Université Paris Cité

Ecole Doctorale 261 « Cognition, Comportements, Conduites Humaines »
Laboratoire de Psychologie du Développement et de l'Education de l'enfant
LaPsyDE, UMR 8240, CNRS

Study of neurocognitive processes involved in inhibitory control, working memory cognitive flexibility, and learning in normal and psychiatric children, adolescents, and adults

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Thèse de doctorat de Neurosciences Cognitives

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Présentée et soutenue publiquement le 16 novembre 2022

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Title: Study of neurocognitive processes involved in inhibitory control, working memory cognitive flexibility, and learning in normal and psychiatric children, adolescents, and adults.

Abstract:

The aim of this thesis was to study inhibitory control (IC), cognitive flexibility (CF), and visuospatial working memory (VSWM) involved in typical and atypical neurodevelopment. Using spatial navigations protocols based on a 'Virtual Carpet Paradigm (VC)', here we report five studies grouped in three thematics:

The first thematic, concerned the study of neurocognitive performances in young (YA) and older adults (OA) using the Walking Corsi Test (WalCT). The first, behavioral study concerned age and sex impact on VSWM, mental rotation, and cognitive strategies during navigation. We found that spatial cognitive performances like VSWM, mental rotation and cognitive strategies were modulated by age and sex. In the second study, we recorded neurophysiological activity using the functional near-infrared spectroscopy (fNIRS). We found that age-related decline in VSWM is reflected by dorsolateral prefrontal activation and cognitive capabilities. We found that VSWM and cerebral oxygenation during the encoding are affected by age. Moreover, cerebral oxygenation and performances were modulated by the type of space (near space and far space) and related to different cognitive functions.

The second thematic, concerned anticipatory orienting strategies and trajectory formation during replanning in a Goal Oriented Locomotor Task (GOLT) in children with Cerebral Palsy (CP), typically developing children, and adults. We found different navigational disorders in CP subjects. These differences were classified in three sub-groups of subjects: those with major navigation disorders (high trajectory variability and abnormal head orientation profiles); those with minor navigation abnormalities generating consistent trajectories; and those who did not differ from controls in any navigation parameter, despite their gait. This classification has important implications for implementing rehabilitation and should therefore address navigation, not only gait.

In the third thematic, we studied the development of IC and CF in children and adolescents with typical neurodevelopment (TD), developmental coordination disorder (DCD), attention deficit and hyperactive disorder (ADHD), autism spectrum disorder (ASD). We designed a new experimental protocol named the "Virtual house locomotor maze (VHLM)". The VHLM required to overlearn a path to reach a target and replan a new trajectory after blocking the previously overlearned path. We analysed quantitative behavioural variables such as tangential velocity, latencies, head-chest orientation before and during locomotion. A first

published study allowed us to identify behavioral indexes of *impulsivity* during the replanning of a new path. In a new extensive study, we designed a task of "negative priming" to the VHLM to assess IC and CF. A total of 109 participants were enrolled in the study whose data are being analysed.

Additionally, five ongoing projects are related to the results of the thesis: a) A study of visuo-spatial memory deficits in ADHD children using the "Virtual City " paradigm in Pisa, Italy; b) An electroencephalography study for assessing brain activity during locomotor replanning with the VHLM in Brussels, Belgium; c) Visuo-spatial memory in vestibular and vertiginous patients using the WalCT in a clinical setting in Paris, France, d) Artificial intelligence methods for quantification of data analysis, in Oujda, Morocco; and e) Exploring Gregarious Positioning behavior, CF and IC using the VHLM in Hospital Salpêtrière, Paris, France. We hope that these paradigms and our findings, may provide new tools for the diagnostic and remediation for children with neurodevelopmental disorders, and the study of aging processes in elderly persons and their pathologies.

Keywords: inhibitory control, spatial navigation, executive functions, spatial cognition, cognitive flexibility, visuospatial working memory, neurodevelopmental disorders.

Titre : Etude des processus neurocognitifs impliqués dans le contrôle inhibiteur, la flexibilité cognitive de la mémoire de travail et l'apprentissage chez les enfants, les adolescents et les adultes normaux et psychiatriques.

Résumé :

L'objectif de la thèse était d'étudier le contrôle inhibiteur (IC), la flexibilité cognitive (CF) et la mémoire de travail visuospatiale (VSWM) impliqués dans le développement typique et atypique. En s'appuyant sur des protocoles de navigation spatiales basés sur le « Virtual Carpet Paradigm (VC) ». 5 études sont rapportées et regroupées en 3 thématiques :

Dans la première thématique, on a inclus deux articles pour étudier les performances neurocognitives chez les jeunes adultes (YA) et les adultes (OA) à l'aide du WalCT. La première étude comportementale étudiait l'impact de l'âge et du sexe sur la VSWM, la rotation mentale et les stratégies cognitives lors de la navigation. On a observé que les performances cognitives spatiales telles que VSWM, la rotation mentale et les stratégies cognitives sont modulées par l'âge et le sexe. Dans la deuxième étude, on a enregistré l'activité neurophysiologique grâce à la spectroscopie fonctionnelle dans le proche infrarouge (fNIRS). L'activation préfrontale dorsolatérale et les capacités cognitives a confirmé un déclin de la VSWM lié à l'âge ainsi que le VSWM et l'oxygénation cérébrale lors de l'encodage. L'oxygénation et les performances cérébrales étaient modulées par le type d'espace (espace proche, espace lointain) et liées aux fonctions cognitives.

Deuxième, on a étudié les stratégies d'orientation anticipatoires et la formation de trajectoire lors de la replanification chez des enfants atteints de paralysie cérébrale (PC), des enfants typiques et des adultes. On a trouvé des troubles de la navigation chez les sujets CP. Ces différences sont classées en trois sous-groupes : troubles majeurs de la navigation (forte variabilité de trajectoire et profils d'orientation de la tête anormaux); anomalies de navigation mineures générant des trajectoires cohérentes; pas de différence avec le contrôle. Cette classification a des implications importantes pour la rééducation et devrait aborder la navigation, pas que la démarche.

Troisième thématique, on a étudié le développement du CI et de CF chez les enfants et adolescents présentant des troubles typiques et développementaux comme le trouble développemental de la coordination (TDC), le trouble déficitaire de l'attention et hyperactivité (TDAH), le trouble du spectre autistique (TSA). Un nouveau protocole expérimental est conçu, nommé « Virtual house locomoteur maze (VHLM) ». Le VHLM sollicite de surapprendre une trajectoire pour atteindre la cible et replanifier une nouvelle trajectoire après avoir bloqué le chemin précédemment surappris. Des variables comportementales comme la vitesse

tangentielle, les latences, l'orientation tête-poitrine avant et pendant la locomotion sont analysés. La première étude nous a permis d'identifier des indices comportementaux d'*impulsivité* lors de la replanification d'un nouveau parcours. Une ébauche d'article dans laquelle on a adapté une tâche d'amorçage négatif au VHLM pour évaluer IC et CF. Au total, 109 participants ont été inscrits à l'étude dont les données sont en cours d'analyse.

De plus, 5 projets en cours sont liés aux résultats de la thèse : a) Une étude des déficits de la mémoire visuo-spatiale chez les enfants TDAH en utilisant le paradigme "Virtual City" à Pise, Italie, b) Une étude électroencéphalographique pour l'évaluation de l'activité cérébrale lors de la replanification locomotrice avec le VHLM de Bruxelles, Belgique, c) Mémoire visuo-spatiale chez des patients vestibulaires et vertigineux utilisant le WalCT dans une clinique à Paris, France, d) Méthodes d'intelligence artificielle pour la quantification de l'analyse des données, à Oujda, Maroc, et e) Exploration du comportement de positionnement grégaire, flexibilité cognitive et l'inhibition cognitive à l'aide du VHLM à l'hôpital Salpêtrière, Paris, France. Nous espérons que ces paradigmes et nos découvertes pourront fournir de nouveaux outils pour le diagnostic et la remédiation des enfants atteints de troubles neurodéveloppementaux, et l'étude des processus de vieillissement chez les personnes âgées et leurs pathologies.

Mots clefs : contrôle inhibiteur, navigation spatiale, fonctions exécutives, cognition spatiale, flexibilité cognitive, mémoire de travail visuospatiale, troubles neurodéveloppementaux.

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ACKNOWLEDGMENTS

I want to start by thanking my advisor and mentor Professor Alain Berthoz without whom this endeavor would not have been possible. Having had the privilege of working with him since 2017, he has encouraged me to grow professionally, academically, and personally and was witness to my struggles and my first articles being published. In addition to being a terrific advisor, he did not hesitate to push me beyond my comfort zone and inspired me daily to keep improving my skills. Since I started working with him, I have been a witness to his empathic, kind, and generous nature, always inspiring me to do better and taught me to acquire new practical skills which have been indispensable these past years. During the Covid pandemic, Professor Berthoz systematically took the time to check in on me and helped me during difficult moments. I am eternally grateful to him for having taken a leap of faith and having given me the chance to prove myself academically and professionally.

Next, I would like to express my deepest gratitude to Professor Olivier Houdé and Professor Gregoire Borst who accepted me as a PhD student and welcomed me to be part of the distinguished LaPsyDe laboratory which is a remarkable team. I want to thank Professor Olivier Houdé for being my thesis director and for his academic supervision he has offered me over the past few years. I am very grateful for his generosity for attributing me extra time for my thesis drafting because of delays caused by the Covid-19 pandemic. I sincerely appreciate Professor Grégoire Borst's valued input, for continuously motivating the team, helping us understand our priorities and duties within the lab and his availability and informative advice.

I am eternally indebted to Dr Jacques Fradin who offered me the opportunity to work with him and his institution by financing my PhD. During my thesis, he inspired me with his altruism and desire to change and improve the world for future generations, wanting to leave it a better place. I wish to express my deepest gratitude towards his continuous kindness and belief in me which gave me strength throughout these past few years. The opportunity to work with him and his institute provided me with the funds necessary to open the doors to new perspectives in research. A special thanks to the whole team of Dr Jacques Fradin, most notably Camille Lefrançois and Stéphanie de Chalvron for their contribution to my research projects and the questionnaire. A sincere thanks to Fanny Fradin for her continuous support, kindness, and assistance regarding administrative issues.

My warmest thanks go to Professor David Cohen who has been an unstinting source of help and guidance. I am immensely appreciative for his constant availability, his kindness, leadership and his willingness as well his steadfast support.

A big thanks to Dr Julie Brunelle, Dr Cora Cravero and Ingrid Zammouri for helping me acquire the necessary participants and their constant support. I must also heartily thank the staff, particularly Chantal Galbert from the department of Pedopsychiatry (Director Pr David Cohen) at the Hospital la Salpétrière who contributed to the technical and administrative assistance of the experiments.

I'd also like to extend my gratitude to Soizic Gauthier for being a supportive and a helpful colleague recruiting participants and remaining steadfastly positive in tough situations.
Special mention to Hugues Pellerin for his help and advice when I was struggling with statistical analysis and technical issues. I am equally grateful for my colleagues, Salvatore Anzalone, Jean Lefèvre, Carlotta Bettencourt, Jianling Zou and Thomas Gargot for the countless interesting discussions on many different topics and who made my time at the hospital much more enjoyable and pleasant.

I would like to express my deepest gratitude to the Centre Interdisciplinaire de Recherche en Biologie (CIRB) of the Collège de France for graciously proving the material and equipment. I think it is crucial that I also thank the Institut de Formation en psychomotricité (ISRP) for providing me with the digital tools and equipment to work on during the time of my thesis.

I owe a debt of gratitude towards Professor Giovanni Cioni and Dr Vittorio Belmonti whose continuous kindness, support and contributions were exceptionally valuable. Given the particular circumstances, their advice, suggestions, and guidance while drafting and publishing articles was insightful and important to me. The unforgettable welcome and hospitality I received from them and Benedetta Del Lucchese as well as their staff while visiting them in Italy made me instantly feel part of the team.

I would like to extend my sincere thanks to Dr Mohamed Zaoui without whose paradigm this thesis would not have been possible and for the very warm welcome at the Collège de France, taking me under his wing while exploring the surroundings. I deeply appreciate his constant availability and helpfulness concerning the various paradigms and protocols as well as any engineering questions I had. I also wish to thank Professor Pierre Blazevic and Djordje Urukalo who encouraged me to stretch my horizons and become familiar with programming in R and Matlab, allowing me to plot the data and the data analysis at the beginning of this thesis. They were always available to assist me with technical issues and I am deeply grateful for their contributions over the years.

It was my immense pleasure to be able to work alongside Dr Anaick Perrochon and Téo Kronovsek for allowing me to learn from their experience and share with me their cheerful personality. I want to express my appreciation and sincere gratitude for having had the opportunity to work with Dr Bernard Cohen who was always gracious enough to give me constructive criticism and helped update and modify our data analysis software. A heartfelt thanks to his whole team for the incredible collection of data and assistance regarding vestibular patients.

Of course, special thanks go to Professor Guy Cheron, Dr. Ana Maria Cebolla Alvarez Mathieu Petieau and their team for their hospitality while visiting them in Brussels and for their implication and enthusiasm while adapting the protocol to their own experimentation.

A heartfelt appreciation to my fellow PhD students, most particularly, Gabriela, Esther, Sabrina, Emma, and Nydia who made my days at the LaPsyDé laboratory more pleasant. A special thanks to Iris whose great sense of humor and kindness brightened my day and to Matthieu who never hesitated to accompany me to try new lunch restaurants.

Lastly, I would like to mention and thank my family who are overseas. Most specifically my mother, Estella Ruby, Anne-Julie, Ivan, Stiven, Ivan Jr, Daniel for their unwavering support and love during these past few years without whom I would not have been able to complete this work.

FOREWORD

General objectives

The aim of this thesis was to study inhibitory control (IC), cognitive flexibility (CF), and visuospatial working memory (WM) involved in typical and atypical neurodevelopment. We explored, mainly using behavioral paradigms, the brain processes involved in the capacity to choose appropriate behavior, and plan or replan a visuo-spatial locomotor trajectory using either a) sequences of visual targets, b) inhibition of unpredicted changes of the goal, and c) replanning of previously over perfected learned paths, in children, adolescents and adults. These two behaviors have been progressively perfected throughout Evolution.

On November the 24th, 1974, after a fruitless day of searching for new sites in the hot African savannah (at Hadar, Ethiopia), a group of archaeologists led by Donald Johanson and Tom Gray made an astonishing discovery. It consisted of a collection of fossilized bones which they realized dated to about 3.2 million years ago. The partially retrieved skeleton was later identified as an *Australopithecus afarensis* which was a key element in understanding human evolution (Jungers, 1982). Indeed, Lucy's skeleton indicated that our ancestors had started walking upright. Therefore, she is evidence of a walking gait that was bipedal (i.e., walking on two feet) and upright related to modern humans (and other hominin species). The story of Lucy and her descendance told by their fossilized remains make us a witness to the challenges that they faced. In fact, bipedalism extended the perception of their surroundings for spatial navigation. This upright position was crucial in a drier climate when rainforests were being replaced by savannahs and safety could only be guaranteed by scanning the horizon for potential danger. Thus, the radical change in environment and the need for self-preservation seemed to have been the trigger for this shift of behavior (Bonnefille et al., 2004). It appears that a crucial moment of human evolution was this transition from quadrupedalism to bipedalism (Schmitt, 2003). Lucy's discovery supported the hypothesis that bipedalism preceded encephalization (Wittman & Wall, 2007). Further brain expansion and reorganization in cortical areas such as prefrontal, parietal, temporal, and occipital provided our ancestors with the evolutionary advantage for developing complex mental functions (Bailey & Geary, 2009; Schoenemann, 2006). These complex mental functions are defined as a set of neurocognitive processes involved during high levels of information integration, in the acquisition of knowledge and in reasoning (E. K. Miller & Wallis, 2009).

If we imagine a normal day in the life of one of our ancestors, we can picture a hunter-gatherer about 1.5 million years ago struggling to survive. The complex mental functions sharpened by evolution were tested and challenged while hunting local game. The pursuit of prey can be defined in scientific terms as a "goal-oriented task". During the searching or tracking of prey (e.g., spatial foraging), it was important to avoid obstacles and to memorize the specific geographic and physical characteristics of the environment and of the previously found paths or traveled routes. These capacities for identifying their surroundings are known as spatial cognition abilities. Spatial cognitive abilities are essential in the exploration and exploitation of the environment during navigation (Babayan et al., 2017).Our ancestors, developed many different mental capacities which proved vital for survival. These capacities were involved in simple daily tasks such as the preparation of the tools and weapons (primitive spears, bow and arrows), planning of the strategies before and during the hunt, and selecting the right time to behave or inhibit inappropriate actions. They were somehow a guarantee to thrive while facing the adversities in complicated and life-threating situations.

Nowadays, the conditions changed from the primitive context of human beings to modern day society. We do not need to hunt for our food or hide from predators to survive, but we are challenged every day by activities that require cognitive efforts such as social interactions, decision making, scholarly tasks, or even driving home safely. This requires *cognitive flexibility* (also called mental shifting or mental flexibility) which refers to the capacity to shift between cognitive strategies for dealing with unexpected problems or circumstances (Scott, 1962; Uddin, 2021). This requires the ability to select pertinent actions and to stay focused and pay attention to our goal while avoiding irrelevant distractions or ignore automatic or inappropriate responses. This ability has also been identified, in the brain, as being part of the *executive functions.*

Among all functional neurocognitive properties which appeared during evolution, IC, WM and CF play an important role because they are involved in crucial activities that required selection, decision making, reasoning, and maintaining, adapting, shifting, updating, or *replanning* cognitive control during a goal-oriented task, which will be a major topic of the present work.

Executives functions are considered to be the determinant of mental and physical health (Allan et al., 2016; Diamond, 2013; Moffitt et al., 2011). Psychologists, neuropsychologists, and psychiatrists evaluate executive functions to establish the correct functioning according to neurodevelopmental characteristics (i.e., sex, age, and educational level). These examinations facilitate the detection of disorders and conditions that impair the typical functioning of the cognitive processes to propose intervention for reeducation or rehabilitation. Paper-and-pencil tests and computerized adaptations are often used to estimate inhibition control (Stroop test, go-no-go test, Wisconsin card sorting test etc.).

Executive functions imply several memory systems: WM, episodic memory, semantic memory and procedural memory. *Working memory* is considered to be a cognitive system that allows us to remember information for manipulating it for a short period of time when performing complex tasks or having to replan our actions (A. Baddeley, 1998, 2012).

Origin of the thesis

This thesis is the result of a very large set of cooperations. It was initiated by a cooperation between Pr. Alain Berthoz in the College de France and Dr Jacques Fradin (Institut de Médecine Expérimentale - IME) with the contribution of Dr Camille François. The IME generously granted a research contract (permanent contract- CDI) to Alexander Castilla. The challenge was to try and find experimental paradigms that could allow a behavioral assessment of two distinct psycho-social behaviors: dominance and submission (Lefrançois et al., 2011, 2013). The hypothesis was formulated that normal subjects who had these two different psycho-social profiles (i.e., dominance and submission) would show very different behaviors in an appropriate visuo-spatial task. This would be specifically clear in a task implying *behavioral inhibition* and *replanning*. As an example, it was supposed that during encoding, a spatial array with a goal orientated task *dominant* subjects would have an *overall global* scan and memory encoding of the array, whereas *submitted* subject would only narrowly encode and learn a *sequential path*. When prevented from doing an overlearned trajectory to a given goal, the dominant subject would easily change the rule and generate a new trajectory inhibiting the learned trajectory and using mental flexibility to organize new path. However, submitted subjects would stick to the leaned path (the rule). This led to the design of a new paradigm created by Alexander Castilla which differs from the classical Walking Corsi Talk and the Magic Carpet previously used (Belmonti, Cioni, et al., 2015; Berthoz & Zaoui, 2015; Perrochon et al., 2014). He used, in the College de France, the Virtual Carpet designed by Mohamed Zaoui and Alain Berthoz and created the Virtual House Paradigm (see description below in Part II) which allowed the study of replanning and inhibition in the locomotor visuo-spatial space.

Following these preliminary attempts, the paradigm was installed at the Hospital Salpêtrière (Département de psychiatrie de l’enfant et de l’adolescent, under the direction of Pr. David Cohen) with the contribution of Pr. Jean Xavier and the staff of the department to explore replanning and inhibition in healthy children and adolescents and in patients with attentional and hyperactivity disorders (ADHD). One of the hypotheses was that ADHD patients would show signs of impulsivity in these tasks. To explore inhibition with appropriate theoretical and methodological tools, the contribution of Pr. Olivier Houdé and Pr. Grégoire Borst from LaPsydé Université of Paris Cité was solicited. They accepted not only to guide the design of a full version of the Virtual House but to accept Alexander Castilla in their Laboratory and take the directorship of his thesis within the Doctoral Program of their Department. The acceptation his thesis was closely associated with Pr. David Cohen and Dr. Jacque Fradin who accepted to generously provide the funding for this thesis.

In parallel, a cooperation was established with the Stella Maris children hospital in Pisa Italy (Pr. Giovanni Cioni) to include the data of similar profiles of children with neurodevelopmental disorders. Alexander Castilla contributed to two projects relevant to the question of planning and inhibition: a) a replanning locomotor task test developed with Dr Vittorio Belmonti on healthy children and Cerebral palsy (CP) patients and b) a “Virtual city paradigm (Thesis of Benedetta de Luchese,2022). The first of these two studies is attached to the present thesis (see annex 2) , including the published paper (Del Lucchese et al., 2021)

An intense cooperation was also developed by Alexander Castilla during the thesis period with Dr Bernard Cohen, an otorhinolaryngologist and director of a master program in the medical Faculty of Hospital Saint Antoine, for the study of visuo-spatial memory in vestibular and vertiginous patients.

Finally, a collaboration to use artificial intelligence methods for the treatment and analysis of the experimental data was established with Pr. Mohammed Rahmoune and his student Ihababdelbasset Annaki from the Ecole Nationale des Sciences Appliquées (Université Mohammed Premier, Oujda, Maroc).

Organization of the thesis

We will briefly review the recent literature on a) cognitive development, b) executive functions, and c) spatial cognition, and, because our work has involved both adults and children, we shall also consider neurocognitive development and four main pathologies. The specific pathologies that were included concern Developmental Coordination Disorder (DCD), Attention Deficit and Hyperactive Disorders (ADHD), Autism Spectrum Disorder (ASD) and Cerebral Palsy (CP)

First, we will introduce the cognitive development theory proposed by Jean Piaget and more specifically, we will detail his theory concerning the cognitive and spatial development. We will also discuss the contemporary perspectives of cognitive development such as the Three system theory of Olivier Houdé.

Concerning executive function, we will specify theories, concepts, and experimental works regarding these mental processes. Then, we will review some work regarding how the brain perceives and guides actions in different action spaces (e.g., near and far spaces), as well as how it processes and integrates the spatial reference frames during spatial navigation and problem-solving (e.g., ego/allocentric referential frames) including WM (Corsi block-tapping task). However, these traditional evaluations are limited in terms of visuo-spatial cognitive processing of the information. In the present work we were inspired by recent work in which, for example, a clear distinction in cognitive performance has been demonstrated when comparing the same task in the reaching space and navigational space (Piccardi, Bianchini, et al., 2014; Piccardi et al., 2010, 2011). Moreover, the acquisition of high-level spatial processing (i.e., shifting from egocentric to allocentric references frame) are related to the brain maturation process, and linked to the development of executive functions (Belmonti, Cioni, et al., 2015).These findings suggest a hypothesis that different brain networks are involved in the cognitive treatment of distinct action spaces (Bennequin & Berthoz, 2017).

Following the theoretical and experimental background of the dissertation, we will discuss our precise objectives and hypothesis. Next, we will describe the paradigm, the protocols and the experimental setup designed to explore the spatial navigation abilities. Then, we will examine the data analysis and data processing and experimental subjects.

Afterward, we will present the scientific articles published and submitted to peer-reviewed indexed journals, together with the articles in preparation for submission. These articles are grouped in three thematic: a) Developmental exploration of spatial cognitive capacities and brain activity in healthy adults using the WalCT, b) Replanning following target shift during locomotion, and c) Inhibitory control and cognitive flexibility in the visuo-spatial locomotor task.

In the **first thematic**, our research studied the exploration of spatial cognitive capacities and brain activity in healthy young and old adults using the WalCT. Two scientific articles were published: the first article was called “Age and sex impact on visuo-spatial working memory (VSWM), mental rotation (MR), and cognitive strategies during navigation” (Castilla et al., 2022). The article was aiming to study spatial cognitive abilities such as VSWM, MR, and cognitive strategies during typical aging using a goal-oriented locomotion task. The second article “Age-related decline in visuo-spatial working memory is reflected by dorsolateral prefrontal activation and cognitive capabilities investigate” (Kronovsek et al., 2020), investigated the effect of age on cerebral oxygenation in the VSWM tasks according to space (reaching or navigational).

In the **second thematic**, we aimed to study *replanning following target shift during locomotion in children diagnosed with cerebral palsy (CP).* For this, we conducted a research entitled: Goal-oriented locomotion in children with spastic diplegia: Anticipatory orienting strategies and trajectory formation (Castilla, Berthoz, Cioni, et al., 2022a). Three main research questions are posed: 1) Can we detect disorders of anticipatory orientation and/or trajectory formation in subjects with spastic diplegic CP?, 2) Are navigation skills distinctively impaired in spastic diplegic CP, independently from gait disorders?, 3) In contrast to independent locomotion, does accompanied locomotion help subjects with spastic diplegic CP cope with their perceptual and balance disorders, allowing them to generate better trajectories?

The **third thematic** is related to the exploration of the *inhibitory control and cognitive flexibility by means of a visuo-spatial locomotor task*. We will present a published article named: A New Paradigm for the Study of Cognitive Flexibility in Children and Adolescents: The "Virtual House Locomotor Maze" (VHLM) (Castilla et al., 2021a). This article is a new protocol for assessing the capacities of planning and replanning trajectories and to study inhibition and mental flexibility using a spatio-temporal index by the means of measuring kinematic behavior (i.e., trajectories, tangential velocity and head direction) during spatial navigation in healthy children. Additionally, we will present the draft outline of another article which discussed the *executive functions and the role of inhibition involved in spatial navigation in typical and psychiatric children, adolescents, and adults* using the VHLM. This paper is being drafted and is expected to be submitted at the end of 2022.

Finally, in the last part of the dissertation, we will integrate our results and discuss them according to the theoretical background in order to synthesize the relevant findings. Future perspectives of research will be considered in the conclusion.

ABBREVIATIONS

ADHD: Attention Deficit Hyperactive Disorder

ASD: Autism Spectrum Disorder

BTS: Basic Trajectory Software version 1

Cb: Patients affected by cerebellar pathologies

CBT: The Corsi Block Test

CCTT: Color Trail Test CTT

CFI: The Cognitive Flexibility Inventory

CP: Cerebral Palsy

CPa : Cerebellar Patients

CPM : Colored Progressive Matrices

DBSCAN: Density-Based Spatial Clustering of Applications With Noise

DCC: Dimensional Change Card Sort

DCD: Developmental coordination disorder

DSM-V: Diagnostic and Statistical Manual of Mental Disorders fifth edition

EC: Eyes Closed

e-CBT: Electronic version of the Corsi Block Test

EEG: Electroencephalogram

EFs: Executive Functions

EMG : Electromyography

EO :Eyes Open

FMRI : Functional Magnetic Resonance Imaging

fNIRS: functional Near-infrared spectroscopy

GMFCS : The Gross Motor Function Classification System

GOLT : goal-oriented locomotor task

GWAS: Using genome association studies

HAC : Hierarchical Agglomerative Clustering

IMD: Internal model deficit

LIP : Lateral Intraparietal Area

LTL: Left Temporal Lobe

LTM: Long Term Memory

MABC: Movement Assessment Battery for Children

MCBT : an electronic version of the Corsi Block Test

MCBT : Modified Corsi Block Test

MCI : Mild Cognitive Impairment.

MR : Mental rotation

MRI : Magnetic Resonance Imaging

MRT : Mental Rotation Test

MTL : Medial Temporal Lobe

M-WalCT : Modified Walking Corsi Test – larger version 7x6m with 18 squares of 3x3 cm (Nori et al., (2015))

MWCT : Modified Walking Corsi Test

NEPSY II: The developmental neuropsychological assessment, second edition

OA: Older Adults

OA-F : Older Adults Female

OA-M : Older Adults Male

OH : Healthy older subject

OLM: Object Location Memory

RIRB: Restrictive and repetitive behavior

RTL : Right Temporal Lobe

SOPT: The Self-Ordered Pointing Task

SPA: Score Point Attribution

STM: Short-term memory

SWM : Spatial Working Memory

TCT : Triangle Completion Tasks

TD : Typical neurodevelopment

TDR : topographical delayed recall

TEA-Ch: The Test of Everyday Attention for Children

TL : Topographical Learning

TMT: Trail Making Test

TSTM : topographical Short-term Memory

V1: Primary visual cortex

V2: Secondary visual cortex

V3: third visual complex

VC: The Virtual Carpet ™ paradigm

VHLM : The Virtual House Locomotor Maze Protocol

VR: Viewpoint Recognition

VSA: Visual-Spatial Assessment

VSDR : Visuo Spatial Delayed Recall

VSL : Visuo-Spatial Learning

VSTM : Visual Short Term Memory Test

VSWM: Visuospatial Working Memory

VWalCT: Virtual Walking Corsi test

WalCT: Walking Corsi Test

WCST: The Wisconsin Card-Sorting Test

WM: Working memory

YA -F: Young Adults Female

YA: Young Adults

YA-M: Young Adults Male

YH : healthy young subject

GENERAL INTRODUCTION

This dissertation was organized in four main parts to present the main topics and elements of the study. In the first part of the dissertation, we provided a brief theoretical background concerning four main subjects of the study which are cognitive development, executive functions (EFs), spatial cognition, and neurodevelopmental disorders. The objective of the part I is to present a short synopsis of the relevant literature to establish the context of the research.

In part II of the dissertation, we described the methods section, and we presented the paradigms and protocols designed to explore the spatial navigation abilities. Moreover, we detailed and illustrated the procedure as well as the experimental setups used to record the locomotor trajectory of the participants.

In part III of the dissertation, we also presented the experimental results and the research articles published in different indexed journals, including the draft of one article in preparation for submission. The section is divided into three thematic: a) Developmental exploration of spatial cognitive capacities and brain activity in healthy adults using the WalCT, b) Replanning following target shift during locomotion, and c) Inhibitory control and cognitive flexibility in the visuo-spatial locomotor task.

Finally, in part IV, we discussed the studies' results and the implications of these findings according to a general theoretical framework. We proposed future perspectives, and we opened the discussion for further investigations based on our findings.

PART I: INTRODUCTION AND ETAT DE L'ART

In this section, we will focus on four aspects of human cognition such as a) cognitive development, b) EFs, c) spatial cognition and d) neurodevelopmental disorders.

a) First, we introduced the theories and concepts regarding the scientific study of cognitive development. We started by presenting the pioneer works of Jean Piaget regarding cognitive and spatial development in children and adolescents. Next, we described contemporaneous perspectives know as post-Piagetian perspectives of cognitive development and IC proposed by Olivier Houdé.

b) Concerning EFs, we began by presenting a brief historical introduction of EFs followed by its definition and its components. Then, we described the three main cores of EFs such as IC, WM and CF based on the concepts proposed by Adele Diamond (2013). Next, each EFs core was discussed individually presenting the definitions, the principal theories, assessment, and how each cognitive function developed during childhood.

c) Next, we provided the scientific literature of spatial cognition that we believed relevant for understanding the background of the dissertation. Firstly, we defined spatial cognition. Then, we outlined different spaces of action (i.e., near action space, far action space, and environmental action space) and its different neurocognitive models such as Berthoz's model, Cutting and Vishton's model and Previc's model. Next, we explained the different spatial reference frameworks such as egocentric, allocentric and heterocentric. Additionally, we presented the experimental background of spatial navigation regarding methods used to assess visuospatial working memory (VSWM) in the near action space and far action such as the Corsi blocking test (CBT), the Walking Corsi test (WalCT) and we analyzed the results. Moreover, we proposed subsequent improvement in the assessment of spatial navigation by means of the Magic Carpet Paradigm. Finally, we described the neural bases of cognitive strategies during the WalCT.

d) In the last part of the introduction, we presented four main neurodevelopmental disorders studied in the dissertation such as the developmental coordination disorder (DCD), Attention deficit and hyperactive disorders (ADHD), autism spectrum disorder (ASD) and cerebral palsy (CP). Each disorder was described according to a diagnosis criterion, the etiology and its EFs profile.

I.1. Cognitive development

I.1.1. Piaget's theory of cognitive development

One of the most famous psychologists of the XX century was Jean Piaget (1896-1980). His contributions impacted multidisciplinary fields dedicated to studying developmental cognition such as psychology, cognitive neuroscience, and education (Piaget, 1947, 1983). He developed different research methods and conducted a series of experiments to study and determine the development of intellectual capacities in children and adolescents. Piaget was interested in how children solve problems and what kind of errors they make while resolving them. His constructivist perspective radically opposed the classical point of view of the stimulus-response proposed by the behavioralists such as Ivan Pavlov (1849-136) and John B. Watson (1878-1958). Instead, Piaget's perspective considered the child as being responsible for his active learning process and "acquisition".

According to him, a child's cognitive capacities evolve from the very beginning of infancy to adulthood in a linear and an accumulative mode passing by a series of progressive stages in a hierarchic order (i.e., in a staircase model). Piaget suggests that cognitive development is possible due to the interaction of four mechanisms. These mechanisms are brain maturation, the manipulation of real and abstract objects, social interaction, and equilibration. According to him, brain maturation is the natural development of the brain which opens new possibilities for the development of intelligence. However, Piaget believes that brain maturation is essential but not enough for cognitive development. He believed that the interaction of other factors such as the physical experience and social interaction are fundamental for development. Concerning equilibration, Piaget defined it as a cognitive capacity to deal with conflicts or differences between the information acquired through experience and new information. Essentially, equilibration is the balance between assimilation and the accommodation of the information.

According to Piaget's theory, the *schema* concept (i.e., cluster of ideas) or unit of understanding is a key element for the construction of the development throughout the stages. The *schema* refers to the organization of knowledge by the mechanisms of assimilation and accommodation. Assimilation is defined as a cognitive mechanism that allows us to include new information from the environment necessary for constructing knowledge. Accommodation is a cognitive process of adapting or changing previous knowledge based on the new information. These two processes open the possibility to incorporate information into a schema or create a new one (Piaget, 1947). These stages were categorized from elemental sensorimotor capacities to the more sophisticated cognitive capacities.

Piaget (1947) proposed four stages of human cognitive development presented in a stair mode (step by step): the sensorimotor stage, the preoperational stage, the concrete operational stage, the formal operational stage:

The *sensorimotor stage* (zero to two years) (Stage 1) is the first stage of development in which the child learns through interacting with the world using the five senses and motricity (motoric scheme). In the sensorimotor stage, the newborn reflexes such as grasping, and sucking are stimulated or triggered by the sensorial experiences (e.g., sound, light, touch, etc.,) allowing them to develop schemas. The schemas in this stage are patterns of behaviors that become more sophisticated progressively to voluntary actions. For instance, in their first months, a child builds a relationship with objects (e.g., toys, teddy bears), "the object exists if the child can see it". Around eight months old, the baby understands that the object continues to exist even when the object was hidden from them (i.e., object permanence). This object permanence was developed thanks to the searching of the objects to attain a goal. The construction of reality evolves from dependent on sight (in the present time) to a 'symbolic' or 'representative' intelligence by the means of creating a mental version of the motoric scheme. This supposes that children can imagine themselves doing actions before doing them. Thus, previous experiences provide the elements for the imagination of future scenarios. This is a crucial moment of the end of the sensorimotor stage, marked by the beginning of the capacities of abstraction. In conclusion, the milestones or achievements in the sensorimotor stage are object permanence, goal-oriented actions, and deferred imitations.

The *preoperational stage* (two to seven years) (Stage 2) is characterized by the development of linguistics aptitudes and the capacity for representing the world (mental representation), the use of the symbolic thinking (more intuitive than logical), and an egocentric point of view with difficulties to take in consideration the third point of view. In this stage, using the child tends to focus the attention on dominant features avoiding general aspects 'perception-bound' like the high of a glass.

For instance, using the "beaker task", Piaget identified that when the infants are asked if the same quantity of water in glass A (normal glass) is transferred to glass B (taller and thinner than glass A), the preschoolers will focus their attention on the height of the glass attributing more quantity to the glass B. Additionally, during this period, the child tends to consider inanimate objects (e.g., teddy bear) as living entities with feelings and thoughts of 'animism'. This can be interpreted as a difficulty to distinguish between reality and fantasy. Progressively in the preoperational stage, the child internalizes the experiences with the world through mental operations based on the previous experiences such as deferred imitation, 'symbolic' games, and drawing objects by heart. For example, in the symbolic game (using the imagination) the child plays with objects attributing other objects' physical characteristics (e.g., a shoe for a car). The capacities of abstraction developed during the internalization of the world will help the child to acquire more advanced reasoning skills.

The *concrete operational stage* (seven to approximately eleven or twelve) (Stage 3) is characterized by the acquisition of logical thinking (reasoning), the understanding of the notions of number, and physical (concrete) proprieties of the objects like weight, volume, and height. The child understands the concept of "conservation" which means that an object does not change when its physical appearance changes. A clear example is the 'volume conservation', now the child realizes that the same quantity of liquid does not change when is in glass B (tall and narrow), or glass A (normal glass). The child is capable to comprehend the 'operative reversibility' of the action or mental operations. It means that the child is capable to think in a backward manner to solve a problem. Additionally, the concepts of 'seriation' and 'classification' are developed in this stage. The 'seriation' corresponds to the capacity to arrange objects according to dimensions, length, and thickness. The 'classification' is concerned with the ability to categorize elements according to their size, shape, color, function, etc. In this stage, mental flexibility starts to take part in the resolution of the elemental problems. However, the concrete operational stage is limited in terms of the lack of hypothetic-deductive reasoning acquired in the formal operational stage.

In the *formal operational stage* (from twelve to adulthood) (Stage 4), logical thinking evolves into hypothetic-deductive reasoning. The use of hypothetic-deductive reasoning allows us to obtain conclusions 'inferences' based on logical reasoning (i.e., if - then) or evidence. During this stage, the resolution of a particular problem becomes more sophisticated in comparison to the previous stage. On one hand, the adolescent can apply a series of combinations of logical rules and examination of variables during the hypothesis testing. On the other hand, the adolescent can judge the validity of the inferences and propose a conclusion. In the formal operational stage, adolescents understand and conceptualize abstract ideas such as politics, philosophy, ethics, and morals. The propositional thinking based on the logic of the statements is a developmental milestone in the formal operational stage. Piaget suggested that efficient reasoning in the last stage of development is characterized by greater mental flexibility and the ability to understand the multiple perspectives of others. Piaget considered that logical-mathematical development is essential for the development of other cognitive domains

I.1.2. Piaget's theory of spatial development

Piaget was particularly interested in understanding how children acquired and develop spatial capacities. He published two books based on a series of experiments concerning spatial development of children (Piaget et al., 1948; Piaget & Inhelder, 1948). Piaget considered that the development of spatial capacities is built progressively depending on the child's experience. According to Piaget, the spatial reasoning is acquired from initial stages of the development and continues to evolve throughout adolescence. Piaget suggested that there are three types of spatial relationships in the development of spatial reasoning: the *topological representations, projective,* and *Euclidean concepts*.

The *topological representation*s are initially developed by children, and it is considered to be the ability to represent an object isolated of the context based on their perception. This ability involved representing an object outside of a comprehensive system or organized layout. Piaget distinguished between several characteristics of the elements concerning the *topological representation*s such as proximity, separation, order, and continuity. The cognitive development of the topological representation in children opened the possibility to acquire *the projective,* and *Euclidean representations*. According to Piaget, the projective and Euclidian representation are developed simultaneously during the child's development (Piaget & Inhelder, 1948).

The *projective relationship* is described as the capacity to adopt perspectives of others or even objects, whereas the *Euclidean concepts* refers to the use of coordinates relative to the distances, size, scale and involving comparison and seriation. The concept of *projective* refers to the ability to imagine a location from another perspective or adapt to another point of view. To test this capacity of coordinate spatial perspectives, Piaget devised the three mountains task (Figure 1). In the three mountains task, the child is sitting in front of three model mountains and the experimenter places a doll in different positions. The child's task is to reconstruct the doll viewpoint by selecting a set of pictures. According to Piaget, children of about four years old cannot distinguish between their perspective and the doll's point of view. Piaget interpreted this as an absence of the ability to change viewpoints due to the child's egocentric tendency of spatial manipulation.

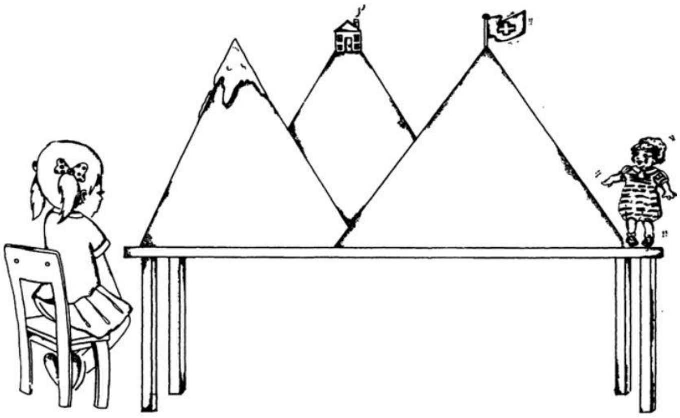

Figure 1. Representation of Piaget's the Three mountain tasks.

According to Piaget's theory of the development of space, children progressively interiorize the knowledge of the environment beginning by the topological representation of space, following by the projective and Euclidean representations. Thus, in the *sensorimotor stag*e, babies are capable of identifying object features such as size, shapes and color integrating them into their senses. Additionally, children improve gradually the visou-manual coordination giving them the possibility to reach the object and manipulated them. Later in the *preoperational stage,* children gradually understand the relationship between the object's size and distance. Moreover, the projective and the Euclidean representations of space become more elaborate. Thus, children are capable to represent space and establish relationships between different objects. For example, the child understands that there are different possible trajectories to reach a point in space. In this stage, the spatial navigation is based on an egocentric point of view. At the beginning of the next stage, the *concrete operational stage,* the development of abstract thinking introduces a broader perspective gradually absorbing other points of view opening the possibilities to better understand the multitude of the different representations of the world. However, it is important to remember that children's egocentric point of view remains dominant and stays centered on their own personal experiences. In the *formal operational stage,* a global perspective of space is achieved, integrating a variety of viewpoints. For instance, a goal can be accomplished by being able to plan and replan (reversibility) several options. At this stage, adolescents can consider sequences of actions, capable of applying logical thinking.

The study of visou-spatial capacities in children and adults have revealed that the perception of the environment is developed progressively with age. Poirel et al, (2011) observed that overestimation and underestimation of lengths.

The theory proposed by Piaget was the foundation for understanding cognitive development. However, some of Piaget's ideas were criticized by posterior researchers opening the door for further investigations as well as further theoretical conceptualizations of cognitive development. One of the main criticisms of Piaget's theory was the overestimation of adolescents-adults' cognitive capacities and the underestimation of children's skills (Borst & Houdé, 2014; Houdé, 2000). For instance, studies in babies suggest elaborate cognitive capacities not predicted by Piaget's theory in the sensorimotor stage (Gopnik, 2012; Téglás et al., 2011). According to Piaget, hypothetical-deductive reasoning is only observed in the last stage of cognitive development characterized by a proficient use of high-order formal thinking. However, adolescents and adults fail 60% of the formal operations tasks devised by Piaget (Byrnes, 2020).

I.1.3. Post-Piagetian perspectives of cognitive development

The scientific evidence compiled in the last three decades studying cognitive development suggests that the 'staircase model' proposed by Piaget does not offer accurate explanations and predictions of cognitive development. The criticism towards Piaget's theory concerning the early cognitive capacities observed in children (nonrelated to the hypothetic-deductive reasoning) and the unexpected errors in reasoning (i.e., regressions) in the formal operational stage in adolescents-adults, opened the possibility of reconceptualization of Piaget's theory. Alternatively, post-Piagetian experimental psychologists and cognitive neuroscientists are interested in understanding and conceptualizing new perspectives capable of explaining cognitive development.

The contemporary Neo-Piagetian approach proposed by Robert Siegler (1999, 2016) suggests that children's reasoning is richer in terms of strategies (e.g., Strategy 1, strategy 2… etc.) than proposed within most cognitive development theories (See Figure 2). Siegler considers that during problem-solving, children have different ways of reasoning based on a collection of strategies (Siegler, 2006). Siegler observed that these strategies competed between them to solve a particular problem. Siegler proposes the analogous overlapping waves strategies of cognitive development in which the acquisition of knowledge is determined by the selection, variation, and discovery of different cognitive strategies. Some strategies have more probability to be used based on previous experiences. According to Siegler, a strategy becomes dominant or frequent when its reliability is very high. For instance, if a particular strategy has a high success rate for solving a given problem, the probability for the strategy to be reused is higher than another alternative strategy that failed to solve the same problem. However, more sophisticated strategies or a new way of thinking can emerge when children rely on analogous strategies or instructions. Thus, cognitive development is associated with two important factors, age and a transfer of experience (Siegler, 2016). Studies of intellectual capacities suggest that the course of cognitive ontogenesis follows a *non-linear development* trajectory. This *non-linear development trajectory* is characterized by a dynamic and irregular way 'crooked' and 'accidental' in the acquisition of cognitive capacities (Houdé, 2019; Houdé & Borst, 2015a; Siegler, 1999).

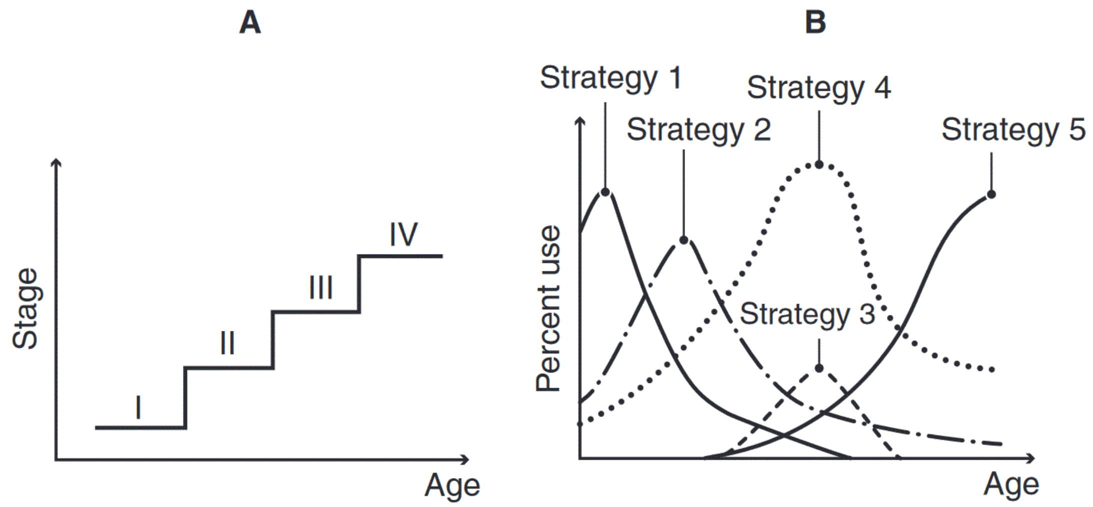

Figure 2. Representation of the (A) Piaget's theory of the "staircase model" incremental process of cognitive development from stage 1 (Biological reaction) to stage 4 (Formal thinking). (B) Non-linear development of cognitive strategies (Siegler, 1999).

This conceptual perspective of cognitive development was strengthened by the experimental findings of human rationality by psychologist and economist Daniel Kahneman. Kahneman is recognized in the scientific community for his important contributions (the Nobel prize of the economy in the psychology of judgment in 2002) in the field of decision-making and human reasoning. Kahneman adopted the concepts previously suggested by Stanovich et West (2000) about human reasoning. The idea of two cognitive systems involved in judgment and choice. These cognitive systems are system 1 (i.e., Intuitive, automatic, and fast) and system 2 (i.e., logic and slow). On the one hand, System 1 (system "hero" for Kahneman) is defined as a heuristic, pre-active, holistic, involved in automatic cognitive processing in the resolution of problems, characterized by fast responses. System 1 guides us to confirm our bias removing doubts. The heuristics responses are useful in a lot of common situations, but they are prompted to errors when they are not adapted to specific problems that require alternative solutions.

On the other hand, System 2 is considered to be a logic system, more demanding in terms of cognitive resources (i.e., attention) and time-consuming but yields accurate results

(Kahneman, 2011). This idea of two different systems or dual processes of reasoning was also studied by cognitive scientists such Jonathan Evans and David Over. Evans and Over (2003) consider that these two systems compete for the control of our decision-making and genera behavior. They also define system 1 as “universal”, or general, observed in other species of animals. System 1 is involved in rapid decisions and spontaneous actions. System 2 is the antagonist to system 1, it is required in hypothetical-deductive reasoning by means of cognitive processes such as WM. According to Kahneman, System 2 is involved in the adaptation of a new set of automatic responses in system 1. So, throughout cognitive development, new cognitive strategies can be learned and overlearned becoming heuristic responses. System 1 helps us in a lot of situations where we need to rely on contextual automatic responses. The A-not-B error task used by Piaget illustrates overlearning behavior in infants which can lead to inappropriate responses (System 1).

In the A-not-B error task, two pieces of clothing are shown to an infant (cloth A and cloth B) (both at the same reach distance). First, the experimenter shows an object (a toy) to the baby. Then, the object is hidden from the infant’s sight using cloth A (right). The experimenter expects the baby to seek the object underneath cloth A to obtain the toy. This procedure is repeated several times using cloth A (i.e., A-A-A-A). Then, the object is shown to the infant and hidden under cloth B (left). Interestingly, infants continue seeking the object under cloth A and not B (Figure 3). This behavior is attributed to a lack of IC not developed yet in infants. Thus, the acquisition of cognitive development is related to the brain maturation capacities of the prefrontal cortex and associated with the capacity to inhibit inappropriate responses (Houdé, 2000).

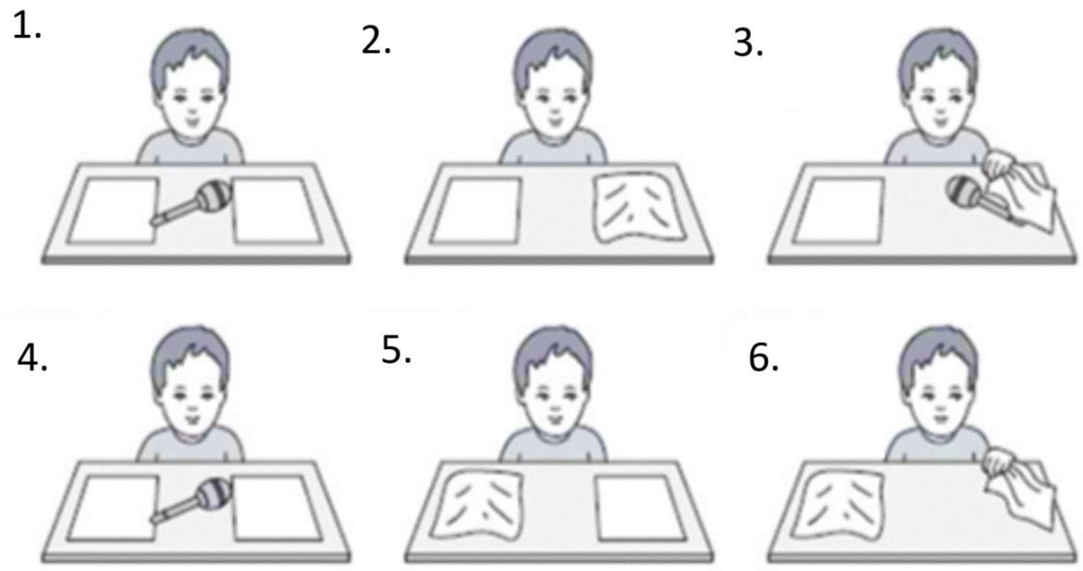

Figure 3. Representation of Piaget’s A-not-B error task. 1.Object in view, 2. Object under cloth, 3. Infant finds object, 4. Object in view, 5. Object under other cloth, 6. Infant searches for object under first cloth.

Another example of automatic strategies adopted by preschool children is the “length-equals-number” bias (Piaget, 1952). During the learning process of numbers and quantities, children associate visuospatial properties with numbers. This is due to the correspondence between numbers and their incremental representation (i.e., one giraffe, two hippopotamus, three crocodiles, etc.). The length-equals-number bias is evidenced using Piaget’s conservation number task. In the conservation number task, when two rows with the same number of elements but different lengths (one row having more space between elements) are shown to children, the children’s task is to decide whether or not the rows have the same number of objects (see Figure 4). Until the age of seven, children incorrectly consider that the longer row contains more elements (Borst & Houdé, 2014; Leroux et al., 2006). The automatization of length equal number overlearned at school will induce errors when the strategy is not pertinent to the circumstances (System 1).

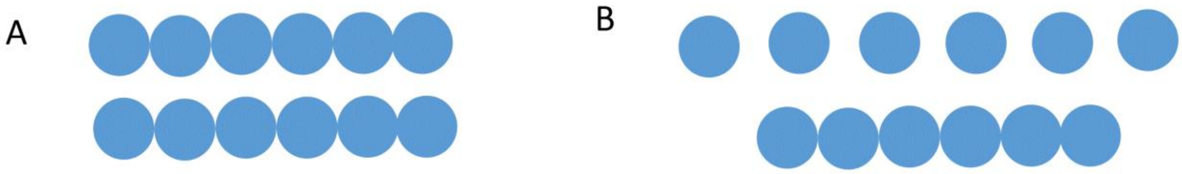

Figure 4. Representation of Piaget's Conservation-of-number task. A. Two equal lines of objects, B. Increasing spacing of objects in one line. Question: "Which line has more objects"?.

According to Houdé et Guichart (2001), children need to inhibit previous overlearned strategies such as length-equal-number in order to succeed in the number conservation task. This was experimentally demonstrated using an adaptation of the number conservation task to the negative prime paradigm (Borst, Moutier, et al., 2013; Tipper, 1985). In the experiment, children performed a computerized number conservation task. Children were asked to identify whether or not the two rows have same number of elements. The experimental design was divided into test and control conditions. Each condition was divided into prime and probe trials. In the prime test trials, children performed the typical Piaget's conservation number task (i.e., two rows with the same number of elements with different lengths – long row vs short row). In the probe test trials, two rows with different lengths and different number of elements (i.e, longer row equals more elements) were presented to children. In the control prime trials, the presentation of the elements was arranged to control the strategy (i.e., elements presented vertically on the screen). This presentation was devised to avoid any inference on the strategy to activate the probe trial. In the control probe trial, the rows were presented horizontally identically as in the test probe trials and conserving the same length-equal-number. The analysis was performed on the comparison between the probe test and probe control trial's reaction time. The results suggested a significant negative priming effect (more time for activate the right strategy) on the test probe trials in comparison to the control probe. This means that the inhibition process of the length-equal-number strategy in the previous prime test influence the decision in the probe trials (Houdé et Guichart 2001).

I.1.4. Houdé's three-system theory and the role of inhibition in cognitive development

Cognitive development is challenged by situations where System 1 (i,e., heuristics, intuitions) and System 2 (i.e., logic thinking) are in competition (Diamond, 1998; Houdé, 2019). The winner in this cognitive competition determines the outcome. If there was positive feedback applying a System 1 strategy, a human being will automatically strengthen and react identically the next time in a similar situation. However, if the individual received negative feedback or outcome, they would consider that the strategy applied is not adapted to the problem (trial and error experience). This is why, they adapt their way to solve a problem by applying other strategies – logical rules (System 2). Thus, when typical adolescents and adults (i.e., Piaget's operational stage) fail during the resolution of a reasoning problem, rather than considering them as illogic or "happy fools" (De Neys et al., 2013), we can consider them as having been misled by heuristics 'hypothesis of Presumption of rationality' or presumption of System 2 (Houdé, 2000). The equilibrium between these two cognitive processing systems is determined by cognitive control. Thus, valid or invalid reasoning is defined by the capacity of performing IC (System 3) (Borst & Houdé, 2014; Houdé, 2019, 2020). System 3 intervenes as a metacognitive control system blocking or stopping the heuristic system (System 1) for activating the algorithmic one (System 2). This three-system theory is proposed by Olivier Houdé based on experimental and neuroimaging data (See Figure 5).

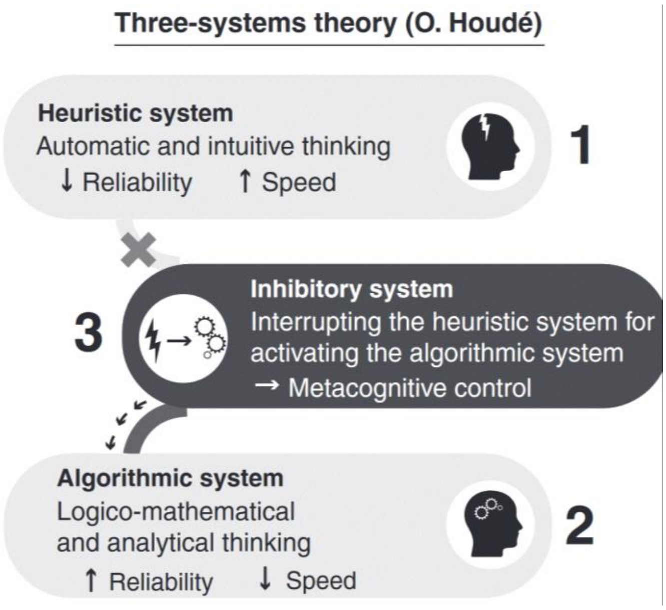

Figure 5. Three-systems theory of cognitive brain. System 3 (Inhibitory system) in the prefrontal cortex controls and mediates the cognitive competence between System 1(Heuristic system) and System 2 (Algorithmic system). System 3 inhibits the heuristic system and actives the algorithmic system (Borst & Houdé, 2014; Houdé, 2019).

This new perspective opens the possibility to understand cognitive strategy processing (system 1 and system 2) as regulated systems capable of debiasing (unbiasing) reasoning. This idea contrasts with Evans' (1983) perspective that is almost impossible to suppress a reasoning bias. Evans considered that biases are permanent due to the rapid and preactivated nature of System 1. However, the theoretical framework of IC (system 3) is based on empirical findings in several cognitive and emotional domains such as object representation (Bell & Fox, 1992; Diamond & Goldman-Rakic, 1989), numerical cognition (Borst, Poirel, et al., 2013; Houdé & Guichart, 2001; Poirel et al., 2012; Roell et al., 2019; Viarouge et al., 2019), reading process (Ahr et al., 2016, 2017; Borst et al., 2015; Houdé et al., 2010), logical reasoning (Houdé, 2000, 2007; Houdé et al., 2000; Houdé & Borst, 2014, 2015a) and emotional processing (Aïte et al., 2018; Draperi et al., 2022).

In parallel with cognitive development, brain development plays a crucial role in the acquisition of IC. Brain imaging studies demonstrated that the prefrontal cortex subserves IC, which is also associated with other high-level capacities in the executive-functions system (WM, CF). Using Magnetic Resonance Imaging (MRI), structural changes have been documented in the prefrontal cortex from childhood to adolescence (Casey et al., 2005). The adequate use of IC is associated to a well-developed prefrontal cortex. This is due to the high cognitive cost of controlling or blocking misleading strategies. The prefrontal cortex's maturation requires more neurobiological processes (i.e., structural architecture and functional organization) in comparison to other brain structures and is only achieved in adulthood (Caballero et al., 2016).

I.2. Executive functions: Vicarious processing of the brain

The history of the term executive functions (EFs) dates back to the nineteenth century and the early twentieth century and it is related to the clinical studies on patients who were reported to have sustained general frontal lobes damage or more specifically prefrontal cortex lesions (Krudop & Pijnenburg, 2015). One of the most notorious cases in cognitive neurosciences was documented by Dr. John Martyn Harlow (1848, 1868) who described a series of behavioral disorders in a patient after suffering a frontal lesion. The tragic accident occurred when the patient Phineas Gage was working at the railroad company and an iron rod penetrated Gage's left cheek destroying the left side of the brain. After his physical recovery from the accident, Gage presented personality changes such as "profane", "irascible", and "irresponsible behavior". However, Gage's cognitive functions like memory, language, etc. were preserved.

133 years after the death of Phineas Gage (1823-1861), the reconstruction of the brain damage by means of neuroimaging techniques revealed a bilateral lesion in the prefrontal cortex (Damasio et al., 1994).

Herman Oppenheim (1880) and Jastrowitz (1888) documented behavioral and emotional changes after the frontal lobe damage. Moreover, the "Frontal lobe syndrome" was formally introduced by Erich Feuchtwanger in 1923. The clinical observations in patients with frontal lesions allowed them to identify atypical behaviors that were not associated with other cognitive faculties (memory, speech, or sensorimotor deficit). These atypical behaviors were characterized as affective dysregulation (irritability), personality changes, and difficulties to learn new behavior. The conceptualization of the frontal lobe syndrome increased interest in the study of behavioral manifestation after frontal lobe damage. However, the term EFs is rooted in the description of the neuropsychologist Alexander Luria (1980) concerning frontal lobe functioning. Luria suggested that frontal lobes are involved in an "executive role" of programming, controlling, and verifying the activity of the brain. In 1982, Muriel D. Lezak conceptualized the term "executive functioning" as the ability to engage in goals, planning and problem-solving, and self-monitoring. Lezak proposed that the frontal lobes were involved in executive functioning of other important behavioral and cognitive abilities. Alan Baddeley (1986) introduced the term "dysexecutive syndrome" as a group of clinical manifestations regarding impairment in the emotional, cognitive, and behavioral domains mainly associated with frontal damage. Baddeley suggested that the dysexecutive syndrome is a dysfunction of such planning, abstract thinking, CF, and behavioral control.

According to Ardila (2008), EFs abilities are involved in "metacognitive" and "emotional/motivational" processing. These two EFs processing are related to the functioning of the prefrontal lobes. Consistent with this idea, EFs are determined according to the presence ("hot component") or the absence ("cold" – "cool" component) of emotional processing (Chan et al., 2008; Zelazo & Carlson, 2012). The "cold" component of EFs is linked exclusively to cognitive processing, whereas the "hot" component is involved in the emotional arousal processing (emotional categorization positive or negative). The hot component in EFs is related to the emotional valence of beliefs, motivation, previous learnings, and desires. In contrast to the hot component, the cold component is related to planning, WM, IC, CF (Peterson & Welsh, 2014; Roy et al., 2012).

In the last decades, the study of EFs has become an increasingly relevant subject of research for cognitive neuroscience and cognitive science. This interest is characterized by the aim of understanding and enhancing the potential of EFs in people who suffer from cognitive decline or/and accelerated their development in children and adolescents (Diamond & Ling, 2016). Several theoretical perspectives have been proposed in order to understand the mechanisms underlying EFs (P. W. Burgess et al., 2000; Diamond, 2013; Duncan & Owen, 2000; Luria et al., 1966; Miyake et al., 2000; Norman & Shallice, 1986). However, due to its complexity, there is still not a common agreement between researchers world-wide to establish a consensual terminology, components number, and conceptualization theoretical framework (Baggetta & Alexander, 2016; Banich, 2009; Braver et al., 2010; Chun et al., 2011; Kassai et al., 2019; McCabe et al., 2010).

According to scientific literature, EFs are also known as *executive control* and *cognitive control.* EFs are a set of high-level cognitive processes involved in the control of actions, emotions regulation, and deliberated reasoning. EFs allow us to learn, to manage thoughts, to be able to produce innovative ideas, to reason without internal or external interferences in a vicarious way (Berthoz, 2017). EFs allow us to predict the consequences of our behavior and anticipated outcomes. EFs are high demanding in neurocognitive resources requiring effort to accomplish a challenging given task. As a consensus, EFs are categorized in three main intercorrelated cognitive faculties such as IC, CF and WM (Borst, 2018; Diamond, 2013; Diamond & Ling, 2016; Lehto et al., 2003; Miyake et al., 2000; Niendam et al., 2012; Traverso et al., 2015; Zelazo & Carlson, 2012). These three categories of EFs are the cornerstones for higher cognitive processes like problem solving, planning, and reasoning (Collins & Koechlin, 2012; Lunt et al., 2012). In addition, EFs are crucial to our integral well-being. Indeed, our mental and physical health depends on a smooth executive functioning. Moreover, academic achievements, prosocial behaviors, personal-growth and wealth are associated with the development of EFs (Moffitt et al., 2011). In this dissertation, we adopted the Adele Diamond's model of EFs based on the three components mentioned above (Diamond, 2013; Diamond et al., 2007; Diamond & Lee, 2011; Diamond & Ling, 2016).

I.2.1. Inhibitory control

IC (Inhibition) is defined as an essential component of EFs (Diamond, 2013; Lehto et al., 2003; Miyake et al., 2000). Inhibition is a cognitive function involved in the control of all kinds of mental processes, behavior, and emotions that require suppression or retention in order to be modulated (Berthoz, 2020b). Inhibitory control allows us to stop or block strong learned habits, internal or external inappropriate impelling, and resist attractive lures. Thus, IC is a key cognitive process that allows us to be focused, avoiding distractions or mental dispersion, but at the same time, allows us to disengage from mental processes (hyperfocus attention). IC helps us to coordinate behavior in order to adapt to any environmental changes, and to be able to exert our free will. IC is an essential brain mechanism that controls or regulates overlearned automatic strategies, giving us the possibility to active cognitive capacities in order to reflect properly (Borst & Houdé, 2014; Houdé, 2019; Houdé & Borst, 2014, 2015b). IC is required in different levels of information-processing, from the selection of the information (basic process) to the execution of the response (higher level process) (Friedman & Miyake, 2004; Nigg, 2000).

It is possible to argue that inhibition is a powerful mechanism provided by evolution. Tt allows to reorganize the brain networks involved in cognitive and behavioral capacities (Berthoz, 2017, p. 97). We can consider IC as being the aptitude that enables us to achieve our goal-oriented behavior by suppressing strong irrelevant responses (Bari & Robbins, 2013; Houdé, 2001, 2004; Luna, 2009).

There is a large and growing body of published studies describing the role of IC as a fundamental aspect in the decision-making process (Cassotti et al., 2016; Constantinidis & Luna, 2019; Shenoy & Yu, 2011), theory of mind (i.e., ability to understand feelings, thoughts, emotions of other people) (Carlson et al., 2013; Carlson & Moses, 2001; Perner et al., 2002), reasoning (Houdé, 2007; Houdé & Borst, 2015b), creativity (Camarda et al., 2018) and the ability to take a third-person perspective (Aïte et al., 2016; Thirioux et al., 2014).

I.2.1.1. **Taxonomy of Inhibitory control**

Taking in consideration the findings suggesting the importance of IC in the general aspects of the live (decision-making, reasoning, theory of mind, etc), the scientific study of IC has become a subject of greater importance for cognitive neuroscience, neuropsychology and the cognitive sciences. This importance is explained by the impact of IC on all the facets in cognitive development including: learning, emotional processing, metacognitive skills, prosocial behavior, and social interaction in all stages of life. However, the conceptualization of IC regarding quality, composition, interpretation and executive functions is still a matter of debate in the scientific community (Howard et al., 2014). Here, we will present in a chronological order different theoretical approaches of a classification of IC including Dempster and Corkill (Dempter, 1993), Harnishfeger (1995), Nigg (2000) , Friedman and Miyake (2004), Munakata (2011), and Diamond (2013).

I.2.1.2. **Dempster et Corkill's taxonomy: Resistance to the interference theory**

Resistance to the interference theory defines inhibition (interference) as a primary or general mechanism capable of control cognition and behavioral functioning (Dempster, 1991; Dempster & Corkill, 1999a, 1999b). This theory highlights three types of different interference:

motor, perceptual and verbal. These interferences are divided according to the information source (exogenous and endogenous), and they depend on the stimulus temporality (i.e., sequential or simultaneous). According to Dempster et Crokill (1999a), there are two kinds of activation of information during task execution. The activation of relevant information that helps the achievement of a particular task, whereas the activation of irrelevant information (task-off information) difficult the performance and avoid the execution of the task. In their, theoretical proposition, the cognitive strategies or plans are based on the context and consider that the changes in the context lead a change in strategies. Therefore, a key aspect is to determine when information is relevant or irrelevant in order to apply the correct strategy. The suppression of irrelevant information depends primarily on the prefrontal cortex. The prefrontal cortex performs control on the type of interference allowing it to focus our attention on the pertinent stimuli. The development of inhibition is progressively increased from childhood to adolescence. The first inhibitory capacity acquired by children is the inhibition of the motor skills. The development of inhibition is fulfilled in adulthood when the prefrontal cortex is fully developed.

This idea of the prefrontal cortex as a main brain network involved in different types of inhibitions is similar to Luria's conception of the frontal lobes functioning (Dempster, 1991, 1993). Luria considered that frontal lobe damage produced a variety of clinical manifestations such as the difficulties to inhibit an inappropriate response. The type of inhibition varied in function of the area of the prefrontal cortex injured (Luria, 1966, 1973). This perspective of the prefrontal cortex role in inhibition has been corroborate by Dupue et Collaborators. According to the Depue et al., (2016) the right prefrontal cortex networks are involved in the regulation of inhibition in cognitive, affective and motor processes. The prefrontal cortex is activated during the inhibition of specific tasks; however, some networks are coactive during the inhibition process.

I.2.1.3. **Harnishfeger's taxonomy**

Harnishfeger (1995) distinguished three main features of inhibition mechanisms: a) a psychological component (i.e., cognitive and behavioral inhibition), b) control and awareness of the inhibition (i.e., automatic and intentional inhibition), and c) clarification between interference and cognitive inhibition. According to Harnishferger (1995) behavioral inhibition refers to the intentional capacity of suppressing motor behavior, delaying gratification, and impulse control. Behavioral inhibition includes all kinds of acts that require suppressing a motor response. In contrast, cognitive inhibition is recruited during cognitive processes such as thinking, planning, mental reflection etc. This cognitive inhibition is involved during the intentional (conscious) or unintentional (not available of conscience) mental processes. The dissociation between cognitive and behavioral inhibition is based on the correlation between performances in inhibition tasks. However, Harnishferger suggested that there is a relationship between these to inhibitory capacities. Cognitive inhibition is considered as being the "facilitator mechanism" of behavioral inhibition and therefore it supports the behavioral inhibition capacities. Both mechanisms will be developed during childhood and become efficient during adulthood.

The *automatic inhibition* is defined as an "preconscious" or attentional process that serves to filtrate and to select information that is transmitted to our conscience. The automatic inhibition is a spontaneous inhibition that can be intentionally recruited by thinking or introspection. Harnishferger suggested that the *automatic inhibition* is involved in a selective attention task such as the Stroop task. In the Stroop task, a list of color names (green, yellow) are written in a different ink color which are then presented to the participant. In the control condition, the color matches the ink color (congruent, green in Green). In the test condition, a color is written in another ink color. The participant's task is to name the ink color for each word and not the word of the color (e.g. Green in red: Green) (see Figure 6). In this example, the color is green, but the ink color is red. The participant's task is to identify the ink color, in this case red and not the word which is green. The *automatic inhibition* allows to the participant to block the written process to activate the name color of the ink. The *intentional inhibition* is a conscious process that is required in the conscious suppression of the irrelevant information.

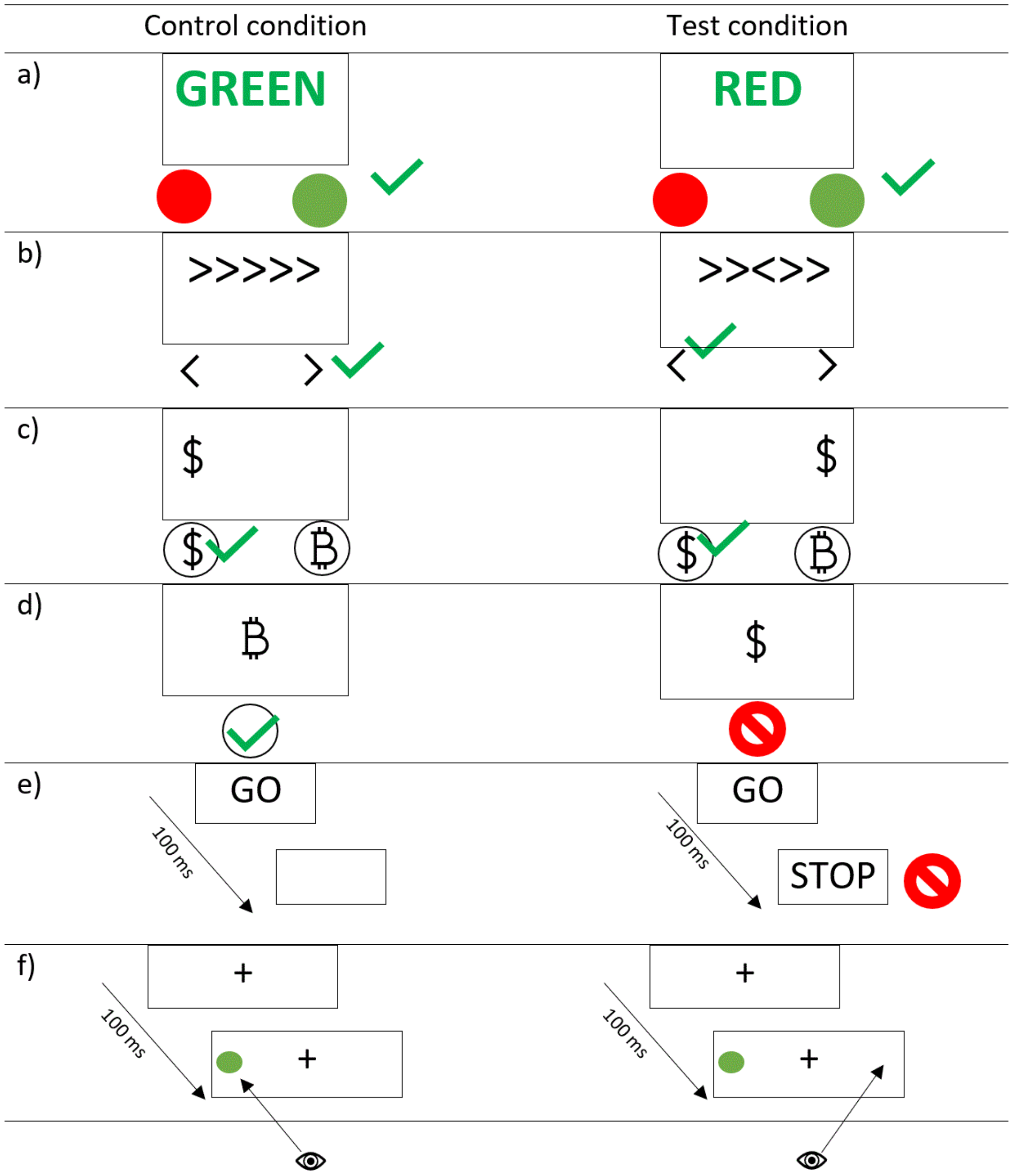

Figure 6. Representation of IC tasks. a) Stroop color test, b) Franker task, c) Simon test , d) stop-signal, e) GO, No-go test , and f) Antisaccade task (From Linzarini (2017)).

The distinction between interference and cognitive inhibition is based on their functional process. According to Harnishfeger (1995), cognitive inhibition and interference are terms which cannot be used synonymously. The term inhibition is associated with the suppression process of irrelevant stimuli. The inhibition process enables to release the WM load by blocking the stimuli non pertinent. Interference is not associated with the suppression of the stimuli. The term interference is related to performance decline due to multi-distraction stimuli. For instance, during a dual task the performance decrements because of the distracting stimuli.

I.2.1.4. **Nigg's taxonomy: Inhibition and disinhibition developmental psychopathology**

Nigg (2000) proposed an integrative taxonomy based on a different series of IC models and concepts in order to provide a contribution to the psychopathological research field. Nigg's taxonomy distinguishes the intentional inhibition (i.e., effortful process) from the automatic inhibition in order to classify them. According to Nigg (2000) IC processes can be grouped into three main categories: a) *Executive inhibition effect, b) Motivational inhibition*, and c) *Automatic inhibition of attention (Table 1)*.

a) The *Executive inhibition control* refers to the intentional capacity of suppress information in order to help high-level information processing such as WM. The *Executive inhibition* control is considered as effortful requiring a lot of cognitive resources to stop the irrelevant stimuli that compete against the appropriate stimuli. The *Executive inhibition* control is divided into *interference control*, *Cognitive inhibition*, *Behavioral inhibition* and *oculomotor inhibition*.

Interference control is involved in the suppression of a stimulus that produces the competition between two responses or during the blocking of distractors that avoid the production of a primary response. *Cognitive inhibition* is defined as the control mechanism that inhibits the irrelevant ideation to protect WM and the attention. Behavioral inhibition participated in the suppression of a stimulus that triggered a motor response. Concerning *oculomotor inhibition*, it is considered as effortfully suppress reflexive saccade.

The *motivational inhibition effect* is related to emotional context concerning the inhibition of *response to punishment cues* (Gray & McNaughton, 2003), *and response to novelty* (Kagan et al., 1998). According to Gray and McNaughton (2003), the behavioral inhibition system is activated during conflict such as signals of punishment, novel stimuli, innate fear stimuli, and signal of non-reward. These conflict resolution takes part inhibiting the behavioral response, increasing arousal, and increasing attention.

Automatic inhibition of attention is involved suppressing inspected stimuli for both attention and oculomotor saccade, inhibiting information at attended locations while attending elsewhere.

Table 1. Inhibition systems in Cognitive Psychology and Cognitive Neurosciences according to Niggs.

Inhibition system & type	Example measure	Possible neural correlate
Effortful inhibition of motor or cognitive response		
1. Interference control (prevent interference due to resource or stimulus competition)	Stroop; flanker tasks; priming; dual-task interference	Anterior cingulate → dorsolateral prefrontal/premotor cortex → basal ganglia
2. Cognitive inhibition (suppress nonpertinent ideation to protect working memory/attention)	Effortful: directed ignoring; ratings of intrusive thoughts; Automatic: negative priming	Anterior cingulate → prefrontal → association cortex
3. Behavioral inhibition (suppress prepotent [automatic/prepared] response; suppress cued but socially inappropriate response)	Stop task	Lateral and orbital prefrontal→premotor
4. Oculomotor (effortful suppression of reflexive saccade)	Antisaccade task; oculomotor tasks	Frontal eye fields/orbitofrontal cortex
Automatic inhibition of attention		
1. Recently inspected stimuli (suppressed for both attention and oculomotor saccade)	Attentional & oculomotor inhibition of return	Superior colliculus → midbrain or oculomotor pathway, respectively
2. Information at unattended locations (suppressed while attending elsewhere)	Covert attentional orienting; neglect/extinction	Posterior association cortex

I.2.1.5. **Friedman and Miyake' taxonomy**

Friedman and Miyake (2004) introduced a new conceptualization of IC based on the empirical evaluation of the taxonomies proposed by Dempster and Corkill (Dempter, 1993), Harnishfeger (1995), Nigg (2000). Friedman and Miyake (2004) suggest three IC processing. These three functions are Prepotent Response Inhibition, Resistance to Distractor Interference, and Resistance to Proactive Interference.

According to Friedman and Miyake (2004) Prepotent Response Inhibition is the combination of behavioral inhibition and oculomotor inhibition suggested by Nigg (2000). This inhibition is presented in all kinds of motor responses, including the suppression of the reflexive saccades. Friedman and Miyake (2004) used three main tasks to explore the Prepotent Response Inhibition which are the Antisaccade task, the Stop-signal task, and the Stroop task. In the Antisaccade task, the participant tries to suppress a saccade (oculomotor response) toward a previous presented cue (Hallett, 1978). In the Stop-signal task, first the participant needs to learn the association between a stimulus with responses (left arrow, press left button or right arrow, press right button). Then, the participant needs to withhold a response when an auditory signal is presented simultaneously with the stimulus (G. D. Logan, 1994), and the Stroop task (Stroop, 1935).

Resistance to Distractor Interference shares the same definition of Nigg's interference control, which is the capacity of suppressing an interference due to stimulus competition or interference due to the source. Friedman and Miyake (2004) studied this capacity using the Flacker tasks, Word naming, and shape matching. In the Flacker tasks, a stimulus (e.g., an arrow) is presented among distractors. Three conditions are presented to the participant, in the neutral condition, a stimulus (directional arrow) is presented among another shapes (squares). In the congruent condition, all the arrows are oriented in the same direction. In the incongruent condition, the arrow is pointing in the opposite direction. The participants' task is to press the arrow key according to the direction of the stimuli (arrow) (Eriksen & Eriksen, 1974). In the Word naming, the participant is required to say the word in green avoid the distractors (M. J. Kane et al., 1994), In the shape matching, the participant identifies whether a white shape matches the distractors or not. (DeSchepper & Treisman, 1996).

Concerning Resistance to Proactive Interference, it is defined as cognitive inhibition proposed by Nigg (2000). Resistance to Proactive Interference or cognitive inhibition is defined as the skill to suppress unwanted information to protect WM. In order to assess this capacity, Friedman and Miyake (2004) used the Brown–Peterson variant, AB–AC–AD, Cued recall tasks. In the Brown–Peterson variant, the participant needs to encode three random trigrams (e.g., ACF). Then, the participant is required to count backward deducing three or four numbers from a given number (100,97,94…) during an interval of time between 3 and 18 seconds, then the participants retrieves the random trigram ACF (M. Kane & Engle, 2000). In the AB–AC–AD task, the participant needs to memorize three 12-item list AB–AC–AD using clued words. For example, the cue word APPLE was paired with the response word tomato in the AB list, avocado in the AC list, and orange in the AD list (rosen & Engle, 1998). In the Cued recall tasks, the participant memorized a clued list of words for recalling (Tolan & Tehan, 1999).

Friedman and Miyake (2004) used 220 participants who were enrolled in the study. Friedman and Miyake (2004) tested the three inhibitory classifications: a Confirmatory factor analysis. The results showed that Prepotent Response Inhibition and Resistance to Distractor Interference were associated. However, Resistance to Proactive Interference was not related with either of them. The author interpreted the results as a common inhibitory ability, but this function was not related to other inhibition functions such as Resistance to Proactive Interference. The author concluded that inhibition related functions are associated to others kind of cognitive abilities. Friedman and Miyake considered that the concept of inhibition is "overextended" in research. The authors suggested that scientists should be more specific when they study inhibitory functions defining the type of inhibition and the tools used to assess the functions.

I.2.1.6. **Munakata's taxonomy**

Munakata et al., (2011) suggested an unified framework of IC based on the functioning of the prefrontal cortex. According to Munakata and collaborators, two different types of inhibitions (targeted global inhibition and indirect competitive inhibition) are supported by the specialization of various networks of the prefrontal cortex. The prefrontal cortex is involved in many aspects of inhibition as well contributing to the executive functioning. This distinction is based on the nature of the connectivity with other brain structures and the type of information processed.

The authors considered that the prefrontal cortex plays an important role in inhibiting but also in the maintenance of the information and the representations of goals and planning. This consideration is important to understand the cognitive processes of behavior control. Thus, the prefrontal cortex is responsible for goal maintaining (abstract information) and inhibition as well as other cognitive processes. Munakata et al., (2011) proposed two different types of inhibition supported by the prefrontal cortex. The first type of inhibition concerns the directed goal-inhibition based on prefrontal cortex projections to the subcortical and archicortical areas. The second type of inhibition refers to the overall inhibition or indirect competitive inhibition within cortical and subcortical regions. In the second type of inhibition the prefrontal cortex projections activate the GABAergic interneurons. Although, the global form of inhibition is supported by subcortical regions and the prefrontal cortex maintaining and contextualizing the moment when to inhibit, the competitive form of inhibition takes part in the prefrontal cortex (and some subcortical) regions assuring the excitation of goal relevant options.

Munakata et al., (2011) suggested three examples to illustrate the first type of inhibitory or directed goal inhibition: suppressing memory retrieval, coping with stressors, and inhibition responses. These three inhibition processes reach the various regions of the prefrontal cortex such as the medial and lateral, dorsal and ventral. Moreover, these inhibition processes recruit two different mechanisms of global directed inhibition. The first mechanism target areas reached by the excitatory GABAergic interneurons of the prefrontal cortex. In the second mechanism, inhibition occurs when the excitatory projections of the prefrontal cortex can synapse onto excitatory neurons which then activate GABAergic interneurons in the target areas. In the third mechanism, according to Munakata (2011), the distinction between targeted global inhibition and indirect competitive inhibition is clearly observed. However, they argue that the two functions are not mutually exclusive, and they can work together.

I.2.1.7. **Diamond’s taxonomy**

Diamond (2013) proposed IC to be an essential element or core of the EFs. Diamond (2013) indicated that IC is defined as the capacity of controlling our behavior, attention, emotions, and being able to resist external and internal temptations. According to Diamond’s (2013) taxonomy, the IC is divided into two main categories: interference control and response inhibition. Interference control is categorized in a) IC of attention and b) cognitive inhibition.

Interference control of attention refers to the capacity to select or direct the focus of attention (Figure 7).

IC of attention is required at a perceptive level of information treatment, being exogeneous (bottom-up, stimulus-driven, or automatic) when a stimulus directed the orientation of our attention. For instance, when we are walking on the street, and we are attracted by a particular advertisement on a billboard. All our attention is directed to the advertisement avoiding all the other information in our immediate surroundings. Conversely, endogenous IC of attention (top-down, active, goal-driven) is required when we consciously decide to ignore a particular stimulus. Endogenous allows us to be focused on a particular task avoiding any distractions.

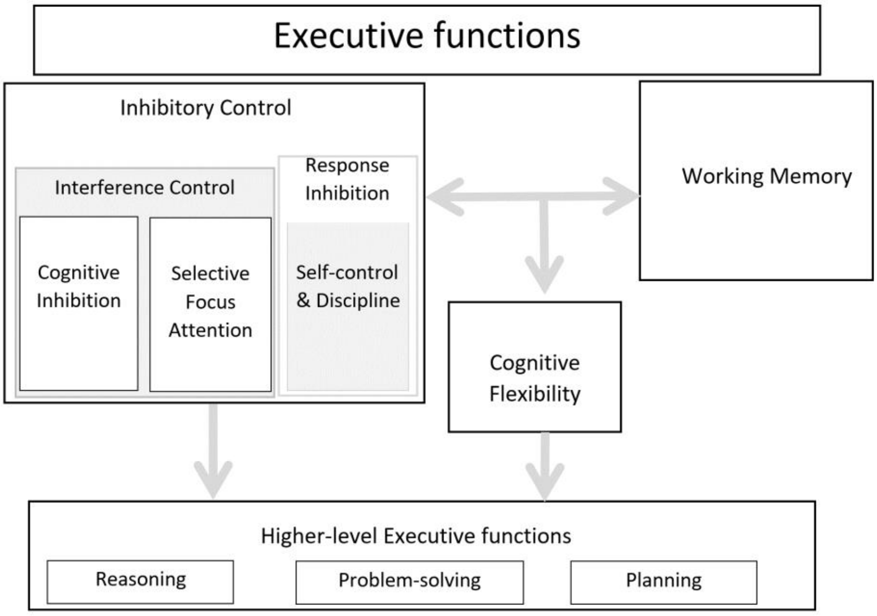

Figure 7. Diamond's model of executive functions and functioning (From Diamond (2013)).

According to Diamond (2013), cognitive inhibition is involved during the control of undesirable thinking and memories. Cognitive inhibition participates by actively blocking the inappropriate ideas or thoughts that comes to our mind (Anderson & Levy, 2009). This capacity allows us to think without any interference. Moreover, cognitive inhibition helps to the intentional forgetting of unpleasant or irrelevant information stocked in memory. Another important feature of cognitive inhibition is its association with the correct functioning of WM capacity. In order for it to work properly, WM needs to be free (avoiding a cluttered workspace) from inappropriate stimuli or interferences. Cognitive inhibition significantly contributes to the information treatment restricting being able to be hyperfocused on one idea at the time and controlling the repletion of old ideas in an infinite loop (Postle et al., 2004).

Self-control or behavioral inhibition is involved during the control of emotions and behavior. This capacity is vital in everyday life because it allows us to behave correctly according to the circumstances and social norms. Self-control is the will to resist temptation and to avoid acting impulsively. Diamond (2013) pointed out that discipline is related to self-control delayed gratification. Discipline and self-control delayed gratification are fundamental for the accomplishment of important tasks that require a huge effort or even sacrifice.

I.2.1.8. **Berthoz's taxonomy: Multiplicity of forms of inhibition.**

According to Berthoz (2020a) in his book "l'inhibition créatrice [i]", evolution has endowed us with multiple forms of inhibition. These forms of inhibitions are present from basic biological operations to the more sophisticated forms of social interaction. The mechanisms of inhibition are required to stop or suppress an ongoing action or process to allow the selection of another action or process which seems more pertinent depending on the context. These forms of inhibition and its opposite, disinhibition, are omnipresent and are at the core of all actions in living beings, such as decision making, learning, and even forgetting. Indeed, these inhibitory mechanisms are a well-functioning process and even define our laws and rules in society. According to the author, the inhibitory mechanisms of the brain are categorized according to a) the neurophysiological processes of inhibition, b) the inhibition that allows for actions, c) the inhibition for decision making and choice, d) the inhibition for learning, and e) the inhibition in the social interaction. Here, we present the main concepts (non-exhaustive) concerning inhibitions.

a) The neurophysiological processes of inhibition include divers forms of suppression of biological processes indispensable for the functional activity of a system. For instance, inhibition is observed at a neuronal level, as in the case of presynaptic inhibition, (when an inhibitory neuron sends as synaptic input to another neuron (axo-axonal synapse). This process, known as Presynaptic inhibition, when an inhibitory neuron sends a synaptic input to another neuron (axo-axonal synapse) to make it less possible to produce an action potential) or postsynaptic inhibition. The neurophysiological process of presynaptic inhibition is often involved in the selection of the information treated by our senses (proprioception, vision, touch, etc).

b) The inhibition that allows actions includes a group of neuronal processes of inhibition involved in a variety of behaviors and is in the control of action (body functions). These processes are the *reciprocal, mutual, lateral inhibition, reactive inhibition, retroactive inhibition, and proactive inhibition. Reciprocal inhibition* refers to the relaxation of muscles on one side of a joint stimulating the contraction on the other side of the joint. *Mutual inhibition* occurs when inhibitory neurons actively inhibit one another in order to halt a decision and allowing the intervention of a specialized system. *Lateral inhibition* is considered to be the excitation of a group of neurons inhibiting the activity of another group of neurons. *Reactive inhibition* is described as the capacity to inhibit an action that is already initiated. This capacity allows us to disengage an impulsive action. *Retroactive inhibition* is considered as the necessary suppression of information to switch between tasks. *Proactive inhibition* occurs when old information interferences with the learning of new information. *Intentional inhibition* is associated with the willingness to stop an ongoing action.

c) In the inhibition for decision making and choice, two functional categories of inhibition are highlighted: the *direct* and the *indirect* form of inhibition. The *direct* category of inhibition in related to the goal-maintaining, whereas the *indirect* category is associated to goal-relevant options (Munakata et al., 2011). The directed global inhibition is supported by subcortical and archicortical areas. The *indirect* inhibition occurs within neocortical and in some subcortical regions. The role of the prefrontal cortex plays is to maintaining abstract information like goals and context. Thus, the prefrontal cortex is involved in the contextualization and in the selection of relevant action. According to Collins and Koechlin (2012), the frontal lobes are involved in the coordination and selection of appropriate behaviors for a given task. Koechlin (2007) suggested three models to explain the prefrontal cortex functioning and its relation to human cognition. The first model is a Bayesian model (i.e., probabilistic), the second model concerns the assessment of the situation, and the third model regards the effectiveness of past actions. Koechlin suggested that decisions are selected and based on the maximization of the reinforcement. The planification of the actions are based on reliability and on the predictively. This approach considers that in decision making the human brain cannot process more than three or four different strategies at the same time (see Koechlin (2020)).

d) The inhibition for learning, according to Berthoz, involves ignoring irrelevant information and knowing when it is ideal to act. The vicariant inhibition refers to the capacity of changing from one task to another. This involves being able to suppress all kinds of information related to the previous task that is not pertinent to the new task. Moreover, the vicariant inhibition helps us to ignore overlearned actions to adapt to a new learning.

e) The inhibition in social interaction is an essential process for understanding other perceptions, emotions and feelings. In order to achieve a correct social interaction, it is necessary to inhibit an emotional contagion and change or adapt to another viewpoint. The adaptation to another point of view involves inhibiting an egocentric point of view and adopting another referential framework, such as the heterocentric referential framework. This inhibition is responsible for suppressing sympathy and instead activates empathy (Berthoz & Thirioux, 2010, 2010).

The inhibitory capacities are acquired during development of the brain. Children acquired the capacity of adapting other point of views when they have the ability to inhibit their egocentric framework. Thus, allocentric and heterocentric referential are related to the maturation of brain structures capable to switch between perspectives. Brain structures such as the prefrontal cortex, the basal ganglia and the cerebellum required considerable maturation in order to perform inhibition. Berthoz suggested that there are critical stages between 7-8 years old and 12-13 years old in which children development elaborated capacities to change referential frames (Belmonti, Cioni, et al., 2015; Poirel et al., 2011). Thus, the abnormal lack of inhibition during the development is an indicator of developmental disorders.

I.2.2. Working memory

I.2.2.1. **Definition of Working Memory**

The notion of memory functioning as the "storehouse of ideas" where the ideas can be stored and processed one at a time was suggested by John Locke (1690) (For historical reviews, see (Logie, 1996; Logie & Cowan, 2015). The formal introduction of the term WM as a cognitive ability was suggested by Miller, Galanter, and Pribram (1960). However, the main theoretical and empirical contributions to the term WM are attributed to Alain Baddeley and Graham Hitch (A. D. Baddeley & Hitch, 1974). According to Baddeley, WM is defined as a limited memory capacity to store and manipulate information for a short period of time contributing to cognition and behavior processing. Baddeley's multicomponent model (2012) suggests that WM has different components: a central executive which is involved in the attentional and cognitive processing of information. The information is selected and classified into two subsystems. The first subsystem is known as the phonological loop whereas the second subsystem is the visuospatial sketchpad or Visuospatial Working Memory (VSWM). The phonological loop stores verbal information contrary to the VSWM, which contributes to the storage of non-verbal information. An important element of WM is the episodic buffer which is involved in the combination of the information to establish integrated episodes (A. Baddeley, 1998, 2012; A. D. Baddeley & Hitch, 1994) (Figure 8).

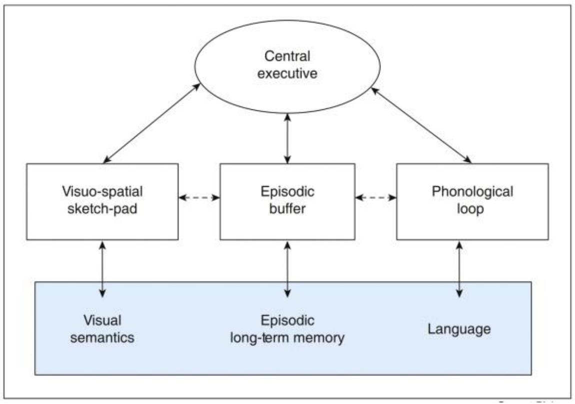

Figure 8. Multicomponent model (A. Baddeley, 2010). It includes links to long-term memory and a fourth component, the episodic buffer that is accessible to conscious awareness.

In the past five decades, the term WM has become more popular in the scientific community due to its important implications. The increase of its popularity goes hand in hand with the rising importance of cognitive neurosciences. Nonetheless, the term WM has caused a lot of controversy regarding its meaning and it is often confused with alternative terms, in other words, the term lacks clarity (Cowan, 2017; Postle, 2015). According to Cowan (2017) there are 9 different definitions for WM (Table 2).

Table 2. Working Memory (WM) definitions arranged in a chronological order (Adopted from Cowen, (2017)).

	Authors years	Working Memory	Definition
1	Laird, 2012; Newell&Simon,1956	Computer WM	A holding place for information to be used temporarily, with the possibility of many working memories being held concurrently.
2	Miller et al., 1960	Life-planning WM	A part of the mind that saves information about goals and subgoals needed to carry out ecologically useful actions.
3	Baddeley, 1986,2000; Baddeley & Hitch, 1974	Multicomponent WM	A multicomponent system that holds information temporarily and mediates its use in ongoing mental activities.
4	Olton et al., 1977	Recent-event WM	A part of the mind that can be used to keep track of recent actions and their consequences in order to allow sequences of behaviors to remain effective over time.
5	Daneman & Carpenter, 1980	Storage-and-processing WM	A combination of temporary storage and the processing that acts upon it, with a limited capacity for the sum of storage and processing activities. When the storage component alone is measured, or the processing component alone is measured, the term WM is not applied, in contrast to the usage within multicomponent WM. Further distinguishing this definition from multicomponent WM, there is not always a clear commitment to multiple storage components, only a separation between storage and processing
6	Cowan, 1988	Generic WM	The ensemble of components of the mind that hold a limited amount of information temporarily in a heightened state of availability for use in ongoing information processing.
7	Ericsson & Kintsch, 1995	Long-term WM	The use of cue and data-structure formation in long-term memory that allows the information related to an activity to be retrieved relatively easily after a delay.
8	Engle, 2002	Attention-control WM	The use of attention to preserve information about goals and sub-goals for ongoing processing and to inhibit distractions from those goals; it operates in conjunction with short-term storage mechanisms that hold task-relevant information in a manner that does not require attention.
9	Unsworth & Engle, 2007	Inclusive WM	The mental mechanisms that are needed to carry out a complex span task; it can include both temporary storage and long-term memory, insofar as both of them require attention for the mediation of performance.

Based on the conceptualizations of WM in the Table 2, WM can be considered as an essential mechanism for updating and establishing coherent relationships between information. WM helps us to mentally reorder and combine different items to make sense and establish new alternatives. Thus, WM is involved in different activities that require applying conceptual knowledge for planning on-going or upcoming decisions. WM underlies all kinds of cognitive and behavioral activities for ensuring the successful completion of the task (D'Esposito & Postle, 2015). Additionally, WM participates in the recall of information stored on the long-term memory necessary for the executive control of behavior (Mansouri et al., 2015). Hence, WM processing is related to numerous daily activities. Its impairment is associated with learning difficulties, psychiatric syndromes, and neuropsychological pathologies (Clark et al., 2007; Peng & Fuchs, 2016; Y. Wang et al., 2017).

I.2.2.2. **Difference between Working Memory and Short-Term Memory**

According to Atkinson and Shiffrin (1968), short-term memory (STM) refers to the capacity of storing information for a short period of time. STM is characterized by its brief duration and its limited capacity. The preservation of the information stored in STM decays over time. However, the duration of STM is still a subject of debate in the scientific community today (Cowan, 2008). The difference between STM and WM are characterized by the treatment of the information. WM allows us to keep information in our mind for combining and manipulating it, whereas STM is involved in the storage and recalling of the information (A. Baddeley, 2012).We can consider the STM as a passive repository system were information is stored. This distinction between WM and STM is observed in two ways. The first difference is observed in the developmental progression of both memories and the second difference is supported by the neuroimaging studies indicating different brain networks activation for WM and STM.

The neural networks associated with WM are the dorsolateral prefrontal cortex, the anterior cingulate cortex, and the posterior parietal cortex (Chein et al., 2011; Kim et al., 2015; Osaka et al., 2003; Owens et al., 2017; Zakia Z. Haque et al., 2021). The prefrontal cortex is related to the process of differentiation between irrelevant and relevant information in cognitive tasks (Curtis & D'Esposito, 2003; D'Esposito & Postle, 1999; Riggall & Postle, 2012). The dorsolateral prefrontal cortex is not associated with temporal storage of the information. In addition, multiple studies suggest that the prefrontal cortex is not involved in the maintenance of short-term storage (Emrich et al., 2013; Ester et al., 2009; Koenigs et al., 2009; Passingham & Sakai, 2004; Serences et al., 2009). Therefore, there is a link between the brain maturation and the development of STM and WM. WM relies on the prefrontal cortex maturation (Buss et al., 2018; Tamnes et al., 2013). Concerning the difference in the development, STM is developed more precociously than WM (Diamond, 2013; Jones et al., 2020). However, it is important to bear in mind that STM intervenes in a larger domain of basic cognitive processing of the information.

I.2.2.3. **Visuospatial Working memory**

The term Visuospatial Working memory (VSWM) refers to the integration, processing, and manipulation of visual and spatial information for a short period of time (A. Baddeley, 2012). This term regroups the visual and spatial processing of information. Moreover, the visual and the spatial processing of the information can be easily distinguished from each other. The visual processing concerns the characteristics of the stimuli such as color, shape, size, texture, recognition of a picture, etc. The spatial processing of the information involves the characteristics of the stimuli like location, the spatial relationship between objects and the movement of visual stimuli in space. VSWM is closely related to the mental rotation capacity both involved during the object rotation and visualization spatial dimensions (Cornoldi & Mammarella, 2008; L. Wang et al., 2018).

VSWM is involved in many daily activities that require encoding and maintaining a mental representation of visou-spatial information (Uttal et al., 2013). This cognitive capacity seems to be particularly reduced during the aging process. The studies comparing older-adults and young adults have revealed that VSWM is especially affected during the aging process (Buckner, 2004; Hedden & Gabrieli, 2004). Thus, according to Wager and Smith (2003) neuroimaging studies in WM established a lateralization of the prefrontal cortex during the tasks that require spatial and non-spatial WM. The right prefrontal cortex is related to the spatial treatment of the information. The verbal processing of the information is associated with the right prefrontal cortex. Concerning the visual WM, the network connected to the maintenance of the visual information is related to the frontoparietal and lateral prefrontal cortex (Daniel et al., 2016; Rottschy et al., 2012).

The relative independence between visuospatial and verbal WM has been reported in behavioral studies with children. Krogsrud et collaborators (2018) suggested that both WMs development differs involving relatively independent neural substrates. According to Krogsrud et al. (2018), the development of VSWM relies on the white matter maturation ensuring the neural connections between frontal, parietal, and subcortical structures. The white matter maturing during development is associated to an increase of VSWM capacities during childhood.

I.2.2.4. **Working Memory measurement**

Here, we aimed to present the representative and widely employed tasks to explore WM capacities. The n-back task (also called AX Continuous Performance Tasks, or AX-CPTs) is considered as one of the most used experimental paradigms to assess WM (Owen et al., 2005). In the n-back task, a series of stimuli (letters, numbers, or words) are presented to the participant and the participant is asked to monitor and to identify whether a stimulus was presented n trials before. The most frequent versions of n-back tasks are the 2-back and the 3-back. For instance, in 2-back tasks, a sequence of letters in a random order are presented to the participant. The participant must respond when the same letter presented 2 trials earlier (e.g., A, K, P, N, P, O, etc.). The control condition are the 0-back task or 1-back versions. The dependent variable analyzed in the n-back task is the accuracy, number of errors and the latency (delay of reaction time). The participants response is recorded each time that they press a button. Emotional versions of the n-back task incorporates emotional features such as faces (Cromheeke & Mueller, 2016), emotional scenes (Hur et al., 2017; Marx et al., 2011), etc.

The Digit Span Backward is a subtest of the Wechsler intelligence scale devised to test WM. In the Digit Span Backward, the participant must repeat a sequence of numbers in a backward manner. For instance, if the sequence of number is 5,9,6,3 the participant 3,6,9,5. The forward version of subtest assesses STM, the participant repeats a sequence of number in the same order. According to Diamond (2003), the numerical order reorganization of a sequence is a curate measure to explore WM capacities. For instance, if the sequence 5,9,6,3 the participant is asked to be reordering it in a numerical order 3,5,6,9.

The Self-Ordered Pointing task (SOPT) is an neuropsychological task developed to study the functioning of the prefrontal lobe related to WM (Petrides et al., 1993; Petrides & Milner, 1982). In beginning of the SOPT, the practitioner presents a series of different items (e.g., boxes containing rewards, abstract designs, or lien drawings). Each series includes between 3 to 12 items. The same series of items is presented each time varying the position of the items (random order). The examinees are instructed to select an item and then continue to select a different item, thus completing the whole series of items without repeating the items selected. If the participant selected an item already chosen, it is considered as an error. The performance considers as the total span score of error produce during the test (T. Ross et al., 2007).

Dual-task paradigms provides an outstanding approach to study EFs, due to the fact that they combine cognitive tasks and motor tasks to explore WM capacities (Woollacott & Shumway-Cook, 2002). These paradigms involve simultaneous treatment such as cognitive processing (e.g., mental operations, digit recall, spatial orientation) and behavioral tasks (walking, gait at postural control) (Huang & Mercer, 2001). Gait developmental differences in typical children vs young adults have been observed when comparing the execution of cognitive task while walking (Schaefer, 2014). This phenomenon is known as dual-task interference.

However, dual-task interference is observed in the opposite direction. Behavioral activities such as walking or postural control can affect the performance in cognitive tasks. This is evidenced by increasing the number of errors and increasing the latency of the response (reaction time) (Hocking et al., 2020; D. S. Reilly et al., 2008; Schaefer et al., 2008). Neuroimaging studies suggest that the prefrontal cortex contributes during the performance of dual-task paradigms (Kübler et al., 2019; Lin & Lin, 2016; Mandrick et al., 2013). Moreover, studies in the gerontological population suggest that poor performance in dual tasks is associated with structural and functional brain impairment and age-related cognitive decline (Allali et al., 2019; Lucas et al., 2019; D. Ross et al., 2021).

I.2.2.5. **Working memory development**

The developmental trajectory of WM varies throughout the lifespan. During childhood the development of WM occurs alongside significant biologicals changes such as brain maturation (Buss et al., 2018; Tamnes et al., 2013) and correlates with aspects of the environment such as education (Finch, 2019; Hunter & Shields, 2022). Studies in babies suggest that during the first year of life, WM is manifested in basic mental operations becoming more sophisticated in later stages of life (Buss et al., 2018; Diamond & Goldman-Rakic, 1989; G. D. Reynolds & Romano, 2016; Ross-sheehy et al., 2003). During childhood, the developmental progression of WM seems to be linear (Best & Miller, 2010; Cowan, 2016; Gathercole et al., 2004).

However, this description of WM development is based on limited information. A different proposition of WM development during childhood suggested that at the beginning of elementary school, the development of WM is steeper becoming curvilinear in upper elementary school (Stipek & Valentino, 2015; Tulsky et al., 2013). During childhood, the increase of WM capacities are related to the development of CF, attentional maintenance, and IC (G. D. Reynolds & Romano, 2016). Interestingly, the memory capacities and processing speed improve later in later childhood. According to Cowen (2016), WM continues to improve progressively across childhood into adolescence. During puberty, the development of WM increases, reaching a level of no relative changes (plateaus) in the middle to late adolescence (Conklin et al., 2007; Gathercole et al., 2004; Isbell et al., 2015; Luciana et al., 2005; Ullman et al., 2014).

As humans become adults, WM capacities remain optimal but reduced in comparison to the WM capacities observed at the adolescence stage. Moreover, an age-related WM decline is manifested after the age of 40 to 50 years old (Alloway & Alloway, 2013; Eriksson et al., 2015; Nyberg et al., 2014; Swanson, 2017). In older adults, WM capacities such as processing speed, selective attention, and distractor suppression are diminished over time indicating difficulties to achieve a task that requires a good amount of WM resources. Concerning the inter-individual differences, some typical children develop early and more rapidly WM than other typical children.

I.2.3. Cognitive flexibility

In this section, we will focus on CF. First, we will discuss its importance and attempt to provide a definition. Then, we will present the most representative tools used to evaluate and measure CF. Next, we will discuss the most relevant findings concerning CF development. Finally, we will introduce the neural bases of CF.

CF is required when daily situations or unexpected circumstances challenge our usual functioning to deal with the problems. In addition, CF is closely related to creativity and being inventive. This capacity allows us to adapt to a variety of conditions. In general, this executive function positively impacts the general aspects of daily life. Moreover, CF is considered a good predictor of academic achievement, mental health, and wealth (Munakata et al., 2013). According to Cartwright et al., (2019) CF is essential for the development of academic and social skills.

However, the lack of or impairment in CF skills is related to a variety of neurocognitive pathologies impacting cognitive development from childhood to adulthood. This is particularly observed in patients diagnosed with Attention Deficit Hyperactive Disorder (ADHD) (Perrault et al., 2019; Willcutt et al., 2005), autism spectrum disorder (ASD)(Hughes et al., 1994; Reed, 2018), depression (Gabrys et al., 2018), pediatric bipolar disorder (O'Donnell et al., 2017; Passarotti et al., 2016), Alzheimer's disease (Swanberg et al., 2004), and Parkinson's disease (Lange et al., 2018)

According to Diamond (2013), CF is one of the three cores of EFs involved in executive control. It is defined as the cognitive capacity to switch between tasks adapting cognitive and behavioral responses according to the context (Buttelmann & Karbach, 2017; Jurado & Rosselli, 2007; Miyake et al., 2000). In scientific literature, CF is related to shifting, switching (task switching), CF, and mental set-shifting. CF is also described as cognitive vicariance which is the brain's capacity to change in a versatile way, one process for another to achieve a goal or solve problems (Berthoz, 2017). Authors like Brown & Tait (2010) and Uddin (2021) put forward that cognitive and behavioral flexibilities are difficult to dissociate because there are intertwined. However, in this dissertation, we will refer to previous terms as CF or cognitive vicariance to remain consistent throughout the text. Thus, CF plays a fundamental role in problem-solving and allow us to adopt different spatial perspectives (i.e., change a spatial locations perspectives) or interpersonal perspective (i.e., adopting other people point of view) (Aïte et al., 2016; Lambrey et al., 2008; Thirioux et al., 2010; Tore et al., 2020).

I.2.3.1. **Cognitive flexibility assessment**

This extraordinary cognitive capacity is studied by means of different psychological, and neuropsychological tests. We introduced a series of tests commonly used to measure CF. However, it is important to clarify that even though the goal in these tests is to measure CF, the results are impacted by the combination of others executive functions such as WM and IC. According to Diamond (2013), CF is based on IC and WM. For instance, the Trail Making Test (TMT) (Reitan & Wolfson, 1993) devised to study CF in which a series of letters and numbers needed to be intercalated one at the time (e.g., A-1-B-2-C-3…) as quick as possible. To achieve this task, the participant is required to inhibit the sequential processing of letters to activate the number processing.

It is important to distinguish between the types of assessment: direct and indirect measurement of CF. Direct measuring refers to all kinds of tasks that can determine the performance of the participant in a particular situation. This directed measuring provides quantitative measuring such as the score, latency in time, accuracy, error numbers, etc. These directed methods are developed in a laboratory controlling the variable that can be involved in the resolution of the task. The direct assessment can measure CF by tasks that demand to switch between rules concerning a series of items or tasks that require switching between stimuli. In the switching between rules, the participant needs to figure out what kind of rule is involved for solving the problem. Concerning the switching between the items, participants can adapt strategies in order to perform the test. The indirect measuring of CF corresponds to all kinds of the questionnaires. These indirect measurements can be self-assessment or hetero assessment.

The classical direct tests used to assess CF are the Wisconsin Card-Sorting Test (WCST, Grant & Berg, 1948)), the Dimensional Change Card Sort (DCC, (Frye et al., 1995)), Brixton Spatial Anticipation Test (P. W. Burgess & Shallice, 1996) ,the TMT (Reitan & Wolfson, 1993), the Color Trail Test (CTT, (D'Elia et al., 1996)).

WCST, DCCS, and Brixton Spatial Anticipation tests are devised to switch between rules. The WCST (Grant & Berg, 1948) is one of the most popular CF assessment used in the clinical and scientific community. In the WCST, a series of cards with different perceptual criteria (color, shape, number) are given to the participant. However, no specific instructions are given to the participant concerning the sorting. The experimenter gives only feedback whether it is correct or not. Once the participant figures out the perceptual criteria of sorting, the experimenter changes the criteria of the sorting, and the participant task is to find again what is the new sorting criteria. According to Miyake (2000), the WCST is also involved in the assessment of higher-level of cognitive processing due to the nature of the task. An adapted version of the WCST was developed for children (preschoolers) to measure CF. This test is known as the Dimensional Change Card Sort (DCCS, (Frye et al., 1995)). In the DCCS blue rabbits and red boats cards are given to children (test cards). The task of the children is to match their car with a target card (blue boats, red rabbits). The assessment consists in two blocks. In the first block, children are asked to match one perceptual criteria (color or shape). If children matched the color criteria in the first block, in the second block they needed to perform the shape criteria.

Brixton Spatial Anticipation Test (P. W. Burgess & Shallice, 1996) an array of two rows and five columns of circles are presented to the participant. The circles were numbered from one to ten. In the initial part of the test, a circle in blue is shown to the participant. The participant is asked to point where the blue circle is moving on the next page. If the participant anticipates the correct circle, then the rule concerning the moving changes. Progressively, the participant learns the rules and integrates them in the test.

The TMT (Reitan & Wolfson, 1993), previously introduced is a good example of switching between tasks. During the test, a series of alphabetical letters and numbers are arranged in a random order on a sheet of paper. The participant's task is to alternate between alphabet letter (A, B, C, D, etc.) and the numerical order (1, 2, 3, 4, etc.). The practitioner measures the time to complete the task. The TMT has been adapted for preschoolers (Espy & Cwik, 2004). In the TMT preschooler version, figures of dog and bones of different sizes are presented to the preschooler on a sheet of paper. The child needs to alternat between dogs and bones according to their size. For instance, a small dog, then small bone, a medium size dog and medium bone. The TMT for preschooler involves a specific task (switch between items) in comparison to the adult version of TMT. A color adult version of the TMT (D'Elia et al., 1996) and an adapted for children named the Children's Color Trail Test (CCTT). The color version of the TMT is a simplified task alternating colors (pink and yellow) in a sequence of numbers (1, 2, 3, 4, etc.). For example, the pink circle number one, then yellow circle number to and pink circle number 3.

I.2.3.2. **Cognitive flexibility assessment**

In clinical assessment, practitioners such as psychologist and neuropsychologist measure CF by means of several executive function batteries like The Test of Everyday Attention for

Children (TEA-Ch, (Manly et al., 2001)), the Developmental Neuropsychological Assessment, second edition (NEPSY II, (Korkman, 2012)), the verbal fluency test of the Delis-Kaplan Executive Function System (D-KEFS, (Delis et al., 2001)),

The TEA-Ch (Manly et al., 2001) developed for children aged from 6 to 16 years old explores attentional capacities (selective attention, sustained attention, inhibition response and, attention control), and flexibility switching from one process to another. The battery includes a subtest called the Creature Counting subtest that allows researchers to evaluate CF. During the test, the participant needs to count according to arrows directions (up, down,). For example, if the arrow points up, the participant counts upwards. The task is to flexibility switch.

The NEPSY II, (Korkman, 2012) is a cognitive developmental evaluation for children from 5 to 16 years old and 11 month. CF and fluency are tested using the drawing fluency subtest. The drawing fluency subtest consists of connecting a series of dots to create different types of figures (start, trees, houses, etc.). The idea is to create as many drawings as possible in a limited amount of time. Additionally, the categorization subtests shares the same principle than the WCST which is used to assess CF. During the test, the child should categorize a series of cards based on the perceptual information. The card can be grouped in different ways. At the beginning, the practitioner shows a categorization, and the child is required to create a new categorization. For instance, if the cards show animals, the possible categorization is to organize them according to sizes.

Verbal fluency assessment is used to measure the CF more particular spontaneous flexibility. The Delis-Kaplan Executive Function System (D-KEFS, (Delis et al., 2001)) is a battery to evaluate general executive functioning in children and adults from 6 to 89. The switch part of verbal flexibility of the D-KEFS are involved in the measuring of CF. In this subtest, the participant should say as many words as they can in a specific amount of time alternating semantically or phonologically prime. For example, the word *mouse* is semantically related to animals, mammals, and rodents or/and phonologically to house….

In the indirect CF assessment different questionnaires have been proposed such us the Cognitive Flexibility Inventory (CFI, (Martin & Rubin, 1995)), Behavioral Assessment of Executive Function Inventory (BRIEF-A, (Roth et al., 2005)), Cognitive Control and Flexibility Questionnaire (CCFQ, (Gabrys et al., 2018)).

The CFI (Martin & Rubin, 1995) is a self-reported questionnaire of 12 items in which the participant responds using a five point Likert scale (e.g., strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree). The questions are devised to determine the degree of the participant's CF considering their normal functioning in different situations. For instances, "I am willing to work on problems that require a creative solution".

The BRIEF-A (Roth et al., 2005)3 is an inventory adapted for children, adolescents and adults. The BRIEF-A assesses the impact of executive functions' impairment in the day life using an ecological approach. This inventory helps with the detection of neurological and psychiatric disorders like learning disabilities, schizophrenia, autism spectrum disorders, depression, mild cognitive impairment, and dementias. The BRIEF-A adult's version (19 - 93 years old) consists of 75 questions categorized in 9 scales such us inhibition, WM, flexibility, emotional control, self-control, initiation, planning/organization, task control and material organization. This inventory can be used in self or hetero assessment. The BRIEF children and adolescent version (5-18 years old) (Gioia et al., 2000) includes 86 questions and 8 scales: flexibility, inhibition, emotional control, material organization, WM, planning/organization and control. Both, the BRIEF and the BRIEF-A include two indices of metacognitive and behavioral regulation index.

The Cognitive Control and Flexibility Questionnaire (CCFQ, (Gabrys et al., 2018)) is a self-report questionnaire that assesses CF, mood and anxiety disorders. The CCFQ is an interesting tool that allows us to evaluate cognitive control, CF, and stress management under difficult situation. In general, this inventory studies the effectiveness of coping strategies associated cognitive control and CF.

I.2.3.3. **Development of Cognitive flexibility**

According to Diamond (2013), CF needs to be supported by WM and IC. Hence, CF develops after IC and WM following a progressive improvement to the adulthood (M. C. Davidson et al., 2006; Garon et al., 2008). CF capacities are dependent on brain maturation specially the prefrontal regions and the connections with posterior regions (Bunge & Zelazo, 2006; Chevalier & Blaye, 2022).

The study of CF starts from a very young age. However, it is mainly focused from the age 14 months (2 years). It had been demonstrated that children from 2 and a half years old can accomplish tasks involving CF such as the intradimensional shifting or within-dimension switching (Brooks et al., 2003; Perner et al., 2002). The test is divided in two tasks, in the first tasks, the child learns an association between a shape and response. For instance, pressing left for a circle and press right for triangle. In the second task, the pressing is inverted, pressing right for a circle and press left for triangle.

Adopting the perspective according to Miyake et al., (2000) and Diamond (2013), the developmental trajectory of CF is characterized by the organization and the development of WM and IC. It seems that children of 3 years old develop their executive functioning organization as an unitary capacity (Willoughby et al., 2010, 2011). This executive functioning evolves to a more differentiated processes becoming a two-factor structuring. From the age of 4 years old, CF is related to inhibitory factor or WM factor (Lee et al., 2013; Monette et al., 2015; van der Ven et al., 2013). The structural differentiation concerning EFs is observed in adolescence and adulthood (van der Ven et al., 2013). During the adulthood the three functions are partially independent. However, the decline of CF is noted during the aging process (Berry et al., 2016; Hülür et al., 2016).

I.3. Spatial cognition

Spatial cognition is a capacity that allow us to orient and navigate through the environment taking in consideration the different distances, landmarks and combining strategies selection to solve possible problems in finding the easiest path for the destination. The human representation of space is a functional property which allows us to adapt to the environment and is key to interaction, navigation, avoiding collision and obtaining a clear knowledge of different distances between objects and humans. Indeed, every behavior that is carried out in an environment takes into account temporal and spatial properties. Thus, the planning of actions and its execution are related to the representation of space. The representation of space is an essential component in the interaction of our surrounding in which the correct anticipation or/and prediction about any future event are essential to correct functioning (Berthoz & Debru, 2015).

I.3.1. Different spaces of actions

There are different neuropsychological models of the arrangement of space that have been proposed as a distinction to how the human brain perceives its environment. One of the models mainly used nowadays is the model of Berthoz, the model of the Cutting and Vishton (1995), and the model of neuropsychology of 3D space by Previc (Previc, 1998). Alain Berthoz proposed the hypothesis of different spaces of actions based on the brain lesion studies and the empirical behavioral observations (See Bennequin and Berthoz (2017) for a review). According to Berthoz and Bennequin, there are at least four different brain networks involved in the construction of 5 spaces of actions. These action spaces are: 1) *body space*, 2) *near action and prehension space*, 3) *far action space*, and 4) *environmental navigation space.*

The *body space* or body schema refers to all the mechanical and dynamic properties of body. The networks associated with the body space are the temporo-parietal junction. This temporo-parietal network is related to the “awareness of the body schema and spatial relationships”. This network was identified for the first time using electrical stimulation in the brain of epileptic patients (Penfield & Boldrey, 1935). The second space of action is *the near action and prehension space* which is considered as a reaching space where objects can be grasped extending the arms. The third space of action is *the far action space,* in this space short displacements (or locomotor trajectories) are needed in order to perform an action. This action space is associated with walking short distances in a room. The fourth space is the *environmental navigation space,* this navigational space required displacement of long distances like cities. Berthoz's hypothesis suggests that each action space is based on a modular organization of the brain networks in which each type of action space requires specific geometries. These types of geometries are composed of Euclidean and Non-Euclidean geometries, and they are regrouped in a general geometry called Topo (Bennequin & Berthoz, 2017).

The model of Cutting and Vishton (1995) proposed three categories of the area surrounding the individual: the first as the personal space (PS), the second as the action space (AS) and the last as the vista space (VS). The personal space is the region that surrounds the person, and it is defined as the region for action (workspace) which is delimited to around 2 meters. This region is an area of interpersonal intimacy where the person allows social interaction. Just beyond the personal space is the AS which is defined as a space of public action. In the AS, the individual has the ability to move and to interact with the context approximately delimited to 30 meters. The VS is characterized by visual perception beyond 30 m.

Previc's model (1998) includes the motor and perceptual integration in relation to egocentric space segmentation with a neuropsychological explanation of brain functioning. Previc's model proposes a division of the space in four key behavior realms: the peripersonal space (PPS), the focal extrapersonal space (FE), the action extrapersonal space (ES) and the 10 ambient extrapersonal space (AES). Previc (1998) defined three of these spaces as "extrapersonal", being regions without the probability to interact instantly with the persons or objects. In this case, the subject needs to move to interact with its environment. The focal extrapersonal is used for visual exploration and recognition of the objects. The action extrapersonal space serves to navigate and orientate oneself toward the objects that are situated beyond the near-body space. Essentially, if we want to take any object out of reach, we need to walk toward the objects' location. The ambient extrapersonal refers to spatial orientation without having specific knowledge of the object. However, it can take topographic references to ensure the navigation in length distances and, thereby, the AES seeks to obtain the adequate locomotion and correct posture. Previc (1998) defined the peripersonal space like being a zone of visuomotor operation near of the body space. The PPS is an area where it is possible to produce direct actions on objects such as to grasp objects or to use a tool. The PPS involves the visual system, the vestibular system, and the proprioception. Therefore, the integration of multiple data can contribute for the estimation and prediction while we produce an action in the near-body space.

The segmentation of the space has been demonstrated in several studies in neuropsychology through behavioral research studies and pathological cases. The theoretical model by Previc (1998) (Figure 9). A) The peripersonal space (yellow region), B) the focal extrapersonal (red region), C) The action extrapersonal (bleu region) and D) The ambient extrapersonal (green region) (). In neuropsychology, the perceptive judgement is used to estimate the boundaries of the peripersonal space.

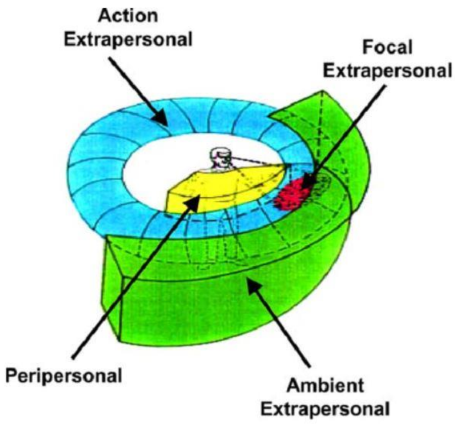

Figure 9. The four realms of perceptual-motor actions in 3D space (from Previc, 1998).

The experimental paradigm of the perceptive judgement was introduced by Warren (1984) to assess the affordance in the visual guidance. In this study, the participants were asked to estimate if they were able to climb different types of stairs. This paradigm was used afterwards by Carello, et al.,(1989). In their study, the participants were asked to estimate the distance of where the object was placed without making a movement, responding only with "reachable" or "unreachable". This task allowed the researchers to estimate the limit of reachability. In fact, the authors observed a perceptual overestimation of the limit of reachability by 10% in correlation with the capacity of action. This overestimation was found independently of degrees of freedom and is corroborated byother studies that have used the same paradigm, for instance Mark et al., (1997), Fischer (2000) and Delevoye-Turrell et al.,(2010). The first evidence of a dissociation of the space was provided by the study of the hemispatial neglect syndrome. This syndrome causes an impairment of spatial cognition generated by damage in the brain specifically at the right parietal lobe. This syndrome is characterized by an intentional or unintentional bias towards the right side. Generally, the patients affected with this pathology can only reproduce the right side of a drawing in a copy task, or their estimation of space is shifted towards the right when they are evaluated in a line bisection task (Mort et al., 2003).

Surprisingly, the patients diagnosed with hemi-spatial neglect syndrome can perform differently in the same task, when peripersonal space or action extrapersonal space were compared (Halligan & Marshall, 1991). The authors noted that there were patients who presented the rightward shift side only in the bisection task in the peripersonal space. However, the same participant did not show any bias when he performed the task using a laser pointer and the stimuli were presented in the action extrapersonal space, meaning without the capacities of action. The opposite pattern was reported by Cowey et al., (1991) and Vuilleumier et al., (1998). In this particular case, the patients were capable of performing correctly the line bisection task in the peripersonal space but they presented difficulties when performing the task in the action extrapersonal space. These findings suggest a clear segmentation of space in relation with egocentric coordinates. This segmentation plays a role in the treating of the space that surrounds the body.

I.3.2. Spatial reference frameworks: egocentric, allocentric, and heterocentric.

Regarding spatial navigation, four spatial referential are distinguished: the egocentric reference frame (or the route strategy), the allocentric reference frame, the heterocentric referential framework and the 3D model strategy (Flash & Berthoz, 2021).

In the egocentric reference frame, each location is encoded according to the subject's perspective (i.e., self-centered representations). This egocentric strategy (or first person point of view) requires a topokinaesthetic memory which updates the self-generated perspective during locomotor movements (Berthoz, 1997). Spatial updating by self-motion is generated from egocentric representations of the environment based on a polar coordinate system (Lambrey and Berthoz, 2007). The use of this perspective involves remembering the landmarks and updating subsequent directions taken during the navigation (Figure 10). The egocentric strategies (or route strategy), organizes and codifies the world from a ground-level local view which means an egocentric perspective.

Figure 10. An egocentric perspective: representing the location of objects in a space relative to the body axes of the self.

In the allocentric strategies, the locations are encoded in a global manner regarding their spatial relationship (i.e., world-centered representations). The allocentric reference frame is useful when creating a cognitive map suitable for navigating in a complex environment (N. Burgess, 2008; O'keefe & Nadel, 1978). The allocentric strategies allows us to detect localization in the environment producing a map-like view (Figure 11). This means that a location is encoded in the brain by considering the distances between elements or objects placed on a map or after the visualisation during navigation (e.g., buildings, mountain, landmarks). Furthermore, the survey strategy is conceived as a "cognitive map" useful to reduce the distances between two places (shortcuts). These two spatial perspectives ego-allocentric have been identified in the human brain and linked to the two main visual streams; the egocentric being restricted to the dorsal stream (where), the allocentric requiring both dorsal and ventral areas (what-where) (Galati et al., 2004). The heterocentric strategy involves imagining someone else perspective. This third perspective required to consider other(s) point of view to imaging their position (Berthoz & Thirioux, 2010).

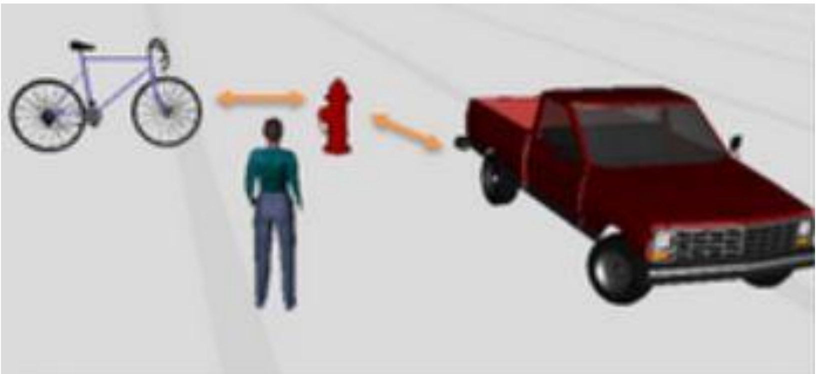

Figure 11. Allocentric perspective: encodes information as map-like view.

The study of the development of the spatial reference frameworks have revealed differences in the estimation of distances depending on the viewpoint and age. Poirel et al., (2011) conducted an experiment based on a comparison task of length estimation in children (from 5 to 12 years old) and adults. In the experiment, a virtual image depicted a park with two different paths; one path was straight, and one path was serpentine and both paths were presented to the participants (Figure 12). The two conditions were presented to the participants a) path with the same length, and b) path with different length. Moreover, the presentation of the virtual image varied according to an egocentric or an allocentric viewpoint. During the experiment, the participants were asked to estimate whether the two paths were the same length or if they differed in length. The analysis of the errors concerning the condition where both paths were the same length observed in allocentric point of view indicated an overestimation for the straight path. Interestingly, this overestimation of the straight path decreased with age. However, when both paths with the same length were observes in an egocentric viewpoint, child (5-year-old) overestimated the straight path, whereas adults underestimate the straight path in an egocentric point of view. The authors interpreted the results according to hypothesis of failing to inhibit the perceptual bias (Houdé, 2000, 2001). The overestimation of the straight path from an allocentric viewpoint suggested that adults relied on a heuristic 'straight path equals longer' perspective. Children under 8 years old overestimate the straight path observed in an egocentric point of view. The authors pointed out that there was an 'overinhibition' learnt at the school in the judgment ''between two points A and B, the straight line is always the shortest path from A to B''. Therefore, the authors suggested that spatial cognition is influenced by bias-inhibition processes.

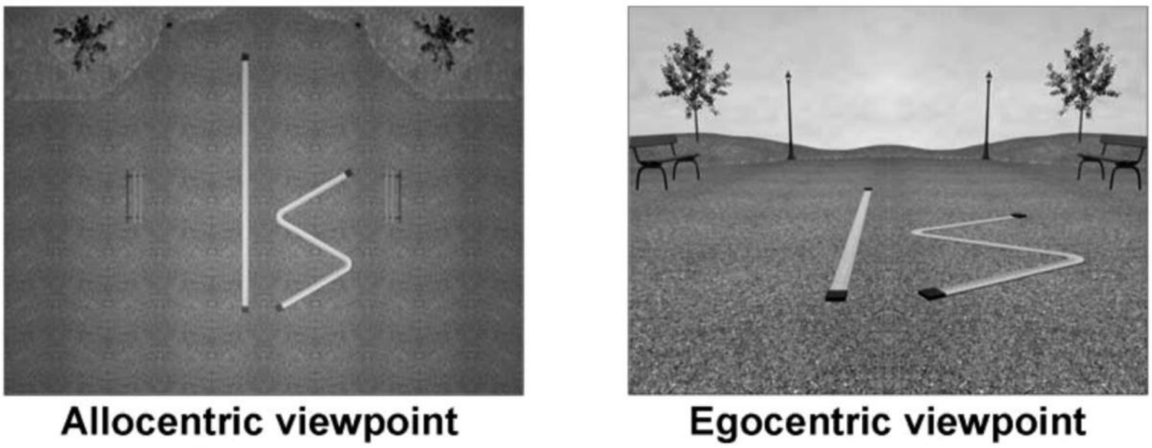

Figure 12. Examples of the stimuli presented in the experiment (Poirel et al., 2011).

The capacity of switching from person-perspective view to third person-perspective view is a crucial capacity for human interactions which allows a correct representation of the world. Lambrey et al, (2008) demonstrated that the visual perspective taking is modulated by distinct brain networks. They were interested in understanding the role of the MTL in the visual perspective taking. The MTL is constituted of the hippocampus, the entorhinal cortex, the perirhinal cortex, the parahippocampal cortex, as well as the temporopolar cortex, which is often described as antero-medial rather than strictly MTL but was considered as part of MTL structures. Fourteen patients with unilateral temporal lesion (seven left temporal lobule and seven right temporal lobule) et twenty-one participants were recruited in the study. All participants completed two tasks: the Object Location Memory (OLM) task and Viewpoint Recognition (VR) task. In the OLM, the participants were asked to memorize a position of a target object in the environment from an initial viewpoint (Figure 13).

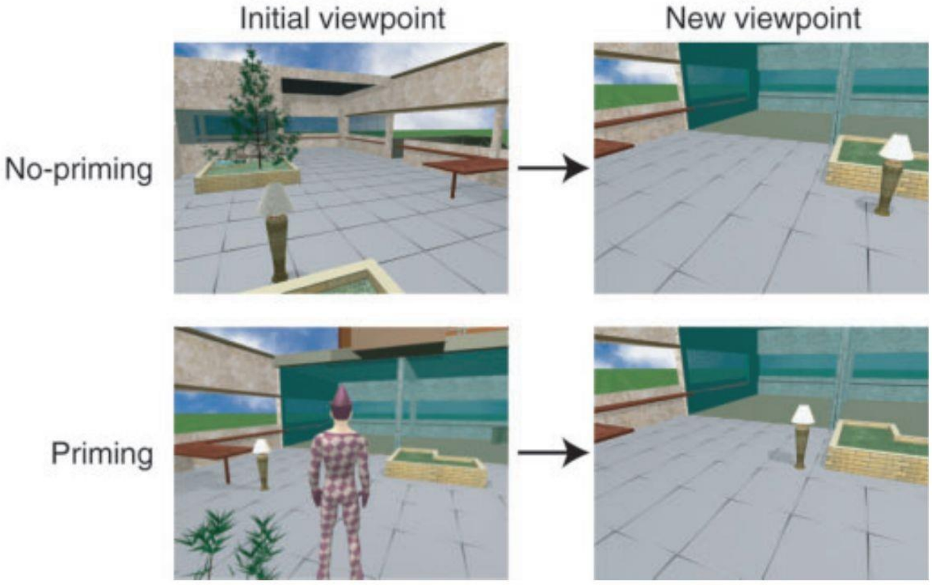

Figure 13. Illustration of the Object Location Memory task. After examining an initial view for 5s, observers switched perspective and indicated from the new viewpoint if the lamp had changed its position. In the priming condition, observers were primed by the avatar occupying their future location in the environment. In the no-priming condition, no avatar was present in the scene and the new viewpoint was unpredictable. The upper and lower examples show non-primed (135 viewpoint change) and primed (0) trials, respectively (From Lambrey et al., 2008).

Then, the same environment was shown from a new viewpoint and the participants had to indicate whether the target object had moved. In the VR, the participants observed an avatar from the initial viewpoint and imaging his perspective, after which another viewpoint was presented then deciding whether the new viewpoint was that of the avatar (Figure 14). In both tasks, different conditions were included: the no-priming condition and the priming condition.

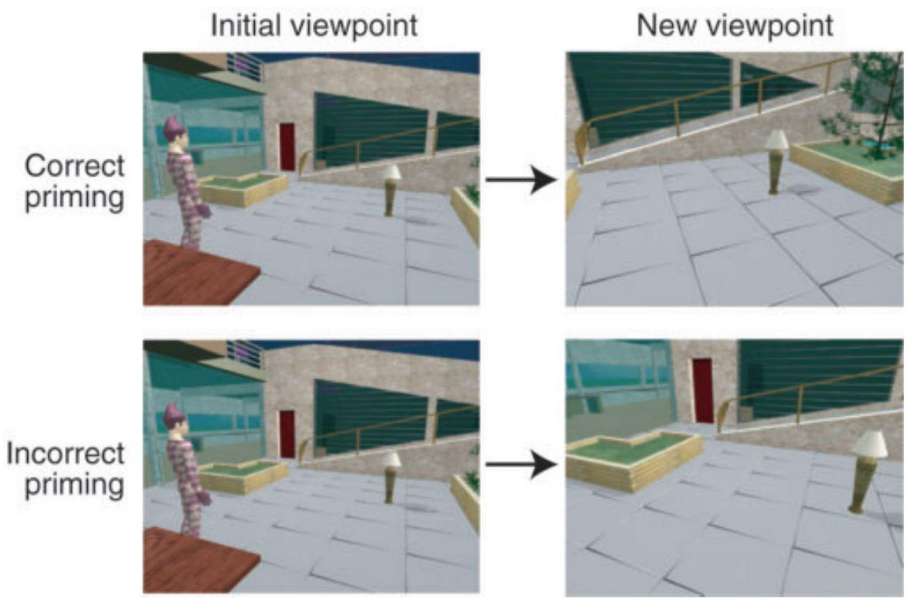

Figure 14. Illustration of the viewpoint recognition task. After examining an initial view for 5s, observers indicated if the new viewpoint was the one, they expected according to the priming by the avatar, if the new viewpoint was the perspective adopted by the avatar. The upper and lower examples show correctly (45° viewpoint change) and incorrectly (90°) primed trials, respectively (From Lambrey et al., 2008).

In the no-priming condition, the new viewpoint was unpredictable from the initial viewpoint. In the priming condition, the new viewpoint was primed via an avatar. The results indicated a double dissociation in the patient's performance (Figure 15). The group of Right Temporal Lobe (RTL) presented impairment in the viewpoint recognition but not in the object location memory task. Contrastingly, the group of Left Temporal Lobe (LTL) patients showed an object location memory task deficit, but they preserved a good performance in the viewpoint recognition task**.**

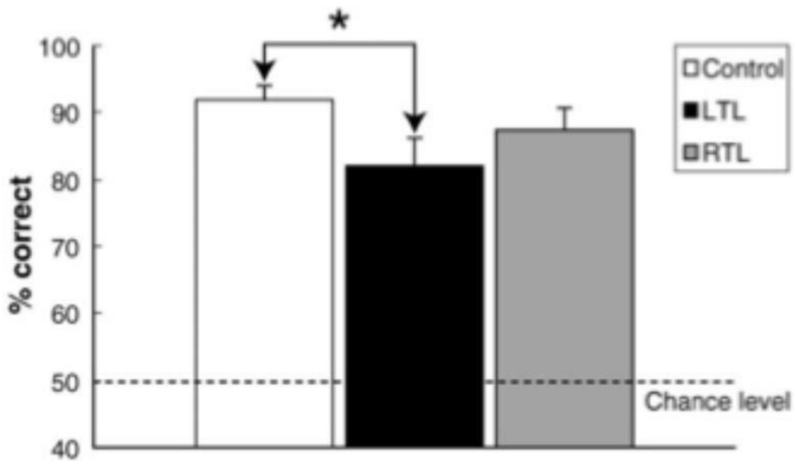

Figure 15. Main effect of group on accuracy in the object location memory task. LTL (left temporal lobe) patients were significantly impaired relative to control subjects. RTL (right

temporal lobe) patients differed neither from control subjects nor from LTL patients. Asterisk indicates a statistically significant difference (P < 0.05) (From Lambrey et al., 2008).

I.3.3. From The Corsi Block-Tapping Test to The Walking Corsi Test and the Magic Carpet Paradigm.

In research and in clinical assessment, the classic paradigm to study the VSWM is the Corsi Block Test (CBT, Corsi (1972)). The CBT test consists of 9 (3x3 cm) wooden blocks arranged in a wooden board (30x25 cm). During the test, the practitioner presented a sequence of blocks tapping one block at the time and the participant was invited to repeat the sequence (Figure 16).

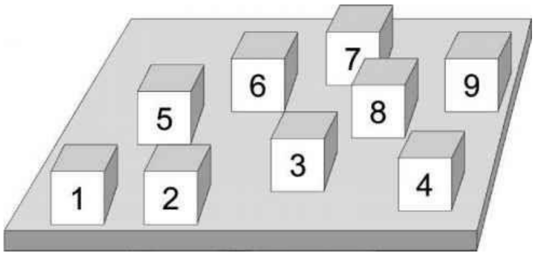

Figure 16**.** Representation of the Corsi Blocks Task (CBT) (Corsi, 1972).

There are two versions of the CBT, the forward and the backward version. In the forward CBT, the participant is required to repeat the sequence in the same order presented by the practitioner. In the backward CBT version, the participant must repeat the same sequence in a backward order starting for the last wooden block tapped (reverse order) (Berch et al., 1998; Donolato et al., 2017). A navigational version of the CBT was proposed by Piccardi et collaborators (2008, 2013, 2019). This navigational version was named the Walking Corsi Test (WalCT). In the WalCT, 9 tiles of 30x30 cm are arranged on the floor in a navigational space 2.5x3.0 (1:10 scale of CBT) (Figure 17). In the WalCT, the experimenter showed each sequence walking and standing on every tile (location) for a brief period. After the presentation of sequences, the participant is required to reproduce the same sequence in a forward or backward fashion (Carbone et al., 2020; Piccardi et al., 2010, 2011, 2013; Piccardi, Palermo, et al., 2014).

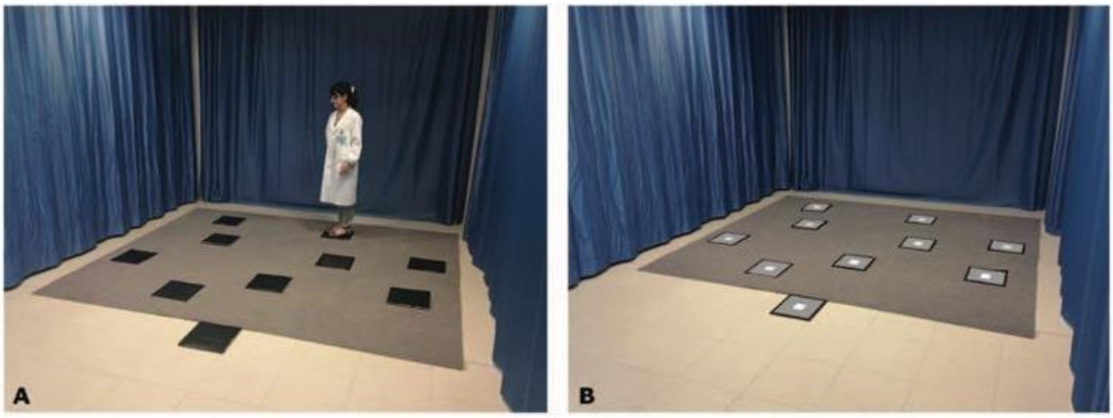

Figure 17. A. Representation of the Walking Corsi Test (WalCT). B**.** Representation of the Magic Carpet(Tedesco et al., 2017).

The WalCT evolved into the Magic Carpet to improve precision, to better control the timing of the stimuli presentation and to avoid the possible influence of the experimenter during the experimentation. The Magic Carpet was developed at the College de France by the Professor Alain Berthoz and collaborators (Berthoz & Zaoui, 2015). The Magic Carpet shares the same principle of the CBT and the WalCT, with the difference that the Magic Carpet consists of 10 translucent tiles with pressure sensors (30cm x 30cm [height ~1cm]). A computer indicated the illumination's sequence produced one-by-one and recorded the signals from the pressure sensors when the participant walks over each tile (Figure 17. B). This method allowed us to make a reconstruction of the trajectories and measure the reaction time in the task and had been used as an experimental protocol in several studies (Belmonti, Berthoz, et al., 2015; Belmonti, Cioni, et al., 2015; Demichelis et al., 2013; Tedesco et al., 2017). The Magic Carpet facilitated the exploration of the spatial cognition in the "near distant extrapersonal locomotor space" (i.e., the area used when walking around in a room) (Belmonti, Cioni, et al., 2015; Perrochon et al., 2014). In this dissertation, we used a new paradigm named the Virtual Carpet ^{tm}. This paradigm will be described and explained in detail in the method section.

I.3.4. Neurocognitive assessment of spatial cognition

The exploration of spatial cognitive capacities revealed important finds in the last decades concerning the brain mechanisms related to the cognitive spatial treatment. Detection of early cognitive decline in patients (non-observed by classical evaluations), differences in cognitive performance between reaching and locomotor space, age and sex related differences are the main contribution of the neurocognitive assessment of spatial cognition. For instance, in patients with early stage of dementia (Alzheimer's disease), the spatial cognitive assessment revealed VSWM impairment in the navigational space, whereas others types of WM such verbal and VSWM in the reaching space were not affected by the disease (Bianchini et al., 2014). It seemed that the spatial cognitive capacities were more vulnerable to the progression of neurodegenerative dementias presenting a premature decline. These results are in line with those of Perrochon et al., (2014) where the detection of mild cognitive impairment was possible due to the assessment of navigational strategies. Aguirre and D'Esposito (1999) described a taxonomy related to the assessment of cognitive functions in a locomotor environment. According to the authors, topographical disorientation is manifested in four types of deficits: a) egocentric disorientation, b) anterograde disorientation, c) heading disorientation, and landmark agnosia. The egocentric disorientation is associated with the deficit to represent space according to a self-reference position. The anterograde disorientation refers to a deficit to encode and recall visual spatial information. The heading disorientation is considered as the deficit to integrate directional information with locations or landmarks. The landmark agnosia is defined as the disability to recognize important features of the environment avoiding the identification of the landmarks.

Thus, the assessment of cognitive capacities when comparing performances in different spaces (reaching space vs locomotor space) has demonstrated a cognitive deficit in adult patients versus typical adults exclusively in the navigational space (Piccardi et al., 2011). Moreover, the assessment of spatial cognitive capacities in children, adolescents and adults shed light on differences relating to the acquisition of navigational strategies development (Belmonti, Berthoz, et al., 2015). In a typical development, egocentric strategies are acquired in early childhood followed by the acquisition of the allocentric perspective in later childhood. The ability to adopt a heterocentric point of view is only acquired when reaching puberty. This developmental trajectory of the spatial referential frames is linked to the maturation of the prefrontal cortex and combined to other cognitive capacities such as the IC, CF, and WM. Additionally, the study of the spatial cognition in children diagnosed with CP suggested that CP children affected with right-brain damage presented more difficulties in the spatial integration than their peers. These findings open the possibility to integrate rehabilitation protocols concerning spatial navigation processing in children with poor navigation performances (Belmonti et al., 2016). A recent study by Bartonek et al., (2021) assessed the topographic WM in CP children and typical developmental children using the WalCT putting forward that CP children presented poor VSWM in comparison to typical developmental children.

Additionally, the assessment of spatial cognition indicated age-related differences regarding VSWM performances between OA and YA in different spaces (reaching space vs locomotor space)(Perrochon, Mandigout, et al., 2018). YA outperform OA in the WalCT, however, the performance of OA in the reaching space were significantly better than in the locomotor space. These results are confirmed by a recent study that evaluated the VSWM in OA versus YA using a backward version of the WalCT (Carbone et al., 2020). Moreover, new technologies such as the functional Near-infrared spectroscopy (fNIRS) were adapted to the WalCT had allowed to study the difference related to the performance between OA and YA. The fNIRS measured the oxygenation level in the brain determining the degree of activation of a specifical area. The activation of a brain structure is associated with higher levels of oxygenation. The analysis of the performances between OA and YA using the fNIRS have shown that VSWM decline observed in OA was linked to a lack of oxygenation levels in the dorsolateral prefrontal cortex compared to YA (Kronovsek et al., 2020).

Experimental contribution in study of spatial cognition

The perception of the space is an important factor to take into considering when studying spatial memory. Indeed, the eye movements are crucial in exploration of the environment. Demichelis et al., (2013) investigated the eye movements during the recalling of a trajectory observed in a map. The authors hypothesized that the eye movements executed during the exploration and learning a route on a map will be implemented to facilitate the retrieval of information learned for the navigation. Thus, visual exploration of a map should influence the efficiency of navigation in the environment from an egocentric or allocentric perspective. Equally, the experimenter hypothesized that the horizontal eye movements are more efficient when exploring and recalling in the given task. Sixteen participants (students) performed two tasks: learning a path on a map (oculomotor task) (Figure 18) and recalling this path immediately after during the locomotor task. In the oculomotor task (OT), a set of grey square targets were shown on a computer screen. The task of the participant was to explore sequentially when a red square appeared and moved over the grey squares. For the learning phase, 4 paths were proposed respectively. Each path was presented on the screen after a map rotation of 0°, 90°,180° or 270° (Figure 19). The locomotor task was the magic carpet. The authors measured the eye movements in the OT and the response time on the magic carpet.

The results indicated that the horizontal eye movement (ocular anisotropy) in the learning phase significantly influenced the performance compared with the vertical eye movements. As was expected, the oculomotor learning generated in the Learning-phase was recalled before the locomotor task, facilitating the navigation performance. The authors proposed that a motor transfer is involved between the oculomotor system and the body movements during the execution of the experiment. The kinesthetic memory contributes to the mental simulation of the walking path. Furthermore, gender differences are observed, men are more susceptible to the ocular learning orientation than women in the horizontal condition showing a short time of response. The path integration is an important element of spatial navigation. Two different strategies have been described involving path integration: continuous and configural strategies

Figure 18. On the left, experimental conditions of the paths' ocular learning. On the right, an example of ocular movements during this learning phase: circles represent visual fixations (the bigger the diameter, the longer the fixation) and arrows the successive gaze moves' directions (the longer the arrow, the faster the gaze move). On this example, the vertical eye movements are visible (6 and 14) which moved away from the central square, twice during the path ocular learning (From Demichelis et al., (2013)).

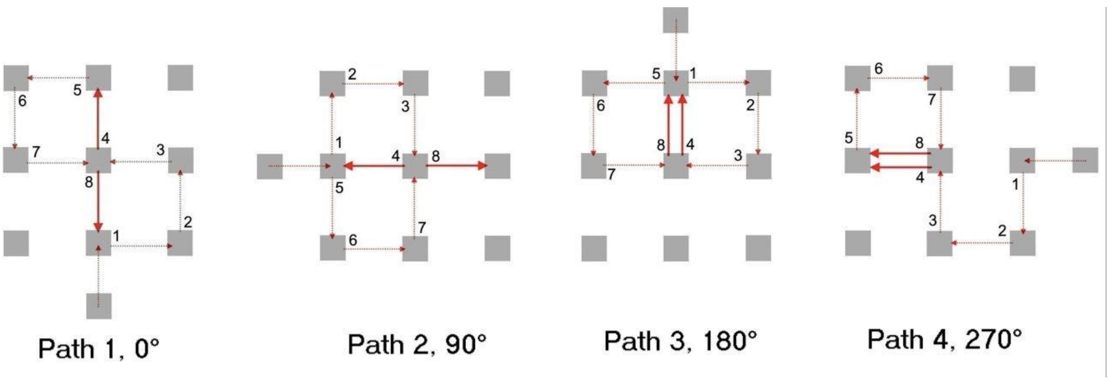

Figure 19. Example of the combination of paths and maps' orientations presented to one subject (From Demichelis et al., (2013)).

The continuous strategy is an online process of updating the ego-move information during the spatial navigation. However, the configural strategy is an offline process in the path integration which required the WM representation of the traversed path. For understanding the process characterized in human path integration, Weiner et Berthoz (2011) compared the continuous and configural strategies. The paradigm used in this study was the Triangle Completion Tasks (TCT) in which blindfolded participants were led along two sides of a triangle (Figure 20). At the end of this outbound path, they are released and asked to complete the triangle by walking back to the starting point. A group of seventeen participants assessed individually were instructed to use the continuous or configural strategies during the experiment. The experimenter measured the head rotation, the response time and the homing errors.

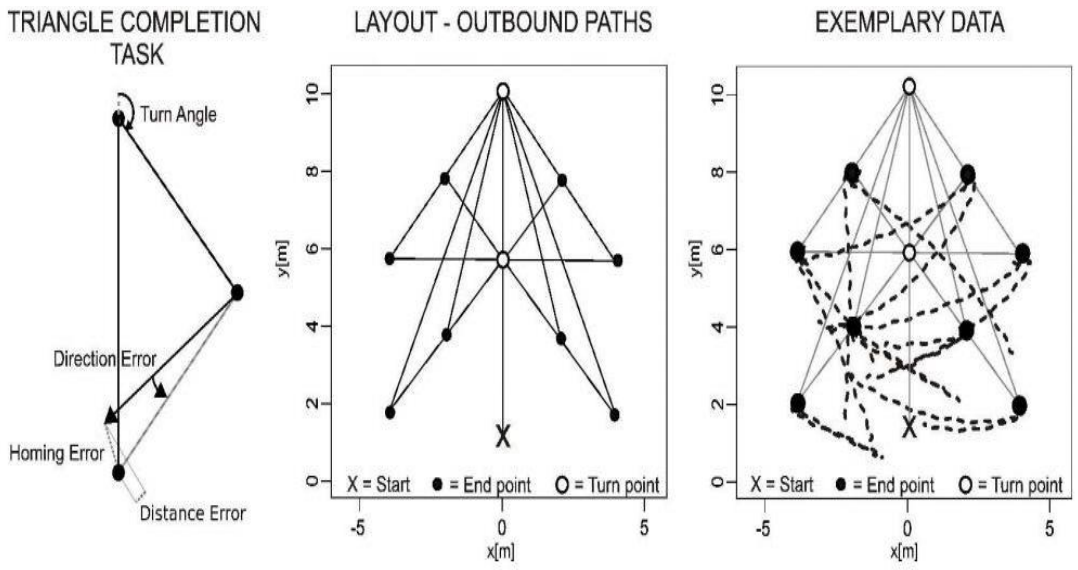

Figure 20. Left: The triangle-completion-task and homing accuracy measures; middle: The layout of the 16 outbound paths; right: Exemplary data of one of the participants in the configural condition (dashed lines represent homing trajectories)(From Wiener et al., 2011).

The results demonstrated that instruction of the task influenced the performance of the participants depending on the use of each strategy. Moreover, when participants used the configural strategy, a dissociable cognitive operation for human path integration was observed. Thus, a clear difference of performances between the continuous et configural is manifested on longer paths (Figure 21). The authors also described the role of the head in the anticipation of the trajectory in the homing direction. Indeed, the authors suggest that the neural mechanisms underlying the path integration are associated with the posterior parietal cortex and the medial temporal structures.

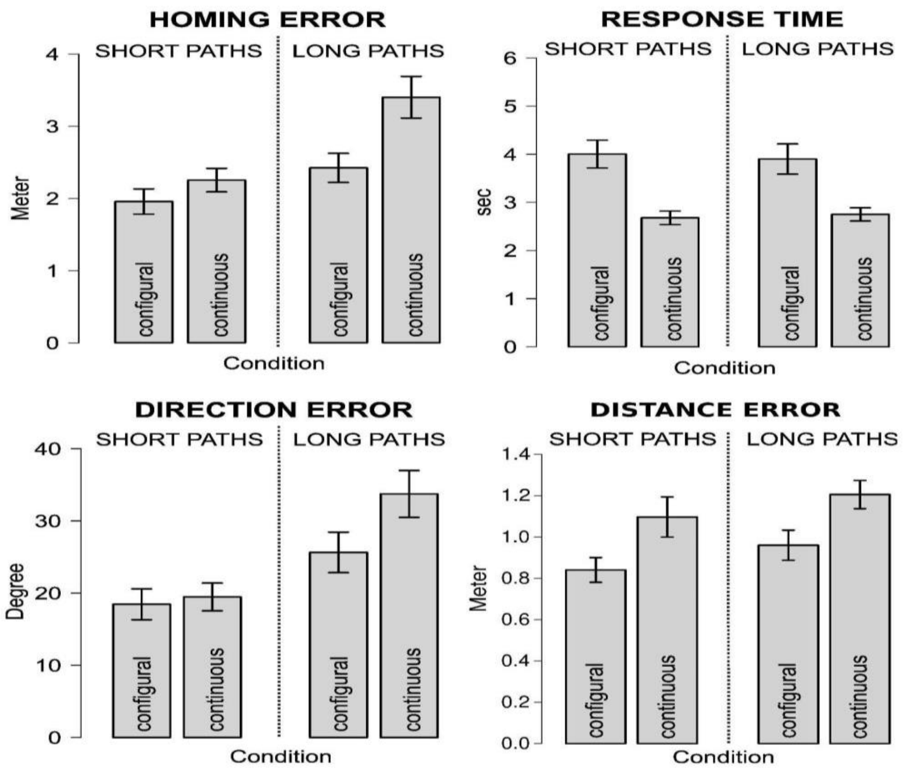

Figure 21. Behavioral results (mean ± sem); Top left panel: homing error; top right panel: response times; lower left pane: direction error ; lower right panel: absolute distance error(from (Wiener et al., 2011)).

The peri-personal space and the extra-personal space were studied during the typical development in children (Belmonti et al., 2014). Taking in account the effects of sequence geometry on performance and the types of error made by subjects at different ages, the authors hypothesized that the sequences geometry will produce disorientation in navigation space in children rather than in adults. A total of 101 children aged between six to twelve years old participated in the study. In addition, eighteen healthy adults (nine females, nine males) were enrolled from a mixed population of university students, medical and paramedical staff, ranging from twenty-one- to thirty-two-year-old. The participants were tested with CBT and the “Magic Carpet” test (Figure 22). Other tests (Digitspan and Raven’s CPM) were carried out other than these two so as to not overload any common spatial memory networks possibly subserving both of them. The authors found that the span increased with age in the CBT and in the “magic carpet”. The results suggested an increase in performance for the male children in the range of age 10-11 for the navigational space. These findings are the evidence of a cognitive shifting which is maturation of executive functions and brain connectivity.

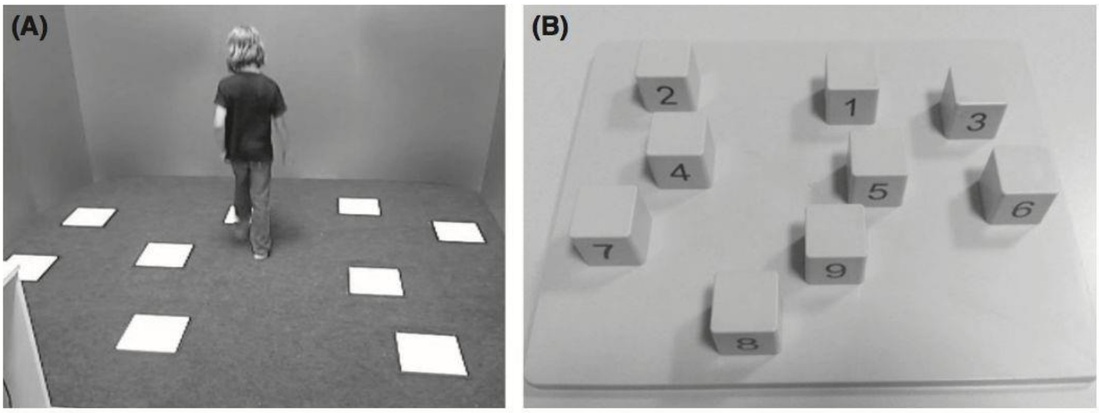

Figure 22. Experimental set-up. (A) The Magic Carpet. (B) The Corsi Block-tapping Test (experimenter's view) (From Belmonti et al, 2015).

In human spatial navigation, the differences between men and women have been widely hypothesized; suggesting that, on the one hand, men use more egocentric representation strategies of the space based in metric distances and cardinal directions. On the other hand, women navigation strategies depend in landmark's positions. These two navigational processes can be distinguished such as Spatial Updating by self-motions and landmark-based orienteering.

To test this hypothesis Lambrey et Berthoz (2007) developed a study to analyze the possible gender-related difference in spatial cognition. The experiment took place in a hexagonal room (Figure 23-24). All the participants explored beforehand the surrounding of the hexagonal room. The experiment consisted of three different conditions: a) Stable-Landmarks (Stable- L), b) Rotated-Landmarks (Rot-L) condition and c) Switched- Landmarks (Switch-L) condition. In the Stable- L, the landmarks were compatible before and after the presentation. In the Rot-L, the images displayed on the three screens rotated in the second presentation. In The Switch-L, two views out of three were switched off after the delay, while the third one remained at the same location. For each condition, the participant was placed in the center of the hexagonal room. All trials started by switching off the spotlight, then three screens displayed images of the outside room for 90s. Next, the screen is turned off for 30s after which the screens displayed images for 90s again. Finally, the spotlight was turned on, allowing the participant to perform the point task. The task of the participant was to point to the direction of each of nine different views in the outside environment. The participants were divided in two groups immobile and the mobile. In the mobile group, the participants received the instruction to close their eyes and rotate on the spot for the 30s while the screens were turn ed off.

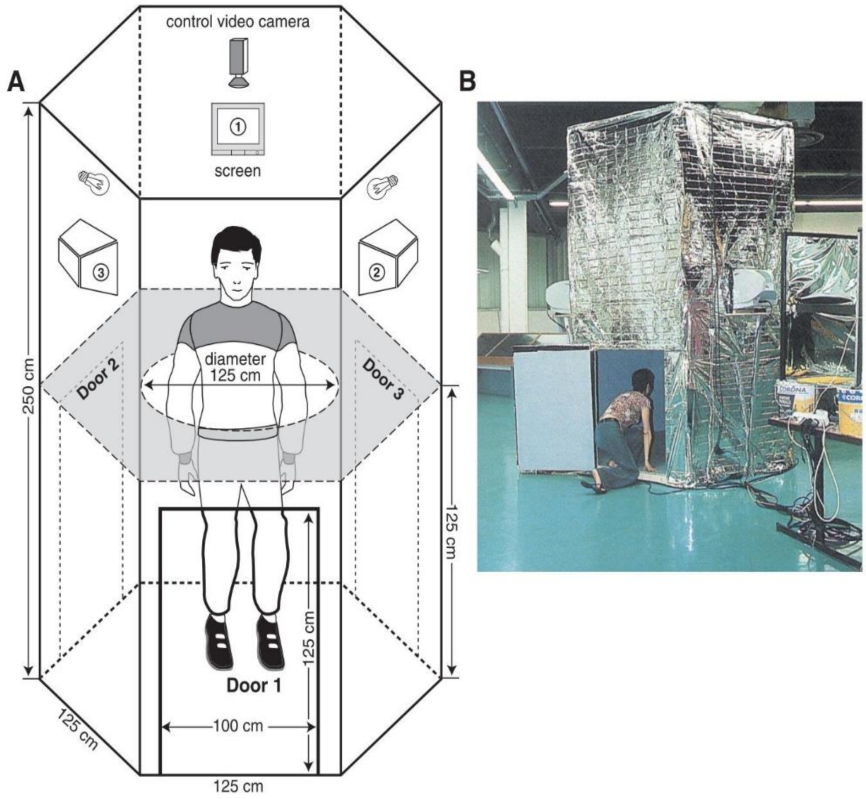

Figure 23. Experimental set-up (diagram and real-world photo). Subjects entered through one of the three doors and then stood up inside the testing room. Three TV screens were positioned on three of the six walls of the structure. These screens displayed the landmark views (from Lambrey et Berthoz (2007)).

The immobile group did not receive any specific instruction to do during the 30s of pause. Nineteen subjects (10 women, 9 men) volunteered to participate in the study. The results showed great proportion in global orientation error in the mobile group because they were unable to correctly update their spatial representation. In the switching condition, both groups performed the same in the awareness of the landmark switch. In general, women made significantly greater global orientation errors than men in the Rot-L.

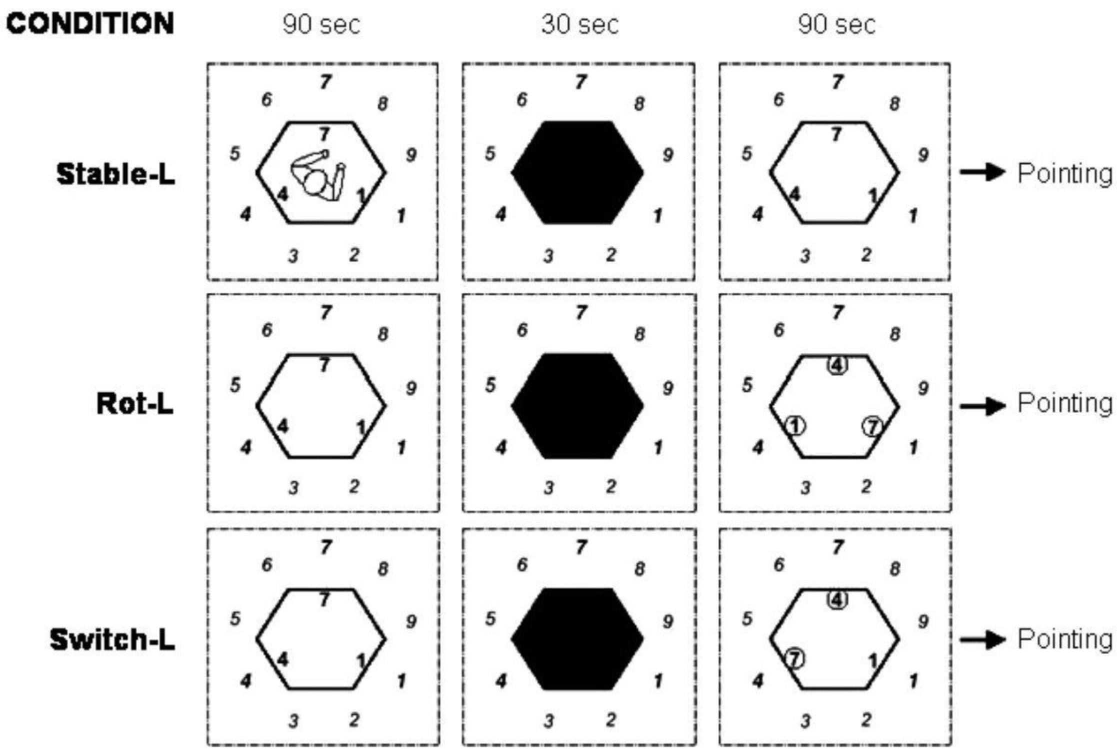

Figure 24. Procedure in the Stable-L, Rot-L and Switch-L conditions. The hexagon symbolizes the testing room. The numbers outside this hexagon correspond to scenes in the real-world environment. The numbers inside the hexagon correspond to the scenes displayed by the screens. First, each screen displayed the image of one view of the environment as if this screen were a window to the surroundings. Subjects were instructed to look carefully at each screen to take in their bearings as precisely as possible. During this phase, the spotlights inside the testing room were turned off and light came only from the video screens. After 90s, the images disappeared, and the screens remained dark for 30 s. Then the screens displayed images of the environment again and subjects had to look once again at each of the screens. After an additional 90 s, the screens were switched off and the spotlights were turned on. This was the signal to perform the pointing task (From Lambrey et Berthoz (2007)).

The authors suggested that women have different strategies than men in the use of egocentric representation of landmark locations. Men’s strategy is based in the internal representation where they expected the landmark to be (Figure 25). The authors hypothesized that women take bearings relative to the actual locations of the landmarks as they appear in the environment. Men used landmarks like an update of the egocentric representation modulating both the actual and expected landmark locations.

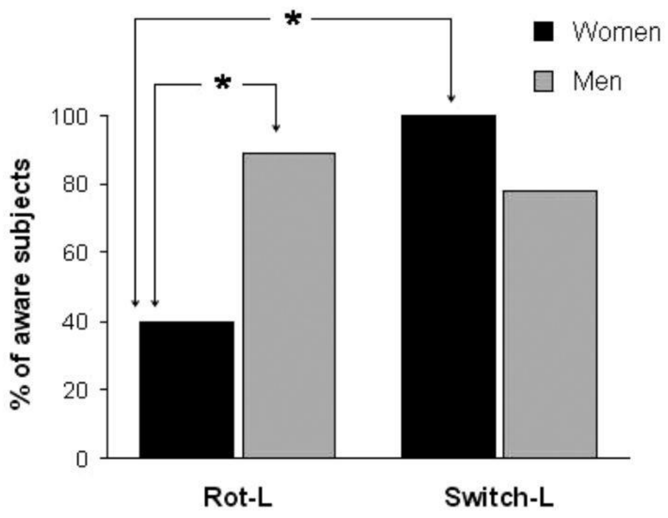

Figure 25. Percentage of women and men who became aware that the landmark views had been displaced in the Rot-L and Switch-L conditions. ∗indicates a significant difference ($p<0.05$)(From Lambrey & Berthoz, 2007).

I.3.5. WalCT as a tool for neuropsychological assessment

The WalCT was proposed as a complement in clinical neuropsychological assessment due to the fact that it can identify the navigation memory impairment in subjects who score normally in the classic memory evaluation. Therefore, Piccardi et al., (2013) had implemented a standardization of the WalCT in an Italian population. The aim of the study was to investigate the psychometric properties of the WalCT as a topographical memory test and compare the CBT to the WalCT in a large sample of 289 healthy Italian participants aged 15–86 years. The participants were subdivided into six group: Youngest (15–25 years), Young adults (26–35 years), Adults (36–46 years), Middle-aged (47–57 years), Older (58–68 years),Oldest (69–86 year). The participants were tested in the CBT and the WalCT. In the CBT, the short- and long-term spatial memory was assessed. In the long-term memory, the learning (VSL) and delayed recall (VSDR) were tested. Similarly, in the WalCT the experimenter evaluated the topographical Short-term Memory (TSTM), and for the long-term memory the Topographical Learning (TL), and topographical delayed recall.

The results show that age is an important factor in the performance of the groups; the younger groups have a better scored performance in comparison with older groups whose performance seems the decline at around 47 years old. The authors observed that the performance for both working spatial memory and learning topographic information has a critical age, estimated at 48-58 years. Gender-related differences were only identified in the WalCT but not in the CBT being that the men outperformed the women. However, this sex difference disappeared at the critical age of 47. Although, they measured different spatial dimensions, the authors suggested that both the CBT test and the WalCT test share similar components such as sequential encoding and planning strategies.

Recently, virtual reality has been used as an important element in the study of cognition in several scientific domains. Nori et al., (2015) developed a study to evaluate reliableness of the exploration of topographic memory. The authors formulated two objectives; the first aim was to compare the effects of the real and virtual reality learning environment during the acquisition of spatial information and the second aim was to determine the gender difference in both environments. Therefore, the experimenters used a virtual version of the WalCT the M-Walking Corsi Test (M-WalCT) which correspond to enlarge version (7x6m with 18 squares of 3x3 cm). In the virtual navigation, the participants were sitting on a chair and imagined movement when they saw an avatar walk through the space. The VR-WalCT was a reproduction of the WalCT with the same characteristics of the room (Figure 26). In the VR-WalCT learning condition, to start the experiment, an avatar showed the participants the 8-step sequence by walking and stopping for 2s on the squares. Eighty healthy participants (forty men and forty women) were selected to perform both conditions (real and virtual navigation).

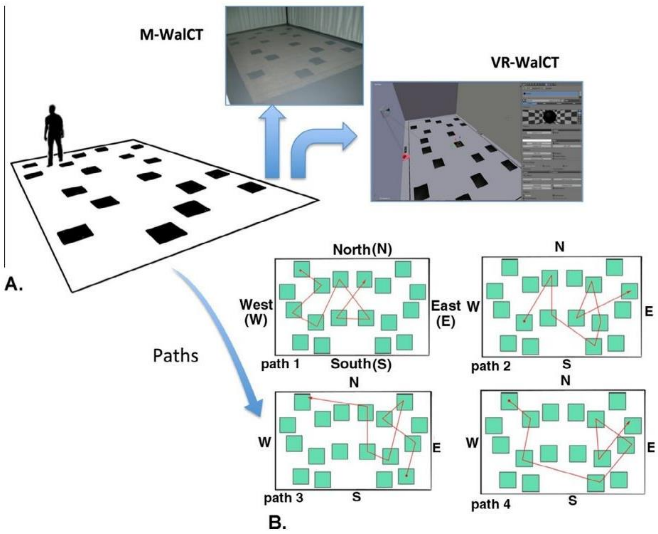

Figure 26. (A) The M-WalCT platform is depicted. A1 shows the real environment and A2 the virtual version; and (B) different paths are represented (from Nori et al., 2015).

The task of the participants was to learn a sequence of 8 blocks shown by the experimenter or the avatar. The results demonstrated that the virtual and real environment are useful to analyze the topographic memory system. Moreover, the results established gender-related differences as it is shown that men outperformed women in this task (Figure 27)

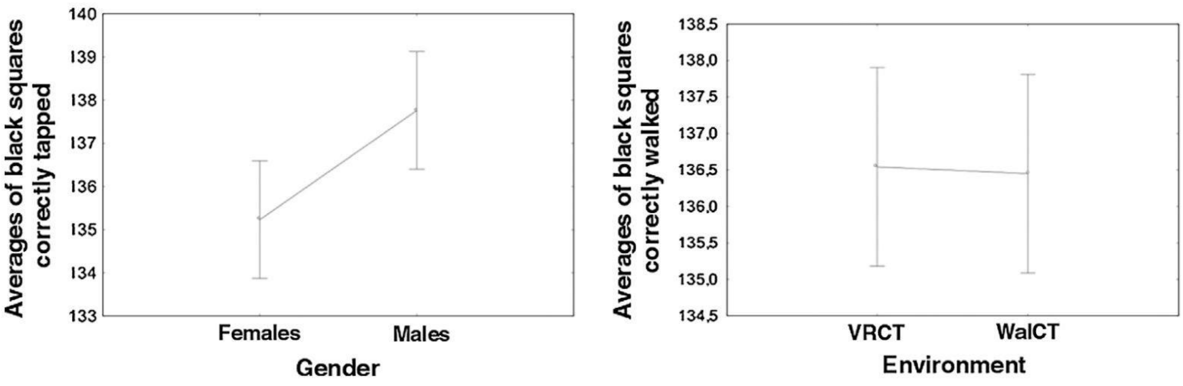

Figure 27. Means and standard deviations for the main effects of gender and environment (from Nori et al., 2015).

To test the effectiveness of the WalCT in the detection of the early stage of dementia, Perrochon et al., (2014) developed a study which aimed to determine whether the assessment of VSWM in the Corsi test and complex navigation task is a good indicator of cognitive impairment in the initial manifestation of a dementing illness. Furthermore, they were interested in analyzing the different strategies used by subjects in different tests and investigated whether these cognitive strategies were related to cognitive decline. The authors hypothesized that the analyses of the strategies used by the participant provide more information than the span score in the WalCT. In the study, 51 participants were selected as sample. This group was subdivided into 15 younger subjects, 21 older subjects and 15 participants diagnosed with Mild Cognitive Impairment (MCI). The MCI had been described as a previous stage before the diagnosis of dementia. The MCI is the intermediate stage between cognitive health and dementia. This pathology is characterized by memory problems, objective cognitive impairment, and the preservation of the daily functioning. Prior to the main test, all participants had undergone a neuropsychological assessment and a physical test of walking for 10 minutes in a standardized environment. Moreover, the mood and state of depression of the participants were also assessed using the Geriatric Depression Scale. The experimental tasks were a newly designed version of the WalCT, using the 'Magic Carpet' and an electronic version of the CBT (Figure 28). In the electronic version or the Modified CBT, the sequences are shown on a computer and the participant repeated the same sequence by pressing the sequence on the MCBT.

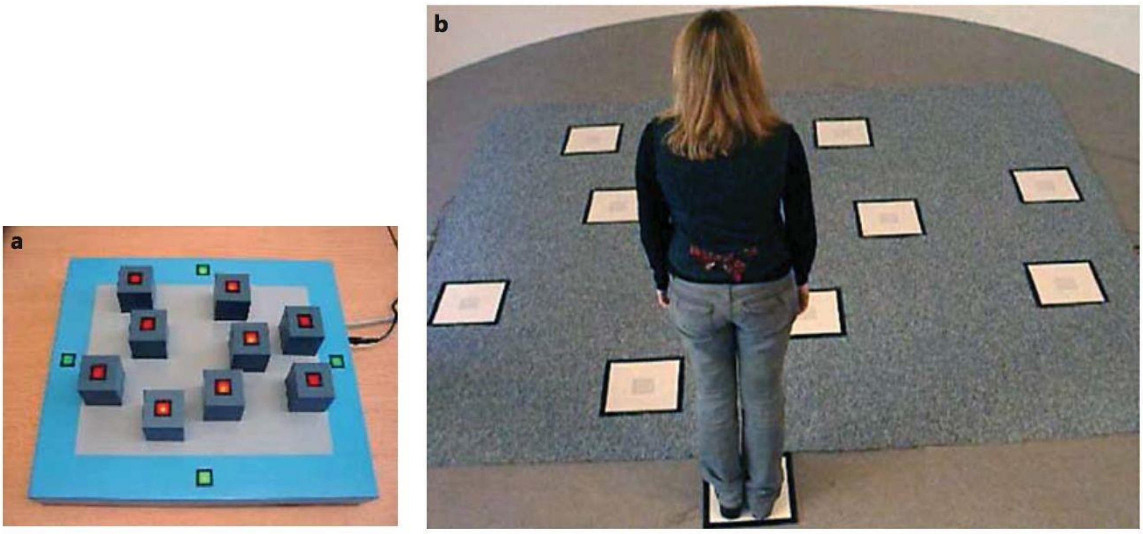

Figure 28. Description of the protocol. A) MCBT is an electronic version of the CBT. The sequences are controlled by a computer. B) MWCT is a larger version (3 × 2.5 m; scale 1: 10) of the CBT. An electronic version of the CBT was organized in an empty room [15, 20]. The MWCT is controlled by a microcomputer through WLAN connection. Nine white squares (30 × 30 cm) were placed on a grey carpet (From Perrochon et al., (2014)).

The level of the difficulty increased after a correct sequence reproduction (two out of three to pass to next level). The criteria of test stops were when two trials out of three at the same level have not been correctly reproduced. Additionally, the experimenter analyzed the *cognitive strategies assessed from the trajectory errors*. Five different types of errors were identified (S1) Localisation (one wrong block is shown); (S2) inversion (two blocks are shown in the wrong order); (S3) approximation (sequences with several errors but with a general configuration similar to the shown sequence); (S4) random sequence (sequences presented without any logic), and (S5) incomplete sequence (sequences with too many or not enough blocks) (Figure 29).

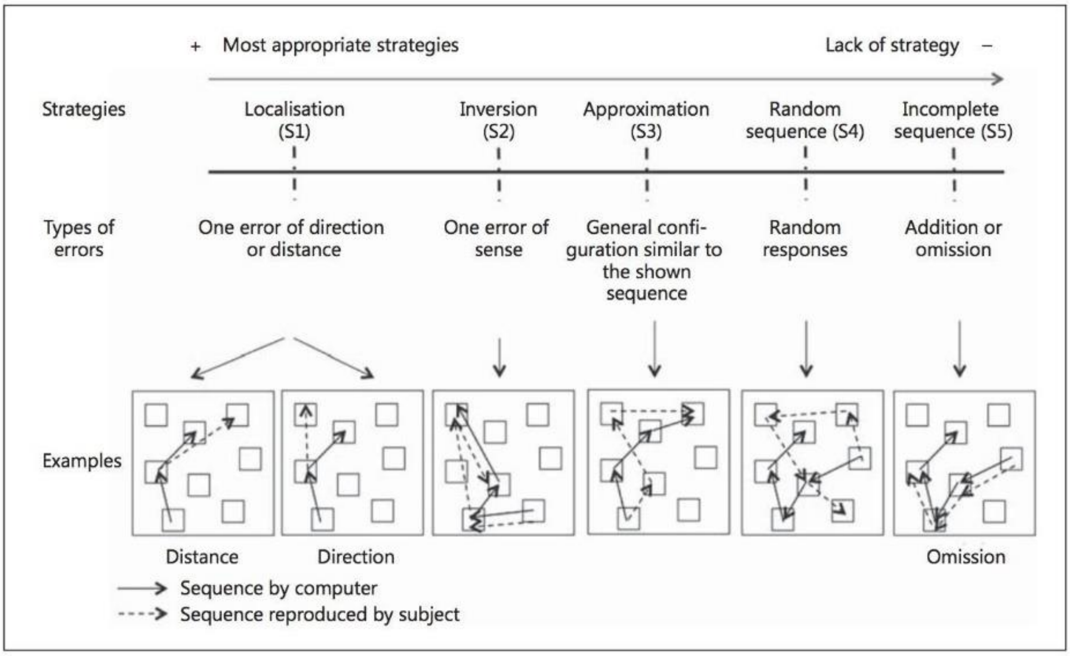

Figure 29. Analyses of the various strategies used in the Corsi test according to the mistakes that were made (From Perrochon et al., (2014)).

The results showed clear differences in the performance of the participants in both tests. The performance on the MWalCT was lower than on the MCBT. The authors explained these differences by the complexity of the MWalCT which demanded an update of sequence coding and planning when the participant navigated in the space. The results indicated an effect of ageing in the performance in the older participants in the MWalCT associated with the decay of the working spatial memory capacities (Figure 30). Moreover, the authors did not observe a difference in the performance between the young group and the MCI group on the MCBT. In addition, the author proposed that the analysis of the strategies used by the participant allowed them to identify a pronounced deficit in the MCI group (Figure 31).

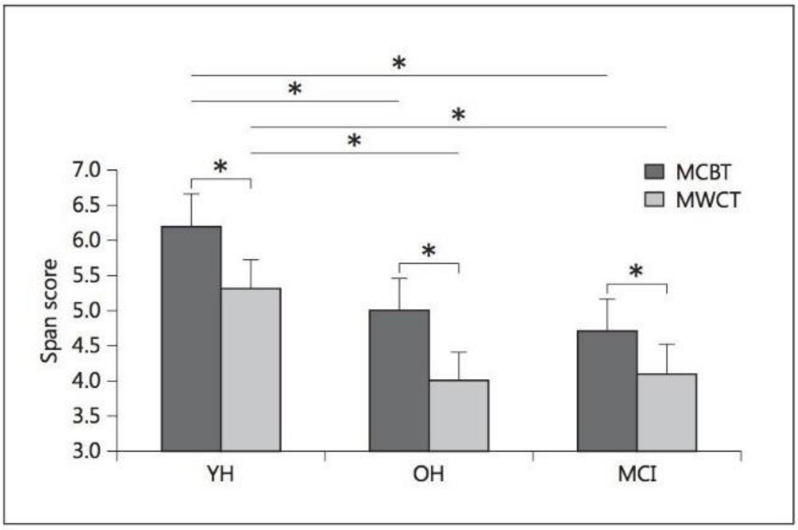

Figure 30. Impact of the complex navigation task on the VSWM of the subjects in each group. OH = Healthy older subject; YH = healthy young subject. ANOVA with a plan of 3 × 2 factors was used. * Significant difference, $p < 0.05$ (From Perrochon et al., (2014)).

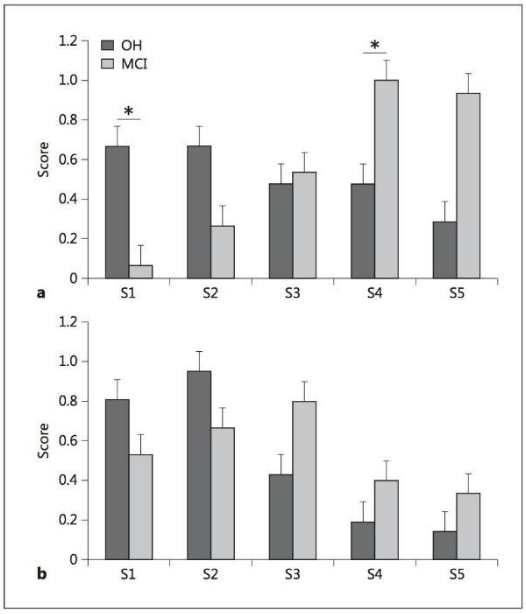

Figure 31. Behavioural profiles in problem solving at the latest stage of the Corsi test. The mean score was calculated during the subject's last and unsuccessful trial series (span + 1), as the mean number of times a strategy was used. a Strategies during MCBT. b Strategies during MWCT. OH = Healthy older subject. Statistics were performed using the Mann Whitney test. * Significant difference, $p < 0.05$ (From Perrochon et al., (2014)).

I.3.6. Neural Bases of cognitive strategies during the WalCT

Perceptual processing and EFs are recruited during the navigation and performance in the WalCT. EFs are engaged in planning, ignoring irrelevant distractions and regulating automatic behaviors (i.e., inhibitor control), in the short term remembering information for manipulated it (i.e., WM), and being able to predict and adjust to eventual changes (i.e., CF)(Diamond, 2013). Neurocognitive and neuroimaging assessments indicate that the frontal lobes are involved in EFs, specifically the dorsolateral prefrontal cortex (Friedman & Robbins, 2022; Kronovsek et al., 2020; Menon & D'Esposito, 2022). The prefrontal cortex is linked to subcortical structures such as the basal ganglia and the cerebellum during the executive processes (McGough et al., 2018; Mirino et al., 2022; Patai & Spiers, 2021). The right medial temporal lobe is key in the representation of the cognitive maps of the environment and memory (Eichenbaum, 2017; Igloi et al., 2010; Lambrey et al., 2003; Maguire, 2001). Moreover, the parahippocampus, hippocampus, retrosplenial cortex, and posterior parietal cortex are the core areas of spatial navigation (Boccia et al., 2014; R. A. Epstein et al., 2017). The hippocampus is engaged in the mental representation of the spatial navigation (cognitive maps), the planning of the actions and the using of past experiences in navigation (Eichenbaum, 2004; O'keefe & Nadel, 1978). The parahippocampus is involved in visual spatial processing, in particular in place recognition, route planning and mnemonic encoding (Aminoff et al., 2013; R. Epstein et al., 1999). The retrosplenial cortex is involved in spatial encoding, memory and the integration of information from egocentric to allocentric spatial processing (Maguire, 2001; A. M. P. Miller et al., 2019; Vann et al., 2009).

Several studies in the field of neuropsychology and neurosciences have described the loss of navigational capacities such as recognition of a familiar landmark and general disorientation after brain damage. An important number of lesions and neuroimaging studies have shed light on an ensemble of structures that are involved in the processing of spatial navigation.

To test the hypothesis that the left medial temporal lobe is involved in the spatial navigation recalling of sequences during the locomotion through the space, Lambrey et al., (2003) evaluated the performance of two groups of patients with unilateral lesion (left-right) in the medial temporal lobe and a control healthy group during a virtual reality task. The virtual reality task was a large-scale virtual maze with a start point and an end point. During navigation, the participants encountered a chair, a flower, a man, a clock, a ladder, a Christmas tree and a portrait. (Figure 32).

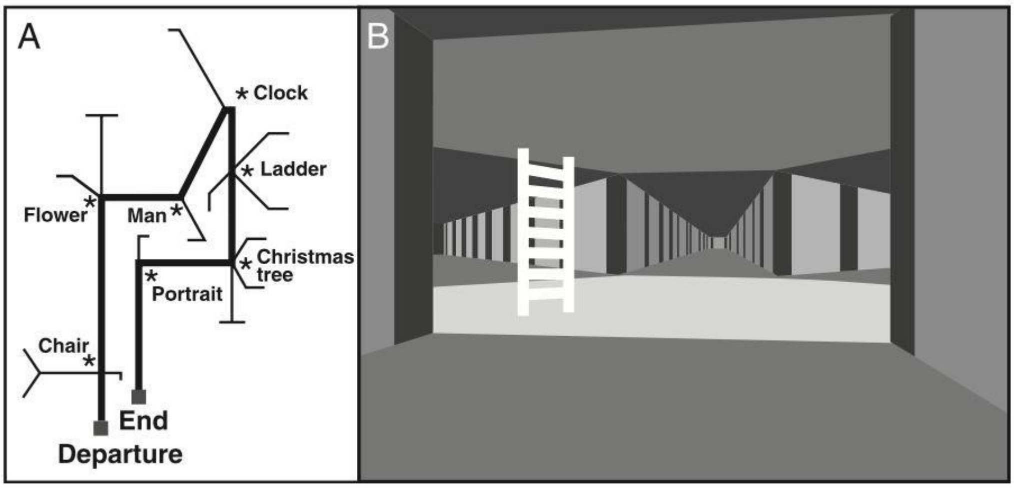

Figure 32. Virtual environment. (A) Map of the virtual maze. (B) Graphic model of the virtual environment (example: view of the crossroads with the ladder). The direction to be taken at crossroads was signposted by green-coloured walls while all the wrong directions were signposted by red-coloured walls. The thick line represents the path followed by subjects(From Lambrey et al., 2003).

The instruction for the navigation task was to pay close attention to the landmark placed on their way. After each trial the participant drew the path on a sheet of paper with their eyes closed eyes. The landmarks recalled on the path were symbolized with a dot. The result indicated that the left medial temporal lobe (MTL) is involved in the sequential memorizing egocentric perspective (Figure 33). In addition, the right medial temporal lobe patients presented a performance between the left medial temporal and the control group. The authors proposed that the functional lateralization presented in the medial temporal lobe is due to sequential encoding for language and equally for the sequential of memorizing landmarks or movements. Thus, the patients presented verbal difficulties to describe the elements seen on the path. The differences observed in the literature and the findings demonstrated that the right medial temporal lobe is involved in memorizing the allocentric coordinates, even though the left medial temporal lobe participates in the route memory or allocentric memory perspective.

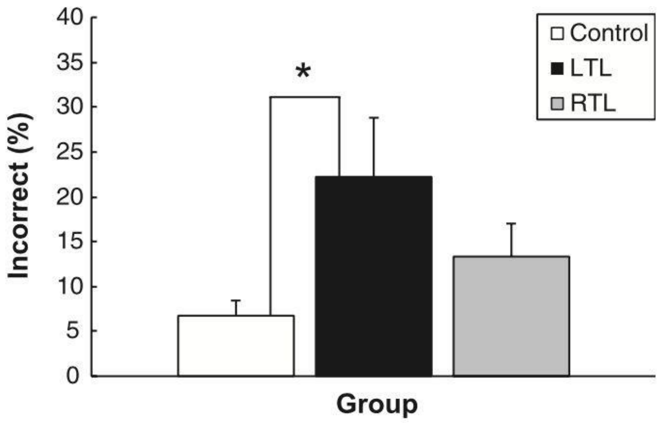

Figure 33. Memory for the sequence of landmarks in control and patient groups. The inaccuracy of memory for the sequence of landmarks was expressed as the percentage of landmarks that were not correctly placed along the path during the map drawing path. Error bars are the standard error of the mean. * indicates significantly impaired relative to the control group ($p < 0.05$) (From Lambrey et al., 2003).

In the study of Piccardi et al., (2010) the authors were interested in understanding the different neural systems involved in spatial memory. The aim of the study was to determine the role of the Medial Temporal Lobe (MTL) areas in object localization in the peri-personal and extra-personal space. The authors suggested the hypothesis that there are two different memory systems for the object localization in the space: one for the proximal space and another for the far space. The study was conducted on a patient group (22 patients) and a healthy group (21 patients). The patient group had undergone unilateral temporal lobe surgery for the relief of intractable epilepsy. The patient group was subdivided in eleven right temporal lobe (RTL) and eleven left temporal lobe (LTL) surgery. The patient group and the healthy group were evaluated with a neuropsychological battery to determine their neuropsychological profile. The experimental testing involved the CBT and the WalCT. In both the CBT and the WalCT tests, the visual short-term memory test (VSTM) and two aspects of long-term memory (LTM) were assessed: learning (VSL) and delayed recall (VSDR). The results indicated that some patients' performance in the CBT and the WalCT did not change in the experiment being lower scored in comparison with the healthy group (Figure 28). Moreover, the lateralization of the brain lesion right or left did not play a specific impact. Piccardi et al., (2010) presented that the right and left hippocampus contribute to the visuospatial memory for sequences in the peri-personal space and in the extra-personal space. Nevertheless, the analysis of the individual performance showed a double dissociation between the CBT and WalCT for VSTM and LTM test (Figure 34, 35).

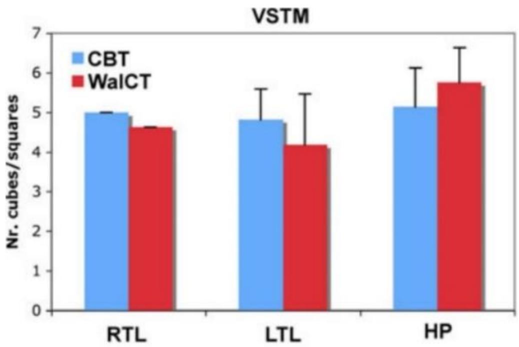

Figure 34. The graph reproduces means and SDs of the number of cubes/ squares recalled in the short-term memory task by each group in CBT and WalCT (From Piccardi et al., (2010)).

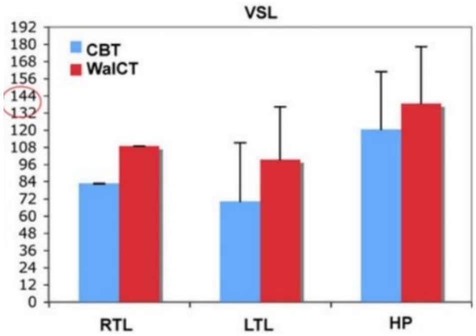

Figure 35. The graph shows means and SDs of the number of cubes/squares performed by each group to reach the learning criterion in the visual learning task. The total score of 144 was the maximum obtainable for both the CBT and WalCT (From Piccardi et al., (2010)).

The double dissociation in the unilateral temporal lobe in surgery patients indicated the existence of two different memory systems, one system for coding, storing, and recalling sequences of objects and movements in a small peri-personal space and the other system for coding, storing, and recalling sequences of locomotor trajectories in a large extra-personal space (Figure 36).

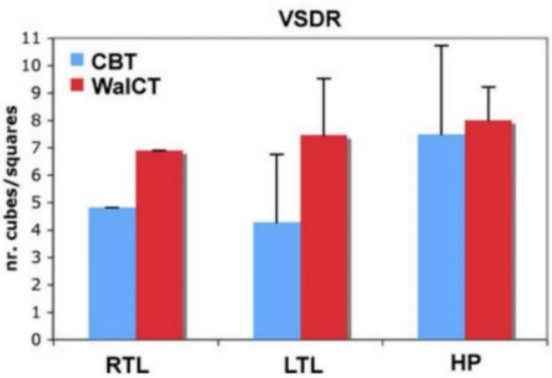

Figure 36. The graph reports means and SDs of number of cubes/squares remembered after 5 min by each group in both tests (From Piccardi et al., (2010)).

The role of the cerebellum in cognition was proposed in the last decade opening a new perspective of the cerebellum. Researcher such as Iglói et al., (2015), conducted a study to determine the involvement of the cerebellum in the navigation strategies, as well to understand its implication in the motor and cognitive human navigation. Based on the previous research, the authors identified the possible connection between the cerebellum and the prefrontal cortex and the parietal cortex via the lobe VIIA (Kelly & Strick, 2003; O'Reilly et al., 2010). Moreover, the authors took into consideration the cerebral activations during the navigation task and the cognitive strategies. The cognitive strategies involved in the navigation are place-based strategies which are associated with the *allocentric perspective* taking and the sequence-based strategies which require the *egocentric perspective*. The place-based strategy is related to the right hippocampus and the sequence-based corresponds to the activation the left hippocampus. Iglói et al., (2014) used the fMRI for measuring the signal BOLD and record a virtual navigation task (virtual starmaze) (Figure 37). The experimenters analyzed the interaction between the cerebellum and the right and left hippocampus. The task of the participants was to move through the starmaze using a keypad and finding the goal and feedback was given after the successful find. In the control trials the participant moved through a determined portion of the alley and turned left or right. The authors found a functional connectivity between the cerebellum and the hippocampus during the use of cognitive navigation strategies. The lobule VIIA Crus shares on the one hand, connections with the right hippocampus and the medial parietal cortex which are both involved in the place-based navigation strategies. On the other hand, the VIIA Crus I is also connected with the left hippocampus and medial prefrontal cortex in the egocentric strategies (Figure 37).

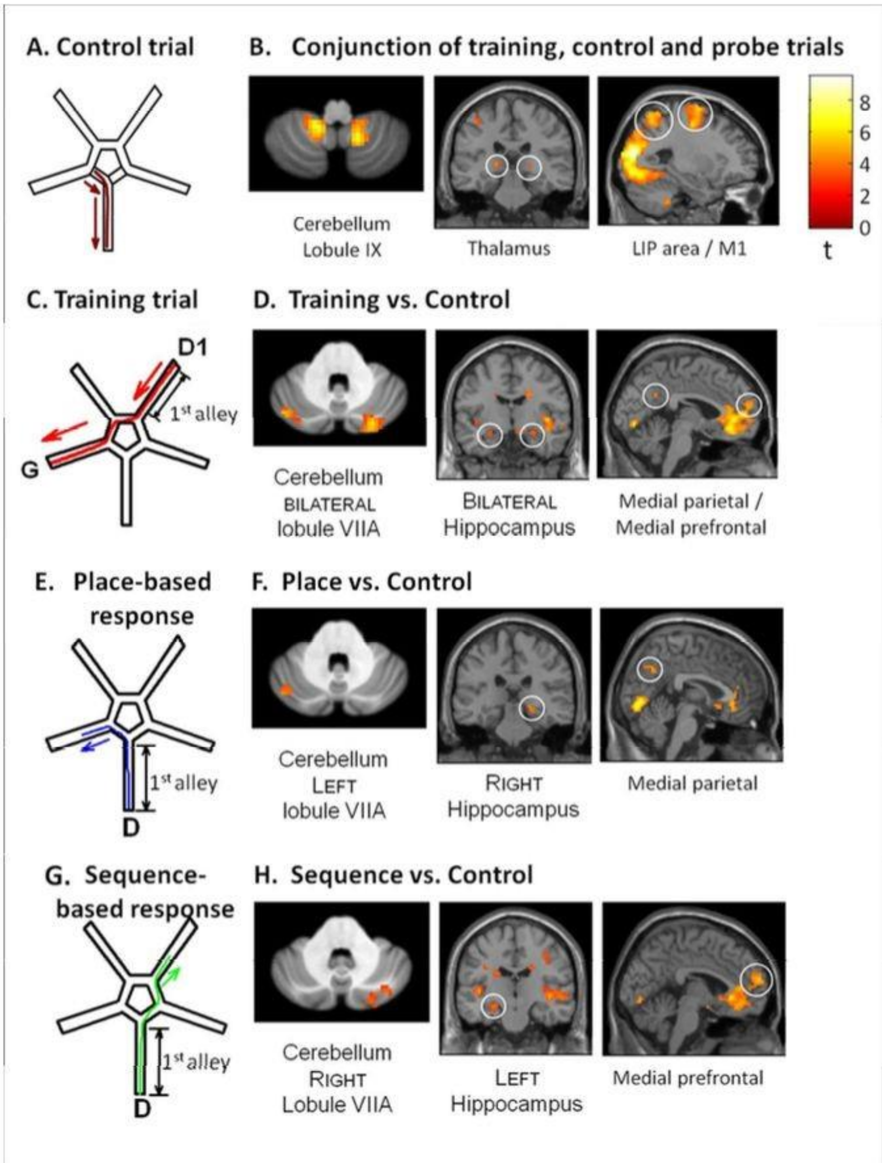

Figure 37. (A) Subject's path in the control trials. (B) Conjunction analysis including first alleys of training, control and probe trials, whatever strategy was used in probe trials. Left: bilateral activation of the posterior cerebellum lobule IX (peaks at MNI coordinates: -12, -58, -41 and 15, -57, -51). Center: Bilateral activation of the thalamus in the white circles (peaks at: -18, -27, 3 and 21, -27, 0). Right: activation of the lateral intraparietal area (LIP) and the primary motor cortex in the white circles (peaks at: -21,-63, 60 and -24, - 6, 63, respectively). (C) Training trials. D1: departurepoint for all training trials; G: goal; in red, the most direct path from the departure to the goal. (D) Activation of structures of interest for training vs. control trials. Left: bilateral cerebellar lobule VIIA Crus I (peaks at MNI coordinates: 27, -81, -36 and -45, -72, -36). Center and right (adapted from Igloi et al., 2010): Bilateral hippocampus (peaks at: 30, -6, -15 and -21, -15, -15), along with medial prefrontal (-3, 42, 0) and medial parietal cortex (0, -54, 30). (E) Place-based path in a probe trial (in blue). D: departure point. (F) Activation associated with place-based responses vs. control trials, in the 1st alley. Left: left cerebellar lobule VIIa Crus I (-45 -72 -36) (From Iglói et al., (2015)).

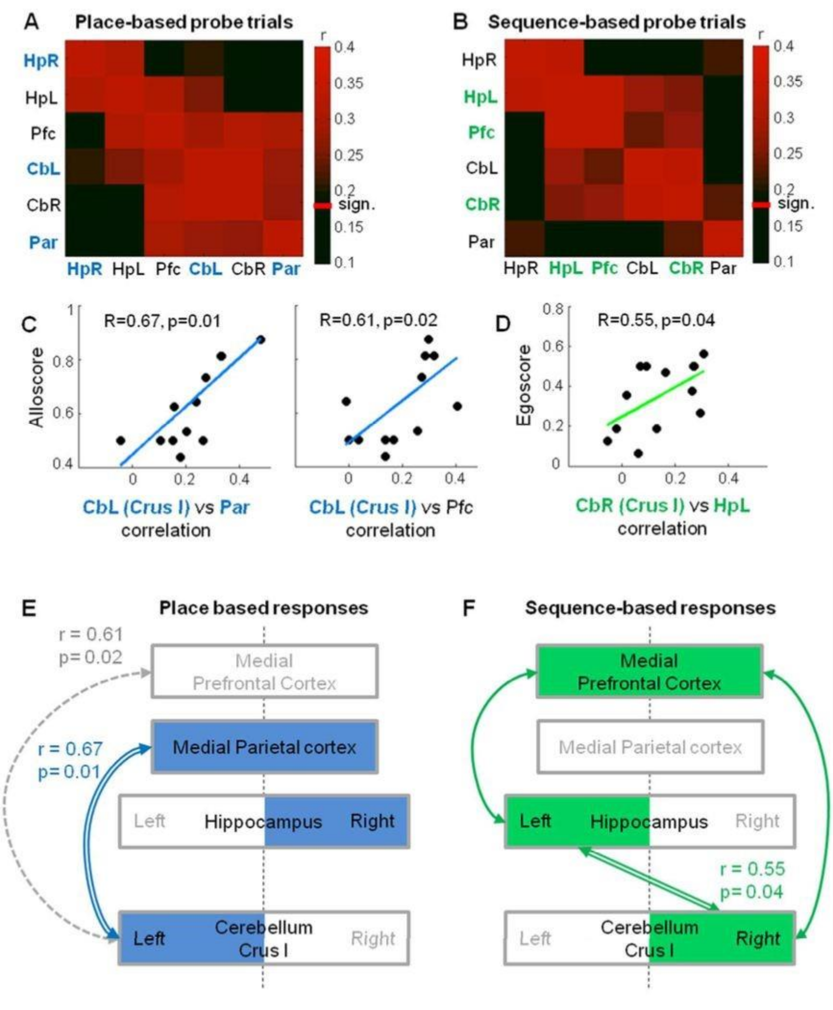

Figure 38. Correlation matrices between the structures of interest for place-based and sequence-based probe trials averaged over 13 subjects included in the connectivity analysis. Correlation is significant above 0.18. The names of the structures found activated in the first alley of probe trials for place-based responses (when compared with control) are highlighted in bold and blue. Names of structures activated for sequence-based responses are highlighted in bold and green. (C) Positive correlation between the alloscore (i.e., tendency to use the place-based strategy) and the medial parietal-CbL (Crus I) correlation on all trials (N = 13) (D) Positive correlation between the egoscore (i.e., tendency to use the sequence-based strategy) and the left hippocampus-CbR (Crus I) correlation on all trials (N = 13) (From Iglói et al., (2015)).

Recently Tedesco et al., (2017) studied whether the cerebellum is involved in the processing of navigational sequential information and whether it is influenced by the modality of the stimuli presentation. The author analyzed the performance of twelve patients with cerebellar lesion and twelve healthy control group on Spatial Working Memory (SWM) tests and the navigation test. The SWM test was the CBT. For the navigation assessment, the authors utilized the WalCT and the electronic Magic Carpet. In the WalCT, the sequence was display by the experimenter whereas in the electronic Magic carpet the sequences were produced by the it is indicated by a computer that lights up the tiles in the sequence. The results showed that the cerebellar patients (CPa) perform like the control in the WalCT despite the fact that the performance of the patients were significatively different in the Electronic Magic Carpet (Figure 39). The authors proposed that the decline of the performance in the Electronic Magic Carpet cannot be attributed to motor problems or cognitive impairment. Moreover, the absence of difference in the performance in the WalCT between the CPa and control groups suggested that also navigational WM is not impaired in patients affected by a cerebellar pathology. They hypothesized that the differences in performances are influenced by the modality of presentation of stimuli. Furthermore, in the Electric Magic Carpet, the easiest way to solve the task is normally to use the allocentric strategy. The authors explained that the difference in performances is probably due to a significant involvement of the cerebellum in sequence processing. The cerebellum interacted with other structures to achieve a cognitive goal. This interaction was interrupted by the cerebellar lesion presented in the patients. Nevertheless, the authors explained that the differences noticed during the performances are probably due to significant involvement of the cerebellum in sequence processing.

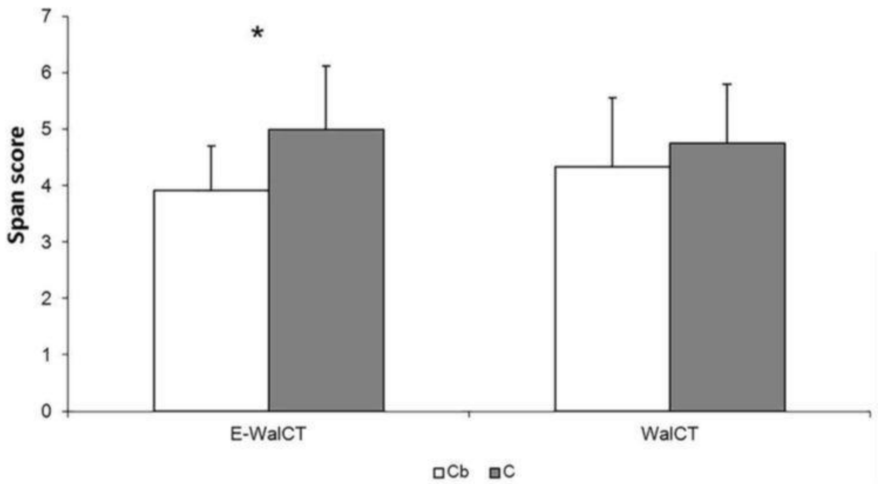

Figure 39. E-WalCT and WalCT performance. Mean span score and standard deviation of patient (Cb) and control group (C) performance on the e-WalCT and WalCT. *p* .05 (From Tedesco et al., (2017))

I.4. Neurodevelopmental disorders

I.4.1. Developmental coordination disorder (DCD)

I.4.1.1. **Definition**

Developmental coordination disorder (DCD) is a neurodevelopmental disorder that affects the children's coordination of voluntary motor skills characterized by preserving the intellectual abilities with a normal neurological examination (Biotteau et al., 2020). In scientific literature, DCD is also known as the developmental motor coordination disorder, developmental dyspraxia and agnosia, and developmental dyspraxia-dysgnosia (Magalhães et al., 2006). DCD affects the psychomotor development of both fine and gross motor skills blocking the acquisition of new motor learnings with and without tool use. This neurodevelopmental disorder is associated with extreme clumsiness and difficulties acquiring psychomotor abilities. In the early stages of human development, typical behaviour such as sitting, crawling, and walking are delayed compared to the development of typical children of the same age. In the later stages of development, children with DCD manifest poor and inaccurate performance during the manipulation of objects such as handwriting, drawing, tying shoelaces, buttoning a shirt, and performing activities like playing games, and riding a bicycle.

The proportion of children affected by DCD varies in function of the population study and the type of definition applied. According to Bank et al.,(2019) between 5% and 6% of school-aged children are affected by DCD. However, different studies suggest a distinct prevalence for DCD of about 5.4 % (Giagazoglou et al., 2011), 6.9 % (Asonitou et al., 2012), and 4.3 % (Cardoso et al., 2014). Concerning the prevalence in adolescence and adulthood, longitudinal studies suggest that DCD continues throughout adulthood (Blank et al., 2019; Kirby et al., 2008). For instance, a group of 468 Dutch adult students (19-23 years old) presented a prevalence 2.8% of DCD (Geuze, 2005). Regarding sex differences in DCD, studies suggest that males are more affected by DCD than females. This difference observed was identified as 2:1 and 3:1 (Faebo Larsen et al., 2013; Gillberg, 2003; Missiuna et al., 2008).

I.4.1.2. **Diagnosis**

According to the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-V)(American Psychiatric Association, 2013), in order to establish a diagnosis of DCD, four criteria must be fulfilled (see Table 3). These criteria are based on extensive research including the behavioural, and cognitive information of DCD. The diagnosis of DCD involves coordinated efforts from several different disciplines such as neuropsychology, pedopsychiatry and psychomotor therapy. The analysis of 176 scientific publications related to voluntary movement disorder shed light on the diagnostic criteria for DCD (Smits-Engelsman et al., 2015). These criteria include a) an interference or difficulties to perform everyday activities, b) the absence of other disorders, c) a score of intelligence scales or IQ above of 69, and d) a deficit in motor skills on the standardized assessment (inferior to 15 %).

Table 3. Criteria for Developmental Coordination Disorder (DCD) according to the DSM-V (2013).

Criterion	Description	Characteristics
A	The acquisition and execution of coordinated motor skills is substantially below that expected given the individual's chronological age and opportunity for skill learning and use.	Difficulties are manifested as clumsiness (e.g., dropping or bumping into objects) as well as slowness and inaccuracy of performance of motor skills (e.g., catching an object, using scissors or cutlery, handwriting, riding a bike or participating in sports).
B	The motor skills deficit in criterion A significantly and persistently interferes with activities of daily living appropriate to chronological age.	Difficulties in self-care and self-maintenance and affects academic/school productivity, prevocational and vocational activities, leisure, and play.
C	Onset of symptoms is in the early developmental period.	Difficulties to achieve motor developmental milestones.
D	The motor skills deficits are not better explained by intellectual disability, visual impairment, or a neurologic condition.	Absence of cerebral palsy, muscular dystrophy, degenerative disorder.

One of the most used psychometric tools to assess DCD is the Movement Assessment Battery for Children (MABC) (Henderson et al., 2007). This battery includes eight items for ages between 3–6-year-old, 7-10 year old, and 11-16 year old. The MABC explores three different areas such as manual dexterity, ball skills, and balance skills. Complementary to the MABC, the other aspect of motricity is assessed like handwriting skills, imitation of gestures, muscle tone. In addition to the behavioral skills, cognitive capacities are also evaluated. EFs, attention, memory and neurological soft signs are also studied. The severity of DCD is determined by the cut-off of the standardized motor test. A score inferior of 5th percentile corresponds to a sever DCD whereas a score between 5th and 15th percentile is considered to be moderate DCD. A probable DCD diagnosis is determined when the score is inferior or equal to 15th percentile. However, to establish a diagnosis in DCD, it is important to consider the high variability of a child's development during the acquisition of motor skill stage before the age of 5. Above the age of 5, it's possible to establish a diagnosis but it's important to consider checking in regularly with regard to the developmental progression of child (Blank et al., 2012).

Concerning the cognitive assessment in children and adolescents diagnosed with DCD, several studies suggest that attentional functioning and EFs are impaired (Hofmann et al., 2012; Querne et al., 2008; Tal Saban et al., 2014; Wilson et al., 2013). Other authors indicated impairment of specific domains in EFs and attentional functioning (Toussaint-Thorin et al., 2013; Wilson et al., 2013). A recent review of the literature presented a deficit in specific domains of the cognition, specifically affecting inhibition control, WM, planning and non-verbal, as well as general EFs impairment (Lachambre et al., 2021). However, deficient cognitive capacities are a criterion of exclusion. Indeed, according to the DSM-V, some DCD children present attentional deficit (Kaiser et al., 2015; Pieters et al., 2012). A recent analysis suggested that children diagnosed with DCD present fundamental impairment in visual-motor mapping and cognitive-motor integration (Subara-Zukic et al., 2022).

I.4.1.3. **Neurocognitive findings**

Brain studies indicated abnormal maturation of motor networks as well as clinical signs of dysfunctional in structural and functional activation patterns in children with DCD. According to Biotteau et al., (2016) a compilation of neuroimaging studies demonstrated abnormal activation of a group of brain structures such as the cerebellum, subcortical (base ganglia), and cortical (frontal and parietal lobes) involved in DCD. Additionally to these brain areas, structural features such as cortical thickness of the right orbitofrontal cortex are associated with symptoms of DCD (Wilson et al., 2017). Genetic factors are associated with the etiology of DCD. However, this assumption of a genetic origin of DCD needs to be further supported (Biotteau et al., 2020).

I.4.1.4. **Etiology Hypothesis**

Four principal etiopathogenetic hypothesis have been proposed to explain DCD. These hypotheses are visuospatial deficit, internal model deficit, procedural learning deficit and EFs impairment.

I.4.1.4.1. Visuospatial and perception action deficit

The first hypothesis refers to a visuospatial and perception action deficit presented in DCD. The exploration of eye-hand coordination and spatial processing by means of wooden puzzles or handling blocks have revealed visuospatial processing deficit in children with DCD (Alloway, 2007; Biotteau et al., 2017). However, it needs to be specified that even though DCD children present lower visuospatial performances compared to control children, not all-DCD children present a visuospatial impairment as a systematic deficit (excluding for extreme slowness). However, this hypothesis is supported by neuroimaging studies that related an abnormal functioning of the dorsal visuospatial stream to DCD (Williams et al., 2017; Wilmut et al., 2017). Additionally, DCD children present lower scores in the assessment of WM and STM compared to other neurodevelopmental disorders (Alloway, 2007; Alloway et al., 2009). Nonetheless, contradictory findings have been reported concerning the visuospatial disorder in DCD. The main problems related to these studies are the sample size (i.e., low number of participants) and the variability concerning the sample. Thus, this hypothesis is difficult to corroborate due to the intervention of compensatory mechanisms achieved by children during development.

The coupling of perception and action have been considered as the main disorder in the DCD children. Several lines of evidence suggest that the coupling of perception and action combined to difficulty to adjust to conditions challenges the adaptability of the children with DCD (Geuze, 2018; Wade & Kazeck, 2018). The development of the coupling perception and action in DCD have been reported as deficient concerning tasks of imitation (J. E. Reynolds, Licari, et al., 2015; J. E. Reynolds, Thornton, et al., 2015). These finding suggests a deficit or atypical activation in the mirror system in children with DCD correlated to a decrease in gray matter in the premotor frontal regions (J. E. Reynolds et al., 2017).

I.4.1.4.2. Internal modeling deficit in DCD

The second hypothesis is internal modeling deficit in DCD. The internal models are central nervous system mechanisms that allow us to adapt to the world. These models enable us to coordinate the input and the output of information creating representations for future actions. The prediction of a movement is based on a forward internal model that allows us to anticipate consequences of movements correcting the ongoing actions (Shadmehr et al., 2010; Wolpert, 1997; Wolpert et al., 1995). Incorrect plans of actions or unexpected environmental changes are corrected online by the sensorimotor information or feedback facilitating rapid online adjusting. Thus, the experience acquired through the actions influence our prediction and consequences. Hence, DCD is associated with an inadequate prediction of online control of movement. The clinical manifestation of DCD such as inaccuracies, slow movements, effortful movement suggest a disruption of predictive motor control (Wilson et al., 2013). This impairment is known as internal model deficit (IMD). A systematic review of 48 research IMD in children with DCD suggested a classification according the effector system involved a) visuospatial attention and oculomotor control, b) control of manual action, c) dynamic postural control (Adams et al., 2014). This classification of the deficit in DCD explains the poor performances and contribute to the adaptation of the specific treatment and intervention.

I.4.1.4.3. Procedural motor skills

The procedural motor skills impairment in children with DCD has been presented as an important factor in the conceptualization of DCD (Goodgold-Edwards & Cermak, 1990). The procedural learning is acquired through three main series of learning stages. These stages are fast, longer, and automatization learning. Thus, all kind of everyday activities that required automatization are divided into motor adaptation and sequence learning (Wolpert et al., 2011). Additionally, procedural learning is adapted according to the type of skill explicit or implicit leaning. In the explicit learning, the new skill required the use of instructions based on a procedure, whereas, in the implicit learning instructions are no require in the learning. According to Doyon et al., (2009) corticocerebellar loop and corticostriatal networks are involved in the processing of a procedural learning. Pathological manifestations in the procedural learning are associated with the disruption of theses networks. Concerning the procedural motor leaning difficulties in Children with DCD. They present difficulties in the acquisition of new motor skills and automatized motor learning. This is characterized by troubles in anticipation, an incapacity to correct online motor actions and integrate pass experiences to a new plan of actions (Biotteau et al., 2016; Wilson et al., 2017). A common tool to assess procedural impairment in DCD is the motor sequence paradigm are used to identify deficits in procedural motor skills (Bo & Lee, 2013). Children with DCD present more variability in the performance and make more difficulties (errors) compared to typical children of the same age.

I.4.1.5. **Executive functions in developmental coordination disorder**

As previously introduced, it has been suggested that EFs are affected in both children and adults with DCD (Leonard & Hill, 2015; Williams et al., 2017). This, deficit in EFs is observed in both Cold EFs and Hot EFs (see EFs section in the introduction). Concerning the cold EFs, it has reported deficit in WM, IC, fluency, and planning in DCD. Regarding hot EFs, children with DCD presented a high sensitivity to immediate reward. This deficit to inhibit the rewarding was associated to emotional characteristic of the stimuli (Rahimi-Golkhandan et al., 2014; Williams et al., 2017). VSWM is affect in DCD due to the visuospatial component. However, other components of EFs are reduced such as CF as well as IC.

Bernardi et al., (2018) conducted a longitudinal study following up on the development of EF in children aged between 7 – 11 years old with DCD. The study assessed verbal and non-verbal EFs two years apart. The results showed that children with DCD presented EFs difficulties compared to the typical control group. Interestingly, the difficulties persisted during both evaluations. The results implied that non-verbal EFs were affected in both evaluations (2 years apart) with children with DCD. This study revealed that EFs impairment in children with DCD are not associated to another developmental disorder being exclusively related to motor deficits. The combination of both motor and cognitive impairment (EFs) in children with DCD needs to be explored to provide an adequate intervention and treatment. In addition, more longitudinal studies are necessary to determine the developmental evolution of DCD.

I.4.2. Attention deficit hyperactivity disorder (ADHD)

According to Barkley (2015b), in 1775, Melchior Adams Waikard introduced for the first time the concept of the syndrome of inattention and hyperactivity-impulsivity for explaining clinical manifestation of disorders related to inattention and behavioral impulsivity. At the end of the nineteenth century, this concept was identified as minimal brain dysfunction, hyperactive/hyperkinetic syndrome, and hyperactive reaction of childhood. In 1980, the DSM-III presented the concept of Attention Deficit Hyperactivity Disorder (ADHD) defining inattention as the central characteristic of the ADHD (American Psychiatric Association, 1980). Nowadays, the term ADHD is used world-wide to refer to a neurodevelopmental disorder characterized by symptoms of inattention and/or hyperactivity-impulsivity.

I.4.2.1. **Diagnosis**

According to DSM-V, the diagnostic for being ADHD includes five criteria and nine symptoms for inattentive and hyperactive/impulsive disorders (See Table 4 for the criteria and Table 5). The disorder onsets in childhood before 12-year-old with 6 or more clinical manifestation (symptoms) for at least 6 months. This disorder is characterized by inattentive signs like distractively, difficulties for paying attention to the details, lack of concentration or difficulties for being focused on task that required attention, and careless to the mistakes. Additionally, the hyperactivity and impulsivity are associated with this ADHD’s symptom. ADHD children have difficulties for stay quiet or remain sit in the same place for a relative short period of time. These symptoms must not be related to emotional issues (e.g., depression or anxiety). However, emotional dysregulation as well as EFs impairment are related to ADHD.

According to DSM-V, the heterogeneity of the ADHD is categorizing in three main groups: predominantly inattentive, predominantly hyperactive-impulsivity and inattentive and hyperactive-impulsivity combined. This heterogeneity in ADHD presentations have been observed as a developmental variability. 168 different symptoms were associated to combined presentation of ADHD. Moreover, Larsson et al., (2011) suggest a sex related difference in the predominance of the symptoms. Girls have more probability to be consider as predominantly inattentive, whereas boys are more likely to be identifies as combined. Additionally, the predominance evolves in function with age. For instances, hyperactive-impulsive symptoms more predominant in younger children underage of 5 years old. Hyperactive-impulsive symptoms presentation are common in preschool children. Inattentive symptoms are persistent in the middle childhood and adolescence and being more apparent in the adulthood (Willcutt et al., 2012). A correlation between age and type of predominance suggests that children of 7 or 8 year old are more likely to be diagnose with a combined presentation while children of 10 or 11 years old are considered as predominantly inattentive (Polanczyk et al., 2010).

Table 4. Criteria for Attention deficit hyperactivity disorder (ADHD) according to the DSM-V (2013).

Criterion	Description
A	The presence of several symptoms (inattentive or hyperactive/impulsive) negatively affect social and academic activities.
B	The presence of several symptoms (inattentive or hyperactive/impulsive) of before 12 years old.
C	The presence of symptoms (inattentive or hyperactive/impulsive) in different environments (e.g., school, home, work etc).
D	The symptoms (inattentive or hyperactive/impulsive) interfere with development of daily activities.
E	The symptoms do not occur exclusively during schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal)

Table 5. Symptoms for diagnosis of attention deficit hyperactivity disorder (ADHD) according to the DSM-V (2013).

ADHD symptoms for inattention	ADHD symptoms for Hyperactivity/Impulsivity
Makes careless mistakes/lacks attention to detail.	Fidgets with or taps hands or feet, squirms in seat.
Difficulty sustaining attention.	Leaves seat in situations when remaining seated is expected.
Does not seem to listen when spoken to directly.	Experiences feelings of restlessness.
Fails to follow through on tasks and instructions.	Has difficulty engaging in quiet, leisurely activities.
Exhibits poor organization.	Is "on-the-go" or acts as if "driven by a motor".
Avoids/dislikes tasks requiring sustained mental effort.	Talks excessively.
Loses things necessary for tasks/activities.	Blurts out answers.
Easily distracted (including unrelated thoughts).	Has difficulty waiting their turn.
Is forgetful in daily activities.	Interrupts or intrudes on others.

According to Larson et al., (2011), 67% of children diagnosed with ADHD present comorbidity of other neurodevelopmental disorders. It has been identified that children and adults with ADHD are more likely to develop health risks and medical conditions such as coronary heart disease, suicide, drug abuse (alcohol, smoking other substances), sleep problems, poor nutrition, type 2 diabetes (Barkley, 2015a; Nigg, 2013). During childhood, the risk of death is doubled for a child with ADHD and five times more likely to die in the midlife (Dalsgaard et al., 2015). If the trouble persists into the adulthood, a decrease of the life span is estimated by 12.7 years (Barkley & Fischer, 2019).

I.4.2.2. **Etiology**

Although none are exclusive to ADHD, biological and environmental factors are linked to the etiology of ADHD, (Nigg et al., 2020). Most of these factors are associated with gestation (Hall et al., 2021). Consumption of alcohol and smoking during pregnancy, prematurity, a polluted environment, and low birth weight are supposed environmental risks for developing ADHD (Scassellati et al., 2012). Concerning the biological factors, genome association studies (GWAS) have revealed several genetic loci (i.e., chromosomal positions, not genes per se) for ADHD. Several genetic variants of which at least 40 % are considered to be involved in the manifestation of ADHD.

Neuroimaging studies demonstrated that brain volume, particularly gray matter, is reduced by 3% to 5% in ADHD patients in comparison to healthy controls (Castellanos et al., 2002). Additionally, it has been pointed out that children with ADHD present a lack of maturation in the frontal region and connections. This late maturation of frontal areas are considered to be correlated to a functional heterogeneity across age (Yap et al., 2021). Moreover, abnormal subcortical volume in structures such as right putamen caudate nucleus, caudate nucleus, right globus pallidus and cerebellum are consistent findings associated with ADHD (Hoogman et al., 2017). Recent findings indicated that dopamine combined with environmental factors is involved in the clinical manifestation of ADHD. This hypothesis proposed that some genes impact dopamine system causing the ADHD symptoms to manifest. According to Faraone (2018), treatment administrated to act on both dopamine systems (catecholaminergic neurotransmission) reducing the symptoms of ADHD. Interestingly, it has been identified in abnormal brain activity in electroencephalogram (EGG) studies, showing an increased power of low frequency activity through resting state.

I.4.2.3. **Theoretical perspectives of ADHD**

For the past three decades, the interest in ADHD has increased steadily and different theories have been proposed to explain the disorder. Here, we will present the two main theories regarding ADHD which are Barkley's executive theory and Sonuga-Barke's dual-pathway model.

According to Barkley's theory (1997, 2012) executive functioning (IC, WM and CF) are crucial components in ADHD. Deficit behavioral inhibition negatively affects other components of EFs such as WM, self-regulation, control of the internal speech. For Barkley' model, lack of inhibition in ADHD concerns three intertwined processes: 1) suppression of the initial response to an event, 2) to stop ongoing reactions or responses given the time to take a decision, 3) avoid interferences or stopping the distractors or inferences. The impairment of inhibition can carry out consequences on the whole level of the treatment of information passing through its selection or filtering to high level processing of the information such WM. Thus, the main absence of behavioral inhibition underlies the deficit in ADHD.

The dual-path way model (E. J. S. Sonuga-Barke, 2002) states that ADHD symptoms are associated with disruption of dopaminergic in at least one of the brain pathways: the mesocortical or the mesolimbic dopaminergic systems. Sonuga-Barke (2002) suggested that a dysfunction in the mesocortical dopaminergic system is related to a deficit in the inhibition process similar to the theory suggested by Berkley. This pathway is supposed to be responsible for the self-regulation of actions and thoughts. The mesolimbic pathway or motivational style pathway is considered to be involved in the motivation and in the role of delay of reward gradient. A disruption in the mesolimbic pathway can lead to a decrease of the value for futures events. The deficit in the mesolimbic pathway is associate to a preference to the immediate rewards showing a deficit for the delayed gratifications. The inattention symptoms are consequences of the increase of the timing (delay) in circumstances where the rewards are not presented in a short term. Thus, a deficit in both dopaminergic systems affect the quality and the quantity of the engagement in a particular task. The temporal processing deficit in ADHD is related to a third pathway. The temporal processing deficit pathway involves the basal ganglia and the cerebellum (E. Sonuga-Barke et al., 2010).

I.4.3. Autism spectrum disorder (ASD)

I.4.3.1. **Definition**

Autism spectrum disorder (ASD) is considered to be a complex neurodevelopmental disorder characterized by a variety of social and communicative atypicalities related to restrictive interests and repetitive behavior (RIRB) and associated with a heterogeneous abilities profile. The symptom of ASD are clinically detectable and there is a high probability for them to manifest by age of 2 years old (Pierce et al., 2019).

According to DSM-V, five diagnostic criteria (A, B, C, D, and E) and three levels of severity are related to the social and communication difficulties in ASD (Table 6). The criterion A for ASD pinpoints impairment of the social communication and social interaction. These deficits are present, affect a multitude of different types of social interactions and are manifested in various contexts (e.g., school, home, playing). The criterion B concerns RIRBs characterized by a stereotyped and recurrent pattern of behavior such as the continuous use of preferred objects (e.g., toys), the use of the idiosyncratic phrases or echolalia. The criterion C suggests that the symptoms are manifested over the course of the development and presented at the early age. The presence of the symptoms are observed when the social interaction challenges the restricted capacity of interaction. The criterion D suggests that important areas of functioning (social and occupational) are affected by the symptoms deteriorating significantly. The criterion E highlights that the symptoms observed in ASD cannot be explained by an impairment of cognitive capacities or a global developmental delay. Although cognitive deficiencies can be observed in ASD, social communication skill are considered being inferior than expected for a general developmental level.

DSM-V does not establish different subtypes of autism. Although Asperger's disorder is no longer consider as form of autism for the DSM-V, the distinction in ASD is determined by the level of assistance needed according to the severity level of the symptoms. Four clinical specifiers or quasidimensional variables are proposed to establish a clinical diagnostic of ASD: the level of cognitive functioning, the existence of simultaneous pathologies (neurogenetic or psychiatric), language level, and severity. The level of cognitive functioning in ASD is consider as a factor of heterogeneity. Regarding language level, verbal impairment can vary from absence or lack of communication to fluent speech. The comorbidity in ASD is associated with neurological and psychiatric conditions.

The World Health Organization believed that the prevalence of ASD is 1 in 68 children in the United States and it is estimated that more than three million people are affected by this syndrome (Baio et al., 2018). In France, more than 600.000 individuals are affected by ASD present cognitive impairment (Bonnet-Brilhault, 2017). Sex differences are observed in autism, the males are particularly more affected, their numbers four to five times greater than females (Werling & Geschwind, 2013).

I.4.3.2. **Etiology**

Several hypotheses have been proposed to explain the origin of ASD, including misconception and speculative causes of ASD such as vaccines, exposure to mercury, lead, gluten, or diary allergies. All the above medical hypotheses have been discarded (Courchesne et al., 2020). Genetic studies in ASD present it to be the result of a genetic condition (Gaugler et al., 2014). However, up to today, there is no scientific consensus about which genes precisely are associated with the symptoms of ASD (Schaaf et al., 2020). It appears that approximately one thousand genes are related to the clinic manifestation of ASD (De Rubeis et al., 2014; O'Roak et al., 2012). Although, genetic tests are recommended to subject diagnosed with ASD (in vast majority being children) to distinguish any genetic predisposition to the development of the disorder.

Regarding environmental factor associated with ASD, it was estimated that 40-50% of variance related to ASD is determined by environmental factors such as drugs, toxic exposures, parental age, nutrition and fetal environment (Deng et al., 2015; Edelson & Saudino, 2009; Gaugler et al., 2014). Nonetheless, the correlation of some environmental factors are strongly supported by in vivo and in vitro studies and other factors need to be explored with additional experimental evidence (Masini et al., 2020).

There is not agreement on the brain areas that could explain all the core symptoms of ASD. Postmortem studies suggest atypical neuroanatomical changes linked to ASD. Brain areas such as the hippocampus, the limbic system, the entorhinal cortex, and the amygdala presented a different pattern concerning cells density as well as smaller cell size (Kemper & Bauman, 1998). Additionally, the study found an atypical enlarged neuron in the cerebellar nuclei, inferior olive, and vertical limb in younger patient with autism. An increased number of cells in prefrontal cortex anomalies were found in ASD children (Courchesne et al., 2011). Functional MRI studies have shown a hypoactivation in the prefrontal cortex and temporal areas combined with enhanced of the visual cortex in patients with ASD (Samson et al., 2012). Others studies found that brain areas such as the prefrontal, posterior cortical and subcortical regions have a low functional integration in individuals with ASD (Langen et al., 2012; Maximo et al., 2014).

Interestingly, new technological advancements and the adaptation of novel paradigms for the assessment of ASD opened the opportunity to automatize the evaluation of motor component related to ASD (Gargot et al., 2022). This perspective considered that motor disturbances are related to clinical manifestation of ASD. For instance, the assessment of interpersonal synchronization and motor coordination capacities in ASD during an imitation

tasks revealed minor impairment in ASD children in comparison to typical and DCD children (Xavier et al., 2018). However, examining the capacity to change from egocentric to heterocentric point of view in ASD subjects using a visou-motor interactive had shown that ASD patients have the ability to change point of view (Gauthier et al., 2018). However, this capacity is delayed in comparison to typical children.

Table 6. Criteria and symptoms for diagnosis of autism spectrum disorder (ASD) according to the DSM-V (2013).

Criteria	Diagnostic features
A	Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive; see text): 1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions. 2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication. 3. Deficits in developing, maintaining, and understanding relationships, ranging, for ex ample, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.
B	Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text): 1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases). 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day). 3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests). 4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement)
C	Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life)
D	Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
E	These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnoses of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.

I.4.3.3. **Executive functions and autism spectrum disorder**

The role of EFs in ASD is a controversial topic and actual subject of debate in cognitive neuroscience. EFs impairment in individuals with ASD are consider are clinical markers for the diagnosis for ASD (Rødgaard et al., 2019). The EFs deficit is present during childhood to the adulthood, however, EFs impairment may vary during cognitive development (Dawson, 2008;

Luna et al., 2007). Nonetheless, the meta-analysis studies suggest contradictory findings concerning EFs in individuals with ASD (Craig et al., 2016; Lawson et al., 2015). This is possible due to the samples size of the studies, heterogeneity in IQ level and diagnosis related groups.

The initial studies of EF and ASD found an executive control deficit in children and adolescent proposing a model for understanding the clinical manifestation in ASD (Pennington & Ozonoff, 1996). This assumption of EFs deficits is believed to be a cognitive marker for distinguishing ADHD and ASD. Thus, compiled evidence of deficits in EFs in ASD was used to establish the executive dysfunction hypothesis (Hill, 2004). The executive dysfunction hypothesis suggested that individuals affected with ASD manifest clinical impairment in distinct domains of EFs. This consideration supports the idea of a fractionated model of EFs in autism. A recent meta-analysis is in favor of the executive dysfunction hypothesis considering a link between EFs and restricted and repetitive behaviors (Iversen & Lewis, 2021). The author found that IC and CF are related to the symptoms of restrictive interest and repetitive behavior. These measures correlated with the parental report. The authors suggested that EFs play a role in the development of behavior. Thus, EFs and developmental factors must be considered as a combination during the study of ASD.

However, others contemporaneous meta-analysis studies suggest a broad impairment of EFs through the life span in individuals with ASD (Demetriou et al., 2018; Lai et al., 2017). Thus, both children and adolescent diagnosed with ASD present a generalized deficit in EFs. An extended deficit as observed in IC, WM, and CF. Although, an important heterogeneity was observed in the analysis. The authors suggest than an underlying shared pathway may influence EFs in autism.

I.4.4. Cerebral Palsy (CP)

I.4.4.1. **Definition**

The conceptualization of Cerebral Palsy (CP) was introduced by Sir William Osler in 1889 to categorize a group of children presenting divers forms of motor and behavior difficulties. In high income countries, the prevalence of CP is estimated to be around 2 ‰ in live births (Sellier et al., 2016). CP is considered as being a permanent neurodevelopmental disability characterized by multiple and different types of display of etiology, functional severity, comorbidities, cognitive and behavioral profiles (Aisen et al., 2011; Mcintyre et al., 2013; Oskoui et al., 2017). According to Rosenbaum et al., (2007) and Bax and Brown (2004) "CP is a group of permanent disorders of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or immature brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy, and by secondary musculletal problems". The Gross Motor Function Classification System (GMFCS) is a diagnosis tool commonly used to determine the level of impairment (i.e., "mild", "moderate", or "severe") related to the pathology (Palisano et al., 2008; P. L. Rosenbaum et al., 2008).

I.4.4.2. **Etiology**

The clinical manifestation in CP associated with motor deficit are accompanied with or without cognitive impairment caused by brain damage inborn or in early life (Stadskleiv, 2020). Genetic and phonotypic heterogeneity are proposed to be the causes underlying in CP (Lewis et al., 2021). Thus, the etiology in CP is related to multiple factors being identified as hypoxic-ischemic encephalopathy, periventricular leukomalacia, brain malformation, intrauterine infections, and neonatal strokes as the most common causes. However, it has been estimated that at least 20% of CP diagnosis lack an etiological diagnosis making it difficult to identify the exact causes of CP (Rosello et al., 2021).

I.4.4.3. **Cognitive assessment of Cerebral Palsy**

The cognitive impairment in CP differs between and within spastic (i.e., muscular weakness), dyskinetic (i.e., impairment of voluntary movements resulting in fragmented or jerky motions) and ataxic subtypes (World Health Organization, 2018). The inherent motor deficit observed in CP children is considered as a bias factor in the assessment of cognitive functions (Sherwell et al., 2014). It is probable that children with CP score lower than typical developmental children at the same age due motor impairment. Thus, underestimation of cognitive performances in children with CP could be the result of a motor deficit.

Children with CP have more probability to develop cognitive impairment in comparison with peers. Official statistics of Western countries indicate that 30% to 40% of children with CP present an IQ less than 70 (Andersen et al., 2008; Sigurdardottir et al., 2008). Additionally, recent studies have reported visual impairment as common deficit in children with CP (Philip et al., 2020). Deficit in dorsal and ventral streams are related to the visual difficulties in CP children. EFs impairment in CP children is associated with lack of myelination of the prefrontal cortex and frontal lobes mostly located in the anterior portion. Additionally, the projection between prefrontal and subcortical structures are related to the EFs deficit presented in CP children (Crichton et al., 2020).

Objective

Brain imaging studies and the differences in cognitive performances observed when comparing homologous tasks such as the CBT and the WalCT in the reaching space and in the locomotor space (Belmonti, Cioni, et al., 2015; Nemmi et al., 2013; Perrochon, Gueguin, et al., 2018; Piccardi et al., 2008, 2010, 2011), provide compelling evidence for discrimination between neural circuits and cognitive processing for reaching and navigational space also in visuospatial memorization and spatial learning. Studies on spatial cognition represented a growing field in cognitive neurosciences, and the assessment of the cognitive abilities remained limited compared to the classical neurocognitive evaluation. Thus, understanding the complexity of spatial cognitive processing, how it is developed during our life span and development, and how it is affected in the neurodevelopmental disorders is vitally important to contribute to establishing a diagnosis and proposing a rehabilitation program.

The aim of this thesis was to study IC, CF, and VSWM involved in typical and atypical neurodevelopment using spatial navigations protocols based on the Virtual Carpet Paradigm (VC) and a goal-oriented locomotor task (GOLT). We presented five studies grouped in three thematics focusing on a) memorization and generations of sequences of visuospatial targets, b) planning and adjusting trajectories when faced with unpredicted changes during the reaching a goal, and c) inhibition and replanning of previously over perfected learned paths.

In the first thematic, we included two studies aiming to study the neurocognitive performances in young (YA) and older adults (OA) using the WalCT. In the first study, we studied cognitive abilities such as VSWM, mental rotation, and cognitive strategies during typical aging using a goal-oriented locomotion task (Castilla, Berthoz, Urukalo, et al., 2022). In the second study, we investigated the effect of age on cerebral oxygenation in the VSWM tasks according to space (reaching or navigational) and determine if EF and cerebral oxygenation were involved in VSWM performances, either in reaching or navigational space (Kronovsek et al., 2020).

In the second thematic, the aim was to study goal-oriented locomotion in children with CP, typical children, and adults. Three main research questions are posed: 1) Can we detect disorders of anticipatory orientation and/or trajectory formation in subjects with spastic diplegic CP?

2) Are navigation skills distinctively impaired in spastic diplegic CP, independently from gait disorders?

3) In contrast to independent locomotion, does accompanied locomotion help subjects with spastic diplegic CP cope with their perceptual and balance disorders, allowing them to generate better trajectories?

Concerning the third thematic, we conducted one study, and we are drafting another study. We aimed to study the development of IC and CF in typical and atypical subjects from children to adults using a navigational protocol. To achieve that, we designed and tested an experimental protocol named the "Virtual house locomotor maze (VHLM)" using the technology of the Virtual Carpet paradigm (VC). We analysed behavioural parameters such as tangential velocity, latencies, head-chest orientation before and during locomotion. We tested the capacities of inhibition and CF during the planning and replanning of locomotors trajectories. We identified behavioural indexes of impulsivity and different strategies during the performance. Regarding the draft of the new article, we adapted a task of negative priming to the VLHM to assess IC and CF in a GOLT. A total of 109 participants were enrolled in the study including typical, attention deficit and hyperactive disorder, autism spectrum disorder, and developmental coordination disorder subjects.

PART II: METHODS: PARADIGM AND PROTOCOLS

In this part, we introduce the paradigms and protocols used during the experimentation. First, we will present the Virtual Carpet Paradigm, the experimental setup, its protocols, and the procedures. Next, we describe the locomotor reaching task the experimental setup, its protocols, and the procedures.

II.1. The Virtual Carpet Paradigm

The VC paradigm was created by Alain Berthoz and Mohamed Zaoui at the College for studying behavior and cognitive functions in the reaching space (peripersonal) and in near locomotor space (Room). The VC is a versatile technological system that allows us to present visual and auditory stimuli (e.g., videos and images) as well as to track and record locomotor trajectories with higher precision by means of sensors.

In this dissertation, we present five studies using two different goal oriented-locomotion methodologies: the VC paradigm (VC) and the locomotor reaching task. Four studies used the VC paradigm:

a) A new paradigm for the study of cognitive flexibility in children and Adolescents: The "Virtual House Locomotor Maze" (VHLM) (Castilla et al., 2021a),
b) Age and sex impact on visuospatial working memory (VSWM), mental rotation, and cognitive strategies during navigation (Castilla, Berthoz, Urukalo, et al., 2022),
c) Age-related decline in visuo-spatial working memory is reflected by dorsolateral prefrontal activation and cognitive capabilities (Kronovsek et al., 2020).
d) The Virtual City Paradigm™ for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study. (Del Lucchese et al., 2021),

The study conducted using the locomotor reaching task was Goal-oriented locomotion in children with spastic diplegia: Anticipatory orienting strategies and trajectory formation (Castilla, Berthoz, Cioni, et al., 2022b).

II.1.1. Experimental set-up

The VC™ paradigm used two laptops, one video projector(s) and one HTC Vive system (system of virtual reality) for the experimentation (HTC® Vive, Taiwan), one software for recording the locomotor trajectories and one software MATLAB for the data analysis and data visualization (Castilla et al., 2022) (Figure 40).

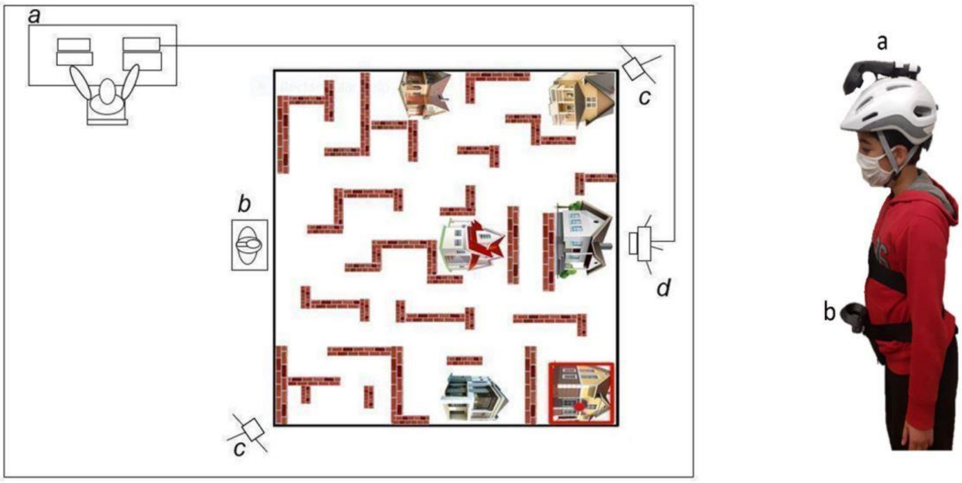

Figure 40. (A) The representation of the experimental setup: (a) control desk location where the experimenter runs the experiment, (b) departure point, (c) two HTC Vive cameras, (d) the video projector. (B) 3D motion sensors motion-tracker. (a) one handheld 3D motion sensor is adapted to a bike helmet and is worn on the participant's head and (b) the second handheld 3D motion sensor is attached to the belt which worn on the participant's waist (Castilla et al., 2021a).

A computer was connected to the video projector for projecting the navigational space on the floor (3 m x 2.4 m) and the stimuli, 9 tiles of 30 x 30 cm. This projection was used as a template to configure the virtual environment coordinates and to present the sequences to the participant. A second computer was connected to the HTC Vive system (i.e., two infrared cameras, two hand-held 3D motion sensors, and one virtual reality helmet). The two cameras were placed diagonally 5 meters (16.4042 feet) apart in order to cover the whole navigational space. The two hand-held 3D motion sensors were used as trajectory trackers recording the X, Y, Z positions every 11 milliseconds (90.90 Hertz) (Niehorster et al., 2017). These 3D motion sensors were fixed upon a head support which was worn on the participant's head and another 3D motion sensor was added to a belt which was worn on the waist. We were able to measure and calculate (a) the position of the participant on the spatial array (X,Y coordinates); (b) the head/waist direction on the horizontal plane (Rotations) in the horizontal component (i.e., Yaw plane).

We used the Basic Trajectory Software version 1 (BTS) for the setting of the navigational space and of the data recording. The BTS used the drives of the HTC Vive system; (a) to generate the virtual targets (e.g., Virtual tiles) in the virtual environment known as *the* *calibration procedure*, and (b) to record the participant's trajectories. The calibration procedure allowed us (a) to measure the records' global navigational space array and (b) to set the target's positions in a Cartesian coordinate system (see annexes 1, for a full description the calibration procedure). Using the coordinates of the tiles, we created an algorithm to establish a perimeter among the center for each tile of 30x30 cm. This setup allowed us to identify the tiles and determine whether or not participants reached a tile target within the sequence.

II.1.2. Experimental protocols

II.1.2.1. **The Virtual House Locomotor Maze Protocol (VHLM^{TM})**

The VHLM^{TM} is composed of 6 houses placed about in a simplified labyrinth delimited by walls created using Microsoft PowerPoint software 2016 (Figure 41). Each house can be identified as a target for the subject by a green dot appearing on the house and surrounding it by a green light square. A beep sound is launched simultaneously to the lighting of the house to increase the attentional focus of subjects on the target house. The projection on the floor delimited the navigational space environment (3.5 x 2.5m). This maze deals with spatial memory of the images of a simplified labyrinth with houses projected on the floor. It requires that the participant generates mental representations of the array, stores them, and can recall them. When the participant has to navigate in the virtual labyrinth redirecting himself to the departure point, the process can even engage mental rotation processes (Carbone et al., 2020; Meilinger et al., 2011).

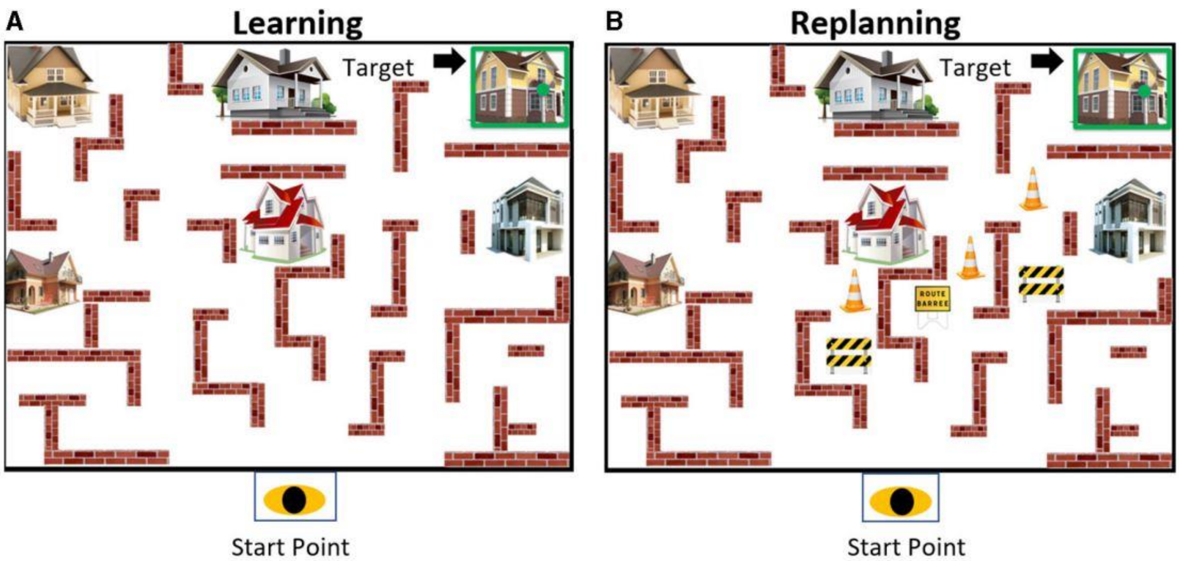

Figure 41. The Virtual Maze layout. (A) The left image shows a target house highlighted in green. The same house was shown 5 times for inducing an overlearned trajectory. (B) The right image shows a target house highlighted in green and the obstacles blocking access to the house by the shortest paths. This induced the necessity to replan the overlearned trajectory (Castilla et al., 2021a).

II.1.2.1.1. Procedure

In the VHLM, the participants were instructed to walk as fast as possible to reach a target house after the presentation of the stimuli (in green and the acoustic signal) and come back to the departure point. Moreover, the participants were asked to avoid crossing the walls, obstacles, and other houses in the whole trajectory. The participants were informed that eventually some path will be blocked, and they can select others alternative path to reach the target house.

II.1.2.2. **The Virtual Walking Corsi Test (VWalCT)**

The VWalCT is an adaptation of the WalCT to the VC (Castilla, Berthoz, Urukalo, et al., 2022; Kronovsek et al., 2020). In the VWalCT, 9 tiles of 30 x 30 cm (i.e., the stimuli) were projected on the floor (3 m x 2.4 m) (Figure 42). During the experimentation, each tile was lit for one second with an interstimulus interval of one second. The number of tiles increased progressively across the length of the sequences by one tile (i.e., sequence of 2 trials of 2 tiles, to sequence of 2 trials of 9 tiles).

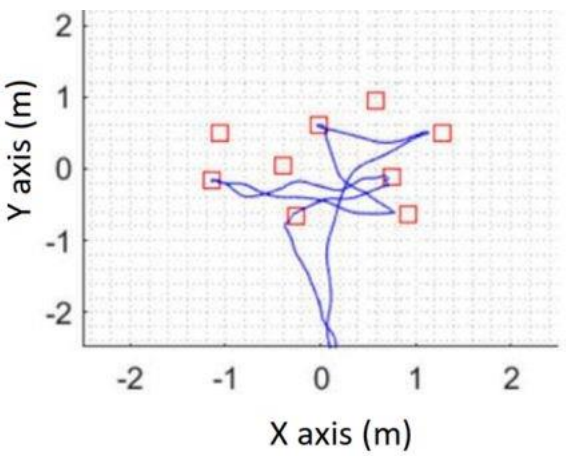

Figure 42. Navigational space and locomotory trajectory for a sequence of six tiles: The red squares represent the tiles' positions in the navigational space. The blue line represents a locomotor trajectory (2D) generated by a participant during the response (Recalling phase) (From Castilla et al., (2022)).

II.1.2.2.1. Procedure

In each trial, a sequence of tiles was presented automatically to the participants. The participants' task was to reproduce the same sequence by walking and standing on each tile for a brief period of time. The participants' trajectories were recorder by mean of the captor.

II.1.2.3. **The Virtual City Protocol**

The Virtual City protocol was developed by Alain Berthoz in collaboration with Giovanni Cioni's research team at the Stella Maris Hospital in Pisa, Italy. It was implemented in the thesis project of Benedetta Del Lucchese from the University of Florence, Italy. The Virtual City is a simplified town consisting of 20 different colored houses, street lanes and crossings projected on the floor for locomotor navigation (Figure 43). It was created based on the VC paradigm using the Unity 5.5.1© platform. The protocol was used in a recent study named "The Virtual City Paradigm ™ for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study" (Del Lucchese et al., 2021). See the full article in the annex 2.

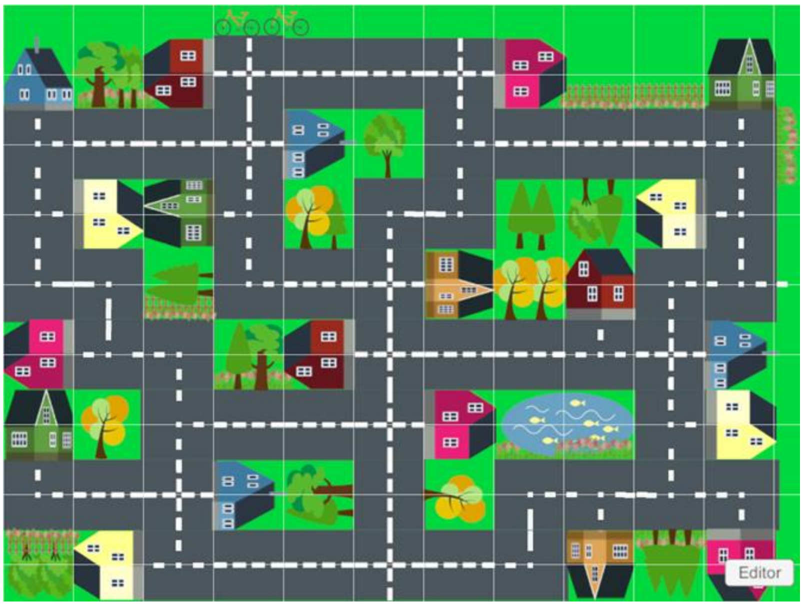

Figure 43. Representation of The Virtual City protocol projection on the ground, consisting of 20 houses (Del Lucchese et al., 2021).

II.1.2.3.1. Procedure

The participants are instructed to attentively observe the Virtual City and to reach the houses that flickered (stimuli) on the locomotor navigation space. The stimuli were presented sequentially (one house after the other each house was flickered for 2500 ms) or simultaneously (i.e., several houses were lit at the same time). Three different conditions were devised for the Virtual City Protocol: a) City Pointing (control condition), b) City Following, and c) The City planning.

a) In the City Pointing, the participant was asked to stand on the starting position then a randomized sequence of houses was presented to the participant. The task of the participant was to point out the flickered houses using a laser pointer. This control condition was introduced to assess the visuospatial exploration capacities of the participants. The participant the was excluded of the study if they scored lower than 80% of the total number of sequences presented.
b) In the City following, the participant was placed on the starting position and a randomized sequence of houses were presented. Then, the participant was invited to reproduce the same sequence in the same order of presentation.
c) In the City Planning, the participant was placed on the starting position then a simultaneous presentation of the houses was displayed. The participant was asked to reach each house presented using a shortest path.

II.2. The locomotor reaching task

The locomotor reaching task has been used to explore navigation capacities and EFs in typical developmental subjects and patients with developmental disorders (e.g., Cerebral Palsy) in near locomotor space (Belmonti et al., 2013, 2016). The locomotor reaching task is a goal-locomotor oriented task designed to evaluate the development of behavioral and cognitive functions in clinical and typical subjects. This protocol allowed us to record kinematic movement during locomotor trajectories.

II.2.1. Experimental set-up

The experimental set-up included a starting point (Start), a visual corridor and three targets (Central, left and right) (Figure 44). Each target was represented by a round plastic lamp adapted with a speaker (30 cm in diameter) placed on a table. A light or visual start signal was presented one at a time accompanied by an acoustic start signal (beep) by a programmable controller. Additionally, this programmable controller gave the output to the motion capture system. The central target was placed on a small table (50 l × 730 w × 70 h cm) in front of the subjects' starting position (Start) at a distance of 3.8 m. The left and the right targets were positioned at a distance of 4.20 m (i.e., 3.3 m on either side and 2.6 m in front of Start). Both targets (Left and Right) laid on two larger tables (250 l × 7,120 w × 90 h cm) evenly positioned laterally to Start, with their long axes facing each other.

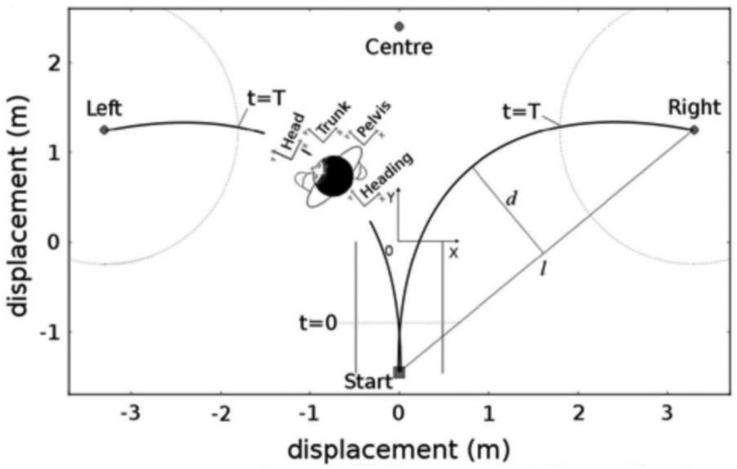

Figure 44. The representation of the spatial layout on the yaw plane (horizontal plane) (Belmonti et al., 2013). Start indicates the starting position. Left, Center and Right designate the three luminous targets. The two vertical bold gray lines depicts the corridor constraining initial walking direction.

II.2.2. Procedure

The participants were instructed to stand still on the Start tile waiting for an acoustic signal and the presentation of a luminous target. After the presentation of the stimuli (acoustic signal and a luminous target), the participants were asked to walk towards the luminous target to reach it and touch it and come back to the Start.

PART III: EXPERIMENTAL RESULTS: PUBLISHED STUDIES

In this section, we will present the scientific articles published and submitted to peer-reviewed indexed journals, together with the article in preparation for submission. These articles are grouped in three thematic: a) Developmental exploration of spatial cognitive capacities and brain activity in healthy adults using the WalCT, b) Replanning following target shift during locomotion, and c) Inhibitory control and cognitive flexibility in the visuo-spatial locomotor task.

III.1. Developmental exploration of spatial cognitive capacities and brain activity in healthy adults using the WalCT

In the first thematic, our research examined the exploration of spatial cognitive capacities and brain activity in healthy young and old adults using the WalCT. The results of our research allowed us to publish two scientific articles:

The first article was called "Age and sex impact on visuo-spatial working memory (VSWM), mental rotation (MR), and cognitive strategies during navigation" published in the *Neuroscience Research Journal* (Castilla et al., 2022). The article was aiming to study spatial cognitive abilities such as visuospatial working memory, MR, and cognitive strategies during typical aging using a goal-oriented locomotion task. In this study, we tested the following hypotheses:

i. The Young Adult (YA) group would perform better than the OA group in WalCT.
ii. MR capacities concerning spatial cognitive maps are closely related to VSWM performances in the navigational space.
iii. Participants with higher performances in VSWM span scores would rely more on place-sparing strategies; contrary to participants with lower performances in VSWM span scores who would rely more on path-sparing strategies.
iv. OA group presented more random errors than the YA when they failed to use spatial cognitive strategies (Perrochon et al., 2014).
v. Sex-related differences in VSWM are only present in the young adult group for the locomotor task (Lambrey and Berthoz, 2007).
vi. YA-F and OA groups were more susceptible to use of egocentric-based strategies during the recalling phase (Colombo et al., 2017; Lambrey and Berthoz, 2007).

The second study "Age-related decline in visuo-spatial working memory is reflected by dorsolateral prefrontal activation and cognitive capabilities investigate" (Kronovsek et al., 2020), investigated the effect of age on cerebral oxygenation in the VSWM tasks according to space (reaching or navigational) and determine if EF and cerebral oxygenation were involved in VSWM performance, either in reaching or navigational space. This study set out to test the hypothesis that:

i. YA would show a better VSWM performance and therefore higher cerebral oxygenation than OA resulting in a stronger increase of oxyhemoglobin (ΔO_2Hb) concentration and a stronger decrease in deoxyhaemoglobin (ΔHHb) concentration.
ii. Performances in cognitive tests would be explicative variables of VSWM performances, especially for navigational space

ARTICLE IN PRESS

Neuroscience Research xxx (xxxx) xxx

Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: www.sciencedirect.com/journal/neuroscience-research

Age and sex impact on visuospatial working memory (VSWM), mental rotation, and cognitive strategies during navigation

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ARTICLE INFO

Keywords:
Visuospatial working memory
Mental rotation ability
Aging effect
Walking Corsi test
Sex differences

ABSTRACT

This study assessed the impact of sex and typical aging on visuospatial working memory (VSWM), mental rotations, and navigational strategies using behavioral information. Fifty healthy participants regrouped in older (OA) and young adults (YA) performed the Walking Corsi test (WalCT) and the Redrawn Mental Rotation Test (MRT) to explore mental rotation abilities. We recorded kinematic data such as locomotion trajectories, and spatial orientations during navigation. We created a new method of data analysis for the WalCT performances and compared it with the classical approach. This original method allowed us to identify cognitive strategies based on errors analysis. Our data suggested that VSWM and mental rotation capacities in locomotion were modulated by age (YA scored higher than OA), and sex (Young Adult Males (YA-M) having higher performance than Young Adult Females (YA-F). We observed a preferential use of cognitive strategies related to sex; YA-F relied more on egocentric strategies whereas YA-M relied more on allocentric strategies. The preferential use of cognitive strategies in the YA group was not observed in the OA group producing more random errors per sequence. The results suggest the effects that age and sex have on VSWM, cognitive strategies, and mental rotation during navigation and highlight the importance of navigational strategies training.

1. Introduction

In addition to classical neuropsychological paper and pencil tests, spatial navigation assessments contribute to complete the estimation of neurocognitive capacities which are essential for diagnosing and rehabilitation (Mattay et al., 2006; Parizkova et al., 2018; Perrochon et al., 2014; Sharp et al., 2006). Spatial cognitive abilities such as visuospatial working memory (VSWM) and mental rotation (MR) are associated when solving complex visuo-spatial tasks (Borella et al., 2014a; Buckner, 2004; Cornoldi and Mammarella, 2008; Kaltner and Jansen, 2016; Meilinger et al., 2011; Wang et al., 2018). VSWM temporally stores (i.e., memorize) and manipulates visuospatial information (Baddeley, 2012; Miyake and Shah, 1999). MR allows us to rotate mental objects in two or three dimensions (i.e., Object-based rotation)(Uttal et al., 2013). In this paper, we consider MR not only of objects, but also MR of spatial cognitive maps (Behrens et al., 2018; Epstein et al., 2017). To our knowledge, this is the first article that studied MR during locomotion in the Walking Corsi test (WalCT).

1.1. VSWM assessment using the WalCT

The VSWM was initially evaluated using the Corsi Block-tapping Test (CBT) in the reaching space (Berch et al., 1998; Borella et al., 2014b; Piccardi et al., 2011, 2010). The CBT consists of a set of nine wooden

Abbreviations: ARE, Angle related error; BTS, Basic Trajectory Software version 1; GDS, Geriatric Depression Scale; MR, Mental rotation; MCI), Mild cognitive impairments; MMSE, Mini Mental State Examination; OA-F, Older adult Females; OA-M, Older adult Males; OA, Older adults; MRT, Redrawn Mental Rotation; VWalCT, Virtual Walking Corsi test; VSWM, Visuo-spatial working memory; WalCT, Walking Corsi test; YA-F, Young adult Females; YA-M, Young adult Males; YA, Young adults.

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https://doi.org/10.1016/j.neures.2022.07.007
Received 24 February 2022; Received in revised form 12 June 2022; Accepted 24 July 2022
Available online 26 July 2022
0168-0102/

blocks (30x30 cm) arranged on a board (2.5x30cm). During the assessment, the experimenter presents a sequence by tapping the wooden blocks and the subject's task is to repeat this sequence identically (Corsi, 1972). The CBT increases its difficulty incrementing the number of blocks per sequence. An adaptation of the CBT to the locomotor space named the Walking Corsi task (WalCT) allowing to study the VSWM during navigation and to explore the spatial cognition abilities (Piccardi et al., 2010, 2008). It was designed for the "near distant extrapersonal locomotor space" (i.e., the area used when walking around in a room)(Nemmi et al., 2013; Piccardi et al., 2010, 2008). During its earlier version, the experimenter walked to a sequence of locations (e.g., tiles in the locomotor space) and the participant's task was to repeat this sequence by walking to the same tiles in the same order (i.e., forward version). Its difficulty increased as the number of tiles (i.e., spatial locations) per sequence increased and the highest score obtained during the execution determined the VSWM span. Since the initial WalCT, other versions of the task have been proposed such as the Magic Carpet paradigm (MC). The MC based on the WalCT test used nine translucent tiles with pressure sensors and a central blue light-emitting diode (Belmonti et al., 2015b; Perrochon et al., 2014). In the MC, a computer generated sequences and displayed them by illuminating the tiles one by one while recording the signals from pressure sensors as the participant walked over each tile(Belmonti et al., 2015a, 2015b; Demichelis et al., 2013; Meilinger et al., 2011; Perrochon et al., 2014). Moreover, the WalCT was compared with an emulate virtual 3D environment showing the same results in both contexts (Nori et al., 2015).

Here, we used an updated version of the WalCT called the Virtual Walking Corsi test (VWalCT) combined with the Virtual Carpet™ paradigm. This particular version enabled us to record the subjects' locomotion, to set the target positions (i.e., spatial locations) in a three-dimensional array, and to present stimuli automatically. These specific features allowed us to extract kinematic information (i.e., trajectories, orientations, and rotations) during navigation. (Berthoz and Zaoui, 2015). This updated version has already been used in several recent studies (Kronovsek et al., 2020; Perrochon et al., 2018). Moreover, in the past year, the Virtual Carpet ™ was adapted to include new protocols such as the Virtual City and the Virtual Labyrinth tasks. These new protocols were specifically designed to study the VSWM, mental flexibility and to determine behavioral index during locomotion (Castilla et al., 2021; Del Lucchese et al., 2021). Preliminary explorations of spatial cognitive abilities, and the VSWM, using the VWalCT have suggested age cognitive decline in OA and sex differences (Kronovsek et al., 2020; Perrochon et al., 2018, 2014).

1.2. Mental rotations

In addition to the VSWM, MR is particularly affected by the aging process, and it is involved in cognitive and behavioral activities (Kaltner and Jansen, 2016). Recently, Carbone et al. (2020) studied spatial cognitive abilities comparing healthy YA and OA using the classical version of the WalCT in a backward manner. They found that object-based rotation capacities and perspective-taking (i.e., participant-based rotation) were closely related to VSWM performances deteriorating with age. The authors suggested that during the WalCT, participants kept changing their perspective basing themselves on an aerial view of the sequence of tiles (i.e., perspective-taking). However, during the performance of the WalCT, MR capacities are involved in manipulating the spatial cognitive maps of the memorized array. Here, we studied MR capacities during the performance of the WalCT (i.e., locomotion) and throughout object-based mental rotation.

1.3. Spatial Reference frames

Furthermore, previous research suggested that navigation capacities involved in spatial reference frames (i.e., *egocentric, allocentric, and heterocentric strategies*) are also influenced by the aging process during the solving of spatial cognitive tasks (Iachini et al., 2009; Perrochon et al., 2018, 2014). Concerning the *egocentric* reference frame, each location is encoded according to the participant's perspective (i.e. self-centered representations). This *egocentric strategy* (or first-person point of view) requires a topokinaesthetic memory which updates the self-generated perspective during locomotor movements (Bullens et al., 2010). In *allocentric* strategies, each location is encoded according to a global point of view (i.e., world-centered representations). The allocentric reference frame is useful when creating a cognitive map suitable for navigating in a complex environment (Burgess et al., 2006; O'keefe and Nadel, 1978). Controversially, it has been demonstrated that during the aging process, the *egocentric strategy* is better preserved than the allocentric strategy (Colombo et al., 2017; Gazova et al., 2013) whereas other findings suggested that both the *ego* and *allocentric* strategies are affected by aging (Fernandez-Baizan et al., 2020; Ruggiero et al., 2016). Indeed, these impairments are attributed to functional and structural changes in the hippocampal and the *parahippocampal* structures occurring during the aging process (Burgess, 2008; Igloi et al., 2010).

Regarding the sex differences in spatial navigational cognitive strategies, both men and woman are able to use allocentric strategies. However, it has been demonstrated that men outperform women in spatial tasks (Fernandez-Baizan et al., 2019; Nori et al., 2015). Females appear to rely more on the *egocentric strategy* while performing spatial cognitive tasks whereas males appeared to rely more on an allocentric processing of spatial information and also demonstrated capacities to easily switch between strategies (Lambrey and Berthoz, 2007; Tascón et al., 2021). Interestingly, this sex difference had not been previously observed in spatial tasks such as an augmented reality task for object-location or map-pointing tasks (Munoz-Montoya et al., 2021).

1.4. Neural Bases of cognitive strategies during the WalCT

During the WalCT, perceptual and cognitive processes (i.e., executive functions or cognitive control) are recruited in order to achieve a goal. The executive functions are involved in selecting an action plan, ignoring irrelevant distractions and controlling automatic behaviors (i.e., inhibitor control), temporarily bearing in mind information for manipulated it (i.e., Working memory), and being able to anticipate and adapt to eventual changes (i.e., mental flexibility)(Diamond, 2013). Neuropsychological and neuroimaging studies suggest that the prefrontal cortex is associated in executive functions specifically in the dorsolateral prefrontal cortex (Friedman and Robbins, 2022; Kronovsek et al., 2020; Menon and D'Esposito, 2022). The prefrontal cortex shares connections with subcortical structures such as the basal ganglia and the cerebellum during cognitive processes (McGough et al., 2018; Mirino et al., 2022; Patai and Spiers, 2021). Concerning the spatial navigation processes, the right medial temporal lobe plays a key role in the representation of the cognitive maps of the environment and memory (Eichenbaum, 2017; Igloi et al., 2010; Lambrey et al., 2003; Maguire, 2001). Specific areas such as the hippocampus, parahippocampus, retrosplenial cortex, and posterior parietal cortex are the core areas of spatial navigation (Boccia et al., 2014; Epstein et al., 2017). The hippocampus is involved in the mental representation of the spatial information (cognitive maps), the planning of the actions and the using of past experiences in navigation (Eichenbaum, 2004; O'keefe and Nadel, 1978). The parahippocampus is involved in visual spatial processing, in particular in place recognition, route planning and mnemonic encoding (Aminoff et al., 2013; Epstein et al., 1999). The retrosplenial cortex is involved in spatial encoding, memory and the integration of information from egocentric to allocentric spatial processing (Maguire, 2001; Miller et al., 2019; Vann et al., 2009).

1.5. New goals of this study: spatial error patterns

This study follows our line of research in the field of spatial cognition. The *span score* analysis in the WalCT detailed a participant's performance when given a sequence by simply measuring the number of tiles successfully reached. However, supplementary error analysis in the VSWM tasks, especially in the locomotor space, revealed additional information about the type of cognitive strategies used during navigation (*ego/allocentric*)(Perrochon et al., 2014). Belmonti et al. (2015c) proposed three categories based on the classification of errors: (a) *place sparing errors* - the participant reached the correct spatial targets in each sequence but not necessarily in the right order (i.e., preserving locations), (b) *path sparing errors* - the participant generated an overall correct trajectory but not necessarily reaching the correct spatial targets (i.e., preserving order), and (c) *random/minimal errors* - the participant generated a trajectory with neither sparing places nor preserving the global itinerary. This classification allowed us to determine which strategy the participant relied on most. It is important to consider that different error patterns can be produced by the same participant depending on the task's complexity and the errors can differ from one sequence to the other (not mutually exclusively).

Error analysis in the WalCT has revealed that mild cognitive impairments (MCI) participants made significantly more random errors than healthy OA (Perrochon et al., 2014). However, little is known about the impact of normal aging on the use of spatial cognitive strategies based on *error patterns* produced during the resolution of the WalCT. Identifying these differences will help us to understand the neurocognitive processes underlying VSWM performances decline through aging.

This paper studies VSWM, mental rotations, and cognitive strategies during typical aging using a goal-oriented locomotion task. The idea was not only to demonstrate the differences between YA and OA in spatial cognitive abilities but also to study their differences in cognitive strategies involved during the resolution of a complex navigational test. For this, we compared healthy YA and OA using quantitative measures to identify the spatial cognitive changes in aging based on the VWalCT. We used two different methods to study the VSWM scores in the VWalCT (i.e., classical vs Score point attribution method). Additionally, we focused on two types of MR capacities, the first type was the Mental Rotation paper Test (MRT) (i.e., *object-based rotation*) and the second MR was of spatial cognitive maps manipulation during locomotion (i.e., *online mental rotation of the remembered array)*.

As previously stated, we hypothesized that the YA group would perform better than the OA group in VWalCT. We also proposed that MR capacities concerning spatial cognitive maps are closely related to VSWM performances in the navigational space. Moreover, we theorized that participants with higher performances in VSWM span score would rely more on *place-sparing strategies*; contrary to participants with lower performances in VSWM span scores who would rely more on *path-sparing strategies*. Concerning the age-related differences, we expected that the older adult group presented more random errors than the YA when they failed to use spatial cognitive strategies (Perrochon et al., 2014). Additionally, based on previous findings, we hypothesized that sex-related differences in VSWM are only present in the young adult group for the locomotor task (Lambrey and Berthoz, 2007). Additionally, younger women and OA were more susceptible to use egocentric-based strategies during the recalling phase (Colombo et al., 2017; Lambrey and Berthoz, 2007).

2. Methods

2.1. Participants

A total of 50 healthy participants were included in this study. They were split into two groups: 31 YAand 19 OA (Table 1). The two age groups did not differ in terms of educational level (t(18) = 1.29; p = 0.25). All participants reported normal or corrected-to-normal vision, absence of motor or gait disorders, without any history of neuropsychological or psychiatric diseases nor any previous use of drugs/medication capable of altering neurocognitive functions. Additionally, the OA group was assessed to verify any cognitive impairment using the Mini Mental State Examination (MMSE) and the presence of depressive symptoms using the mini Geriatric Depression Scale (GDS). The participants carried out a global cognitive functioning assessment using a battery of neuropsychological tests (e.g., ZOO map, Trail Making Test (TMT), REY's figure, Stroop test, etc), including: electronic Corsi Block Tapping-test (e-CBT) (see (Kronovsek et al., 2020). There was no difference in the scores for depression (t(40.75) = −0.17; p = 0.86), the scores remaining within normal limits (mini Geriatric Depression Scale (GDS) score > 1). All participants were enrolled as volunteers in the study. They were recruited at the University of Limoges and the geriatric associations in Limoges - France. Written informed consent was obtained from each participant after they were briefed on the nature of the experiment and the operating mode of the experimental setup. The experiment lasted from forty to sixty minutes per participant allowing breaks or stops when required. The experiment was carried out following the ethical standards established by the Declaration of Helsinki ("World Medical Association Declaration of Helsinki, " (2013).

Table 1
Demographic and cognitive characteristics of the study participants.

	Variables (unity) or [rank]	Young adults (n = 31)	Older adults (n = 19)	P-value
Demographic,	Age (years)	22.9 ± 2.8	70.2 ± 3.4	<
psychologic	Sex (%	[19;31]	[65;77]	0.001
and	females)	61.3% (n =	70.8% (n =	0.051
cognitive	Year of	19)	17)	0.79
characteristics	education	14 + - 1.9	12.+ −3.5	
	MMSE [0 −		28.2 ± 1.4	
	30]	1. ± 0.2	0.1 ± 0.3	
	GDS [0 − 4]			
Cognitive tests: Mental	MRT [0 −	5.9 ± 3.7	2.2 ± 1.5	<
Rotation	24]			0.001
Planning	ZOO [max 8]	6.1 ± 2.8	3.9 ± 3.2	<
				0.001
Planning	REY C [0 −	35.7 ± 0.6	35.2 ± 1.4	0.07
Visual memory	36]	25.9 ± 4.9	18.0 ± 6.2	<
Inhibition	REY R [0 −	50.6 ± 7.1	66.6 ± 12.9	0.001
	36]	37.9 ± 5.2	47 ± 8.7	<
	STROOP D	79.6 ± 17	132.1 ±	0.001
	(s)		30.2	<
	STROOP R			0.001
	(s)			<
	STROOP I (s)			0.001
Cognitive flexibility.	TMT A (s)	22.1 ± 6.9	40.1 ± 14.6	<
Visuo-spatial	TMT B (s)	50.5 ± 18.4	87.6 ± 59.2	0.001
exploring				< 0.01

Means ± standard deviation and [range]
MMSE = Mini Mental State examination; GDS = Geriatric Depression Scale; MRT = Mental Rotation Test; REY C = Rey copy; REY R = Rey restitution; STROOP D = Denomination; STROOP R = Reading; STROOP I = Interference; TMT = Trail Making Test.
Each participant scored above the age-and education-adjusted MMSE normal cut-off suggesting an efficient global cognitive functioning. Despite a barely significant difference in years of education, our groups showed similar education levels (50th–75th percentiles) based on the interquartile range of years of education in each age group (INSEE; the French national institute for statistics and economic research)

2.2. Experimental set-up

This study used the Virtual Carpet™ paradigm (Berthoz and Zaoui, 2015) (Fig. 1). Two computers, one video projector (W316ST Optoma® projector, Taiwan), and one HTC Vive system were used in the experimentation (HTC® Vive, Taiwan) (Castilla et al., 2021; Del Lucchese et al., 2021).

A computer was connected to the video projector for projecting the navigational space on the floor (3 m x 2.4 m) and the stimuli, 9 tiles of 30 x 30 cm. This projection was used as a template to configure the

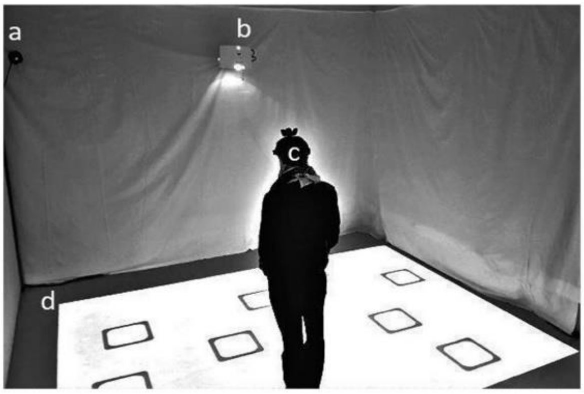

Fig. 1. Experimental set up: a) Camera HTC Vive, b) Video projector, c) 3D motion sensor HTC Vive and d) the navigational space with 9 tiles.

virtual environment coordinates and to present the sequences to the participant. A second computer was connected to the HTC Vive system (i.e., two infrared cameras, two hand-held 3D motion sensors, and one virtual reality helmet). The two cameras were placed diagonally 5 m (16.4042 feet) apart in order to cover the whole navigational space. The two hand-held 3D motion sensors were used as trajectory trackers recording the X, Y, Z positions every 11 ms (90.90 Hertz) (Niehorster et al., 2017). These 3D motion sensors were fixed upon a head support which was worn on the participant's head and another 3D motion sensor was added to a belt which was worn on the waist. We were able to measure and calculate (a) the position of the participant on the spatial array (X,Y coordinates); (b) the head/waist direction on the horizontal plane (Rotations) in the horizontal component (i.e., Yaw plane).

We used the Basic Trajectory Software version 1 (BTS) for the setting of the navigational space and of the data recording. The BTS used the drives of the HTC Vive system; (a) to generate the virtual targets (e.g., Virtual tiles) in the virtual environment known as *the calibration procedure,* and (b) to record the participant's trajectories. The calibration procedure allowed us (a) to measure the records' global navigational space array and (b) to set the target's positions in a Cartesian coordinate system. Using the coordinates of the tiles, we created an algorithm to establish a perimeter among the center for each tile of 30x30 cm. This setup allowed us to identify the tiles and determine whether or not participants reached a tile target within the sequence in the VWalCT.

2.3. Stimuli

In the VWalCT, 9 tiles of 30 x 30 cm were presented to the participant. (Fig. 1). For each trial, a sequence of tiles were lit by means of the projector. Each tile (i.e., a stimulus) was lit for one second with an interstimulus interval of one second. The number of tiles increased progressively across the length of the sequences by one tile (i.e., sequence of 2 trials of 2 tiles, to sequence of 2 trials 9 tiles) (Table 2). A complete experimental session included two trials per sequence (2 trial x 8 sequences). Two types of sequences were presented: a) a set of sequences that required body rotations (more than 90 degrees) and b) a set of sequences that required less body rotations (less than 90 degrees) during locomotion (linear vs not linear) (Kronovsek et al., 2020).

2.4. Procedure

The experimenter read the instructions to each participant, and they were asked if they fully understood them and whether they had any questions before running the experiment. Each participant was assessed individually. The experiment protocol was divided into two parts: (a) the Redrawn Mental Rotation Test (MRT) which is a paper-and-pencil test to assess MR capabilities (Peters et al., 1995) and (b) the VWalCT for the locomotor space(Castilla et al., 2021; Kronovsek et al., 2020).

(a) In the MRT, each item was presented with a *target stimulus* (on the left) and four *sample stimuli* on the left from A to D (Fig. 2). The participant was asked to identify which two of the four sample stimuli (i.e., 2 correct stimuli = 1 point by item) were rotated versions of a target stimulus. We measured the score out of a total of 24 items.We presented 12 items in 3 min.
(b) In the VWalCT, participants were positioned on a Start Tile (ST) at 1.5 m away from the test projection space during the encoding phase. Then, participants were asked to memorize (i.e., Encoding phase) sequences of tiles that were lit in a certain order and to repeat these sequences (i.e., Recalling phase) after the start signal (i.e., beep) sounded. Participants were instructed to walk to each tile in the correct order, stop briefly on each tile, and return to the Start Tile (ST). The stopping task criterion was determined as being two consecutive failed trials in the same sequence (Berch et al., 1998).

2.5. Data processing

2.5.1. Error patterns classification

The error patterns were categorized based on the methodology of Belmonti et al. (2015c). A total of 668 trials were performed in the VWalCT (212 trials for OA and 456 trials for YA). The error sample consisted of a total of 151 errorsfrom all the sequences. This paper used

Table 2
Sequences of the VWalCT presented in experiment (Kronovsek et al., 2020).

Sequences	Trial 1	Trial 2
2	2 7	3 6
3	1 7 6	6 2 4
4	5 1 4 7	7 3 6 2
5	6 3 2 8 4	5 2 4 7 6
6	9 5 8 1 7 3	8 1 3 2 6 4
7	3 8 1 6 2 7 5	7 3 9 6 2 8 1
8	5 2 4 8 7 6 3 9 6	8 3 1 2 9 7 4 5
9	9 7 4 3 8 5 2 6 1	6 2 3 4 8 9 5 1 7

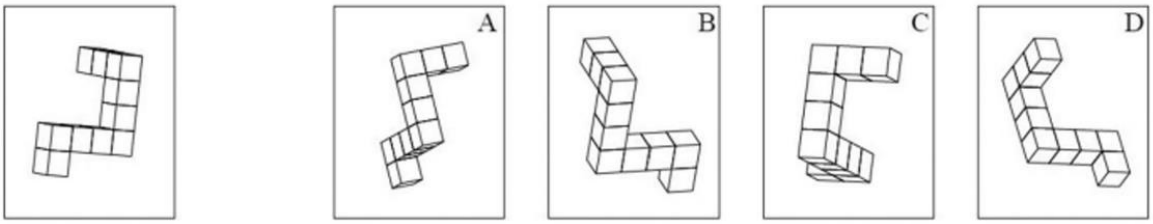

Fig. 2. Redrawn Mental Rotation Test (MRT)
Illustration adapted from Peters et al. (1995).

archival data from Kronovsek et al. (2020).

Firstly, we identified four individual errors (i.e., *Omission, Permutations, Substitution, and Insertion*) made during the recalling phase in order to be associated in specific clusters. *i) Omission:* a stimulus presented (i. e., a tile or spatial location) in a sequence is not retrieved, and the total of stimuli in the response is lower; *ii) Permutations:* two stimuli are retrieved in an inversed order (i.e., tile 3 instead of tile 2 and vice-versa)*; iii) Substitution:* a stimulus presented in the sequence is substituted by another in the response; *iv) Insertion*: adding tiles not presented in the sequence and increasing the length of the response.

Secondly, the individual error patterns were clustered in three main categories: (a) *Place-sparing errors patterns*, (b) *Path-sparing error patterns* and (c) *Random/minimal errors patterns* (Fig. 3):

Place-sparing error patterns: The participant reached the correct targets in each sequence but not necessarily in the right order (i.e., preserving locations). It is composed of three error patterns which are: i) Place identity error (pattern 1): it is constituted of exclusively *permutation errors*; ii) Place approximation (pattern 2): it is denoted by *permutations* and *substitution* of tiles near the location presented in the sequence; iii) Place intrusions (pattern 3): it is characterized by *permutations* and *substitution* of locations far from the location presented in the sequence.

Path-sparing patterns: The participant generated a globally correct trajectory but not necessarily with the correct targets (i.e., preserving order). *Path-sparing patterns* are composed of three error patterns which are: i) *Path approximation* (pattern 4): it is constituted of only *substitutions* and/or *insertions* of tiles near the location presented in the sequence; ii) *Path shortening* (pattern 5): it is characterized by presenting *omissions* only; iii) *Path deviation* (pattern 6): it is denoted by *substitutions* or *insertions* far from the correct path. *Random/minimal error patterns* (pattern 7), which combine responses without any specific strategies or total disorientation. They are determined by more than fifty percent of the *omission* errors in the response or retrieve less than two correct locations in the correct order.

2.5.2. Mental rotation during locomotion

In the MR analysis, we first identified the "*theoretical* path" for each sequence corresponding to the ideal performance. Then, based on this path, we identified the maximum amount of errors that could be made following body rotation greater than 90 degrees (*maximum possible angle-related error: m-ARE)*. For example, in the Fig. 3 we can see that according to the theoretical path, the participant has to make five body rotations of more than 90 degrees to achieve the sequence. Thus, he can make a maximum of five ARE on this sequence. For each participant, we have summed up the maximum ARE they can produce for each sequence they performed. It allows us to obtain the maximum ARE (m-ARE) the participant could have produced on their whole test session. Then we summed up the errors (i.e., Omission, Permutations, Substitution, and Insertion) on tiles directly following a 90 degrees or more body rotation for each sequence they performed. It allowed us to obtain the total number of angle-related errors (t-ARE) produced. For each participant, we then computed a ratio (ARE-r) based on the total number of angle-related errors (t-ARE) produced divided by maximum possible angle-related errors (ARE-r = tARE/ m-ARE).This ratio allowed us to identify the tendency to commit errors while recalling the locations following rotations greater than 90 degrees. The closer the ratio is to zero, the less likely the participant is to produce any angle-related errors. By calculating this ratio, we compared participants with high and low performances on the VWalCT regardless of the fact that higher performers encountered more tiles within the whole test session than poorer performers. We expected that a body rotation of more than 90 degrees during the locomotion required updating the information encoded from the initial visual perspective (i.e., the participant in the start point view) (Meilinger et al., 2011).

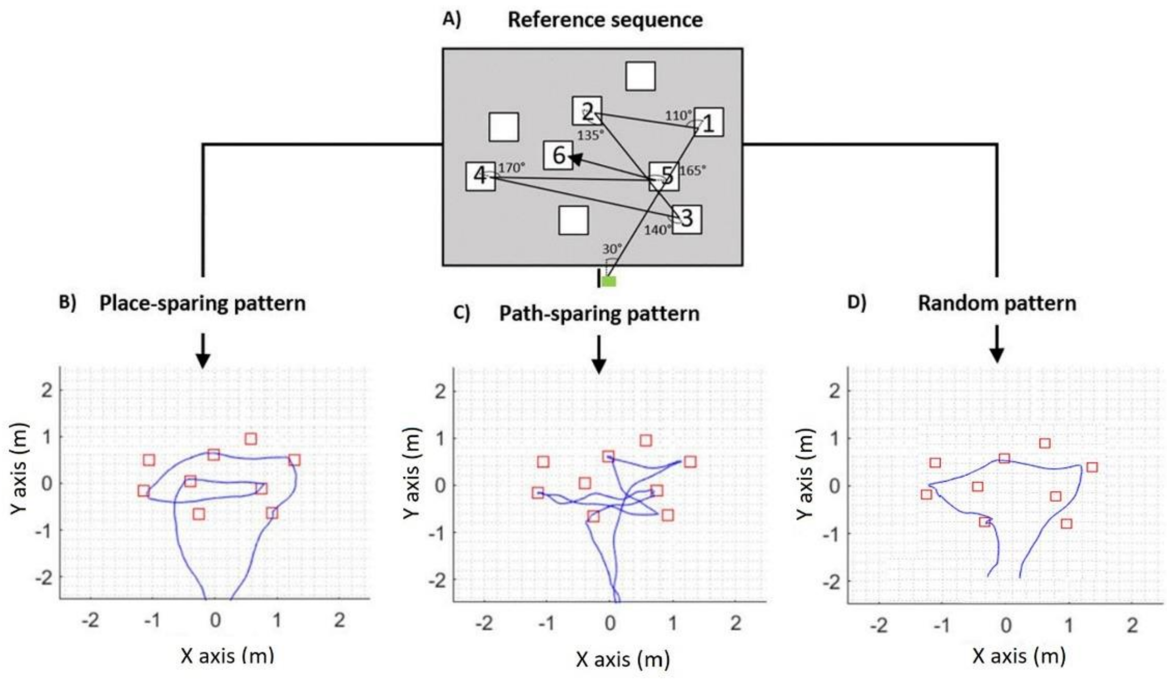

Fig. 3. Representation of global error patterns during navigation for a sequence of six tiles: A) Sequence presented to the participants, the green square represents the start point,the squares represent the tiles and the degrees represent the body rotations in a theoretical trajectory. The degrees are computed according to a single body rotation from one movement direction to another, B) Place-sparing, example of a trajectory performed by a YA-M (23 years old), C) Path-sparing errors, example of a trajectory performed by a YA-F (23 years old) and D) Random errors, example of a trajectory performed by a OA-M (70 years old). The numbers on the tiles indicate the order in which the sequence was presented to the participant during the Encoding phase. The red squares represent the tiles' positions in the navigational space. Each blue line represents a locomotor trajectory (2D) generated by three different participants during the response (Recalling phase).

2.6. Statistical analysis

All statistical analysis was performed using the open-source statistical software R version 4.0.3 (2020) for Windows (www.R-project.org). Prior to the statistical analysis, the scores in classic span analysis, the SPA and MRT were normalized. The statistical analysis was divided into 1) VSWM performances analysis, 2) the mental rotation analysis, and 3) the error patterns analysis.

2.6.1. VSWM performances analysis

The VSWM assessment was obtained based on the numbers of tiles in the last sequence repeated successfully by the participant in the VWalCT (Perrochon et al., 2018). Additionally, we developed a novel methodology to study encoding strategies based on the tiles' retrieval. We called this methodology *Score Point Attribution* (SPA). If a tile was reached in the correct order, the score was 2 points, if the tile was reached in the trial but recalled in the wrong order the score was 1, and it was 0 if the tile was not reached at all. The sequence score was the sum of the tiles recalled in a trial and the global score was the sum of the total points in the sequences. We performed a Pearson correlation analysis between VSWM span scores and SPA.

Next, we classified the performances using a median split method based on the VWalCT classic span score. The median split method consists in categorize a sample group above or below the median base on a continuous predictor variable (Iacobucci et al., 2015). We analyzed the errors produced by the group of higher performers and the group of lower performers (i.e., Level of performance). Then, we compared errors committed by age group (i.e., YA vs OA) and sex. We determined the differences using the classic VSWM span score and the SPA score by group (YA vs OA), and the sex in using a non-parametric Kruskal-Wallis H test at 5 % significance level.

2.6.2. Mental rotation analysis

The MR analysis was divided into two sections: the first section concerning the MRT, and the second section concentrated on the MR of spatial maps during locomotion (i.e., *Online mental rotation of the remembered array)*. For the MRT, we used a non-parametric Kruskal-Wallis H test at a 5 % significance level.

For the *online mental rotation of the remembered array,* we performed a Pearson correlation analysis between ARE-r and MRT scores. Then, we performed two ways ANOVA (age*sex) on the ratio as the assumptions required for these analyses were met.

2.6.3. Error patterns analysis

We used trajectory analysis to identify each error during the trials. We used a frequency analysis Chi-square test (i.e. X^2 test) of the error patterns by age group (OA, YA), sex, and group performance ("higher" / "lower" performers).

3. Results

3.1. VSWM performances analysis

3.1.1. Classical VSWM span score

In the VWalCT classic span, we found significant differences between age groups (YA vs OA) (means and standard deviations are respectively 6.5 ± 1.6 vs 4.6 ± 0.8; $H(1) = 17.460$; $p < 0.001$, $\eta^2 = 0.343$) (Fig. 4C). Additionally, we did not observe any effect of sex for the classical span score (5.4 ± 1.4 for females vs 6.3 ± 1.9 for males; $H(1) = 2.523$; $p = 0.112$). We also checked sex differences within both age groups. We found no significant differences of span scores between YA-F and YA-M (respectively: 7.1 ± 1.8 vs 6.1 ± 1.3; $H(1) = 2.762$; $p = 0.097$), neither in the OA group (males: 4.8 ± 0.8 vs 4.5 ± 0.8 for females; $H(1) = 1.409$; $p = 0.235$). To summarize, we found a difference between age groups (YA vs OA) but not between sexes.

3.1.2. Score point attribution (SPA)

The calculation of SPA gave an age difference between groups with a higher score for YA (YA 111 ± 41.6 vs OA 59.5 ± 15.3; $H(1) = 22.3$, $p < 0.001$, $\eta^2 = 0.443$) (Fig. 4B). No global effect of sex was found (males: 108 ± 50.8 vs 82.4 ± 34.3 for females; $H(1) = 3.17$, $p = 0.075$). However, we found a significant effect of sex in the YA ($H(1) = 4.62$, $p = 0.0315$, $\eta^2 = 0.125$), with YA-M showing higher SPA than YA-F (respectively 130.33 ± 47.37 vs 99.47 ± 33.62). No significant sex

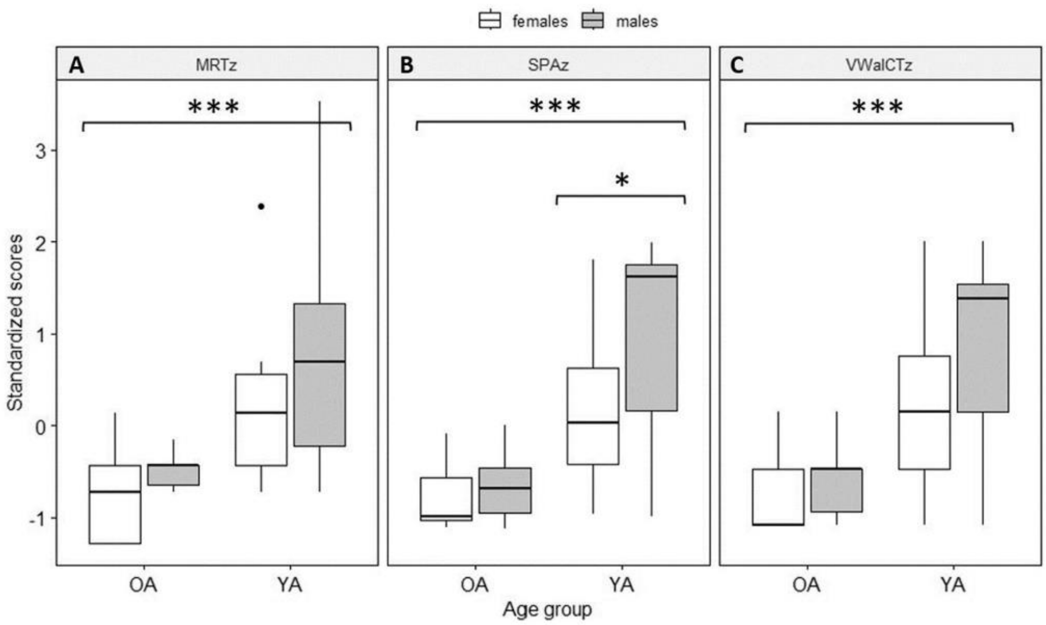

Fig. 4. Standardized scores for by group of age and sex: A) Redrawn Mental Rotation Test (MRT), B) Score point attribution –(SPA), and C) Classical span score Virtual Walking Corsi test (VWalCT). * Symbolizes significance at $p < 0.05$ and * ** at $p < 0.001$.

differences were found in the OA (males: 64 ± 17.7 vs 57.46 ± 14.32 for females; H(1) = 0.282, p = 0.595). To summarize, we found a significant difference in the SPA between age groups and a sex difference only in the YA group.

3.2. Mental rotation analysis

3.2.1. Mental rotation paper test (MRT)

Concerning the MRT, we observed age differences in the scores. YA performed significantly better than OA (respectively 5.94 ± 3.70 vs 2.26 ± 1.59; H(1) = 15.3, $p < 0.001$, $\eta^2 = 0.298$) Fig. 4A). We found that there was no difference between sexes (males: 5.89 ± 4.36 vs 3.78 ± 2.78 for females; H(1) = 2.63; p = 0.105). We also analyzed the sex effect on the MRT score within age groups. We found no significant differences of MRT scores between OA-F and OA-M (males: 2.83 ± 0.75 vs 2 ± 1.83 for females; H(1) = 1.18, p = 0.277) as well as in the YA (males: 7.42 ± 4.64 vs 5 ± 2.69 for females; H(1) = 2.55, p = 0.110).). Finally, the score at MRT and the score at VWalCT strongly correlated (r = 0.67; $p < 0.001$).

3.2.2. Mental rotation during locomotion

Here, we report the results of an analysis of the errors due to MR requirements while navigating. We found that ARE-r shared significant negative correlations with MRT score (r = - 0.36; p = 0.009), VWalCT span score (r = - 0.39; p = 0.004) and SPA (r = −0.48, $p < 0.001$). We observed an age effect ($F(1, 46) = 28.04$; $p < 0.001$) with OA showing higher ARE-r (0.343 ± 0.142) than YA (0.188 ± 0.082) (Fig. 5). We did not observe any sex effect ($F(1, 46) = 0.18$; p = 0.677). There was an age*sex interaction ($F(1, 46) = 10.95$; p = 0.002).

By looking at simple effects, we observed an age effect within both OA and YA female groups ($F(1, 46) = 5.59$; p = 0.022) and male groups ($F(1, 46) = 33.4$; $p < 0.001$). OA-F were more likely to make angle-related errors compared to YA-F (0.31 ± 0.11 vs. 0.22 ± 0.07 respectively). OA-M were also more likely to produce angle-related errors than YA-M (0.42 ± 0.17 vs. 0.14 ± 0.08 respectively). Furthermore, there was a sex effect in the OA ($F(1, 46) = 5.76$; p = 0.020) and in the YA $F(1, 46) = 5.37$; p = 0.025). OA-F were less likely to make angle-related errors compared to OA-M (0.31 ± 0.11 vs. 0.42 ± 0.17) but YA-F were more likely to make angle-related errors compared to YA-M (0.22 ± 0.07 vs. 0.14 ± 0.08). To summarize, we found a group difference for ARE-r. OAwere more likely to produce angle-related errors than YA. YA-F were more likely to produce angle-related errors than younger males and we observed an opposite pattern of results within the elder population.

3.3. Error patterns analysis

The errors were analyzed as: (a) error patterns analysis by the level of performance, (b) error patterns analysis by group YA vs OA, and (c) error patterns analysis by sex. The frequency analysis revealed that the *path-sparing pattern* (43.7 %, 66 errors out of 151) was significantly more frequent than *place-sparing* (41.1 %, 62 errors) and random (15.2 %, 23 errors) patterns within the whole sample (X^2 (2, N = 151) = 22.424; p = 0.000).

3.3.1. Errors patterns analysis by the level of performance

The median split categorization on span score showed a median of 4 for the OA group and a median of 6 for the YA group. Globally, the split categorization identified 29 “Lower performers” and 21 “Higher performers”. We observed a significant effect of the level of performance on the frequency distribution of error patterns (Fig. 6A). The Higher performers showed more place-sparing patterns than the lower performers (53.6 % vs 30.4 %), and less path-sparing (31.9 % vs 53.7 %) and random patterns (14.5 % vs 15.9 %) (X^2(2, N = 151) = 8.995; p = 0.011). The distribution of the patterns significantly differed within both lower (X^2(2, N = 82) = 17,878; $p < 0.001$) and higher performers (X^2(2, N = 69) = 15,913; $p < 0.001$) samples.

We checked for differences in the distribution of error patterns within age groups.

No significant differences in the distribution of error patterns were observed in the OA group (X^2(2, N = 52) = 1.8; p = 0.406) (Fig. 6B). However, we observed a significant difference in the distribution of error patterns between the level of performance within our young sample, higher performers made more place-sparing patterns (62.8 % vs

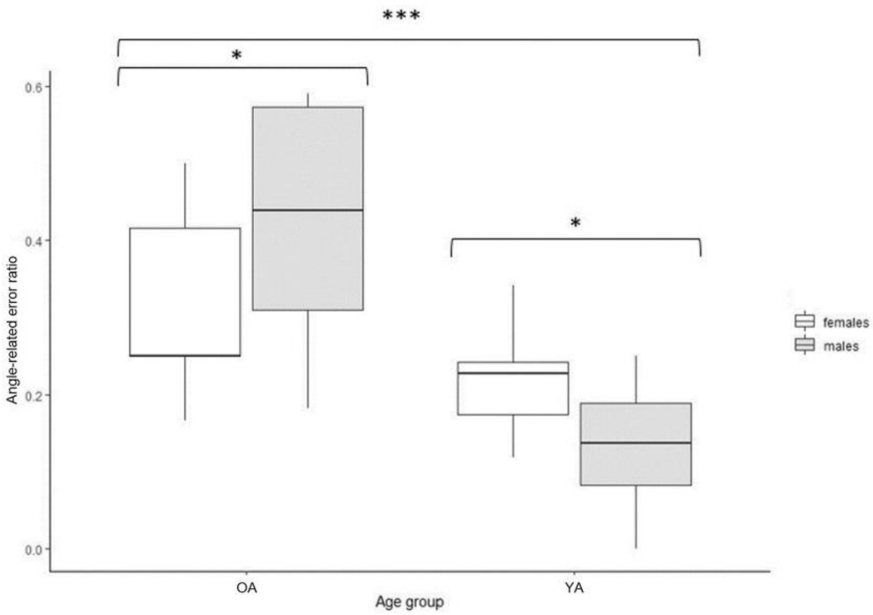

Fig. 5. Angle-related error ratio (ARE-r) for age groups (YA and OA) and sex. * Symbolizes significance at $p < 0.05$ and * ** at $p < 0.001$. This ratio allows us to observe the tendency of each participant to commit errors while recalling the tiles following rotations greater than 90 degrees that he will encounter during the test.

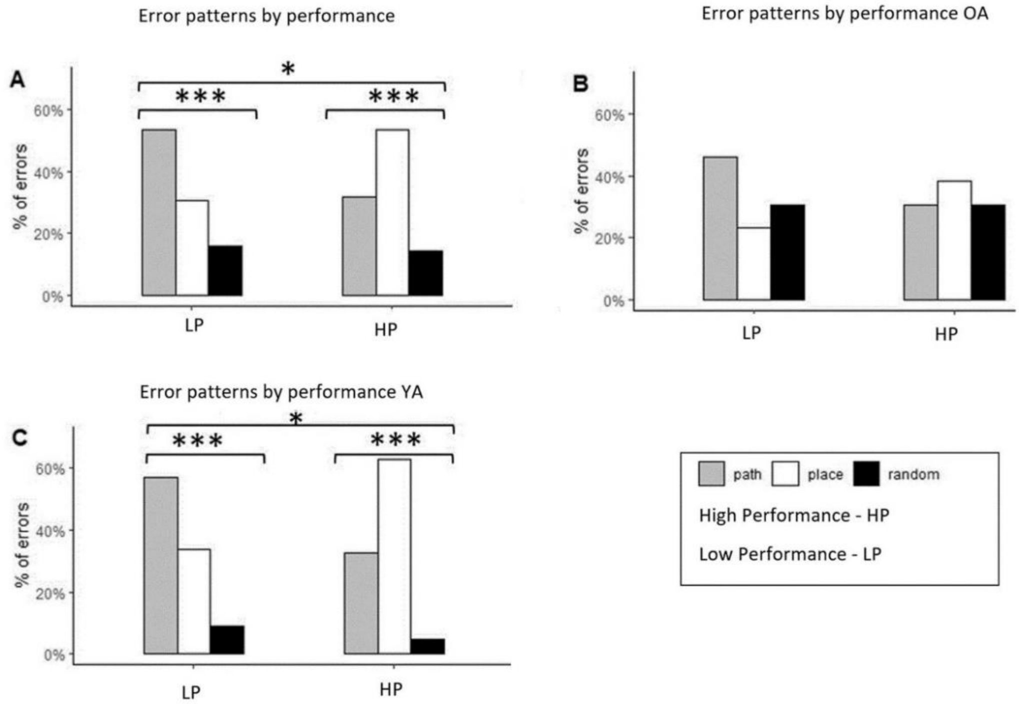

Fig. 6. Percentage of errors by the level of performance in Young Adults (YA) and Older Adults(OA) group. A) Error patterns by performance. B) Error patterns by performance for the OA. C) Error patterns by performance for the YA group. * Symbolizes significance at $p < 0.05$ and * ** at $p < 0.001$.

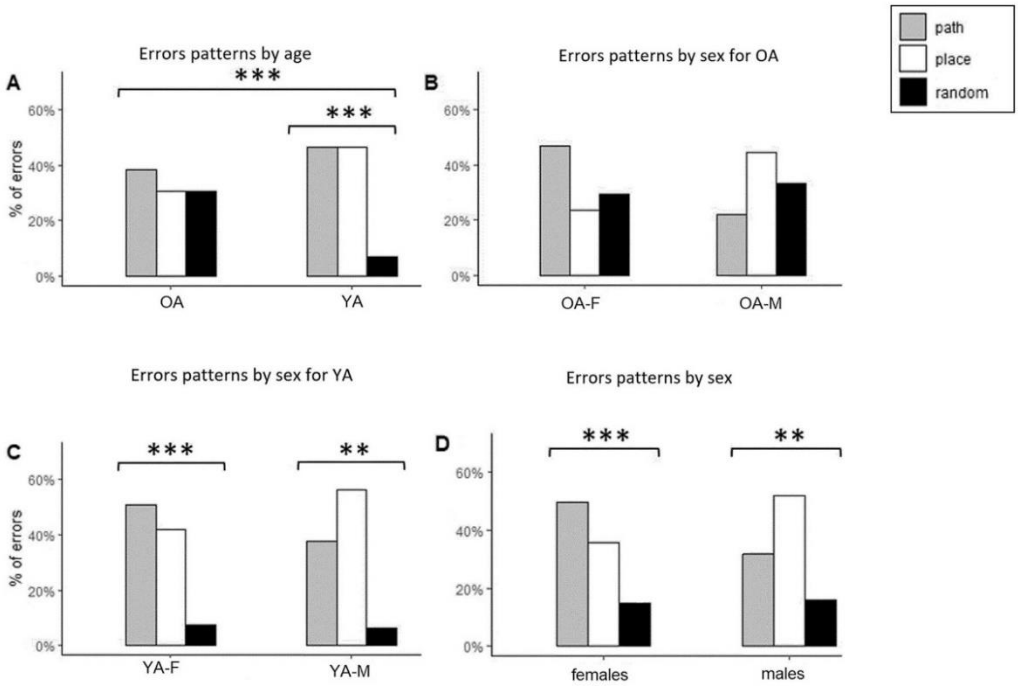

Fig. 7. A) Error pattern frequencies by age in Olde Adults (OA) and Young Adult (YA) groups, B) Error pattern frequencies by sex in Old AdultsOA, C) Error pattern frequencies by sex in YA, and D) Error pattern by sex (female and male groups). VSWM performances within the whole sample of errors. * Symbolizes significance at $p < 0.05$, * * at $p < 0.01$ and * ** at $p < 0.001$.

33.9 %) and less path-sparing (32.6 % vs 57.1 %) and random patterns (4.6 % vs 9 %) than lower performers ($X^2(2, N = 99) = 8.154$; $p = 0.016$) (Fig. 6C). The distribution of error patterns significantly differed in young higher performers ($X^2(2, N = 43) = 21.814$; $p < 0.001$) and young lower performers ($X^2(2, N = 56) = 19.536$; $p < 0.001$). To summarize, a clear strategy selection was identified only in the young group showing that the higher performers produced more place-sparing errors, and the lower performer produced more path-sparing errors.

3.3.2. Errors patterns analysis by age group

We observed a significant difference in the distribution of error patterns between age groups. YA showed more place-sparing (46.5 % vs 30.8 %) and path-sparing (46.5 % vs 38.4 %) patterns than OA but less random error patterns (7 % vs 30.8 %) (X^2 (2, N = 151) = 15,116; $p = 0.001$) (Fig. 7**A**). Moreover, we observed significant differences of frequencies for error patterns within the YA only ($X^2(2, N = 99) = 30{,}727$; $p < 0.001$). The frequency of the three patterns did not differ for OA ($X^2(2, N = 52) = 0615$; $p = 0.735$). To summarize, we found that the OA produced more significant random errors than the YA. Additionally, the YA presented equal proportion in the error patterns selection for place and path-sparing.

3.3.3. Errors patterns analysis by sex

We observed no significant difference in the distribution of error patterns between sexes in our whole population (X^2 (2, N = 151) = 4.553; $p = 0.103$). However, within the female sample, we observed a significantly higher occurrence of path-sparing patterns (49.5 %) compared to place-sparing (35.6 %) and random (14.9 %) ones ($X^2(2, N = 101) = 18.436$; $p = 0.000$). For the male sample, we also identified significant differences in frequencies of error patterns with place-sparing patterns being the most represented (52 %) followed by path-sparing patterns (32 %) and random patterns (16 %) ($X^2(2, N = 50) = 9.760$; $p = 0.008$).

We also verified if there was a sex effect on the distribution of error patterns in both YA and OA groups. First, regarding the distribution of error patterns, we did not observe any sex effect in the OA group ($X^2(2, N = 52) = 3.619$; $p = 0.163$) (Fig. 7**B**). The patterns were similarly distributed among OA-F ($X^2(2, N = 34) = 3.059$; $p = 0.217$) as well as among OA-M ($X^2(2, N = 18) = 1.333$; $p = 0.513$).

Second, we did not observe any sex effect in the distribution of error patterns within YA, ($X^2(2, N = 99) = 1.837$; $p = 0.399$) (Fig. 7**C**). However, the distribution of error patterns significantly differed among YA-F whom made more path-sparring error (50.7 %) than place-sparing (41.8 %) and random ones (7.5 %) ($X^2(2, N = 67) = 20.985$; $p < 0.001$). We also observed differently distributed patterns among YA-M who made more place-sparing error patterns (56.3 %) than path-sparing (37.5 %) and random ones (6.2 %) ($X^2(2, N = 32) = 12.25$; $p = 0.002$).

To summarize, we observed a preferential use of place-sparing strategies compared to other strategies by YA-M and a preferential use of path-sparing strategies by YA-F.

4. Discussion

The aim of this paper was to study spatial cognitive abilities such as VSWM, MR, and cognitive strategies during typical aging using a goal-oriented locomotion task. For this, we compared healthy YA and healthy OA using quantitative measures to identify spatial cognitive changes in aging based on the navigational strategies applied in the VWalCT.

4.1. VSWM performances

The VSWM performances in the VWalCT were analyzed using two different methods: the classical *Visuospatial working memory (VSWM) Span score,* and *the Score point attribution method (SPA).*

4.1.1. Classical VSWM Span score

As expected, the results of the classical span score shed light on a significant difference in the VSWM performances between the YA and the OA in the VWalCT. This finding suggests an important advantage for the young group because they were able to recall more correct sequences than the older group (Kronovsek et al., 2020; Perrochon et al., 2018; Piccardi et al., 2014a, 2014b, 2011). It seemed that spatial cognitive assessment lead to the detection of an initial cognitive age related decline in typical participants around 47 years old (Piccardi et al., 2014b). Moreover, it has been shown that spatial disorientation, VSWM impairments and the occurrence of more inadequate spatial strategies could be among the initial symptoms of MCI at early stages of the Alzheimer disease (Bianchini et al., 2014; Iachini et al., 2009; Perrochon et al., 2014). Complementary to these results, no sex differences were evidenced with the classical VSWM score span method analysis. However, this result appeared inconsistent with previous research indicating that there was a sex difference in the WalCT and in spatial navigation (Piccardi et al., 2014b).

4.1.2. SPA performances

In addition to the classical span score analysis, the SPA analysis revealed an age and sex difference only in the YA group. It also showed that the OA group had lower VSWM performances in comparison with the YA in the SPA. Concerning the OA group, the results suggest that there is a significant decrease in cognitive abilities regarding the processing of spatial information. Their performances were characterized by the incorrect recalling of spatial locations, spatial locations' order, and the direction between various locations. These results are corroborated by a decline in the VSWM capacities during aging (Perrochon et al., 2018, 2014; Piccardi et al., 2013). Moreover, there were no sex differences observed in the OA group.

In contrast to the classical span score analysis, a sex difference was observed in the young adult group. The YA-F showed significantly lower SPA in comparison to YA-M. We noted that for equivalent VSWM span scores between males and females, the YA-F made more errors or more significant errors (i.e., wrong locations and wrong correct order) than YA-M during their failed sequences. These findings suggested that the YA-F recalled less spatial information (i.e., correct spatial locations) than the YA-M. It could be possible because the SPA scoring system allowed us to analyze more quantitative information about the recalling process (i.e., spatial location and order) than the classical span score analysis. Thus, it seems that the *SPA is a reliable quantitative method to analyze spatial cognitive skills during navigation.* Taken together, these results confirmed our hypothesis about age-related differences in VSWM and it is consistent with previous neuroscientific literature (Iachini et al., 2009; Nori et al., 2015; Piccardi et al., 2014b).

4.2. Mental rotation abilities

4.2.1. Mental rotation paper test (MRT)

Cognitive processing in the VWalCT involves updating, and recalling of spatial information when moving, and it requires complex *mental* rotations processes(Carbone et al., 2020; Gallou-Guyot et al., 2020; Piccardi et al., 2008; Röser et al., 2016). Our analysis of the MRT revealed important differences between the OA group and the YA group. The YA group showed better MRT performances than the OA group. Moreover, we found a positive correlation between MRT performances and the VSWM span (Carbone et al., 2020; Kronovsek et al., 2020). However, we did not find any sex effect on MRT rotation abilities (Jansen and Heil, 2009).

4.2.2. Online mental rotation of the remembered array

The percentage of success per sequence analysis in the VWalCT suggested that the recalling of the sequences were modulated by the number of body rotations required for a given sequence. The performances of both groups (OA and YA) were impacted when they were tasked to reproduce sequences requiring more important body rotations during navigation. Initially, the participant has encoded and stored (memorized) a sequence of locations from his/her view perspective. During locomotion, we believe that the difficulty of the task increases when the demand for body rotations increases and requires the participant to mentally update their spatial map.

In line with these assumptions, our assessment of *online mental rotation* revealed important differences in age and sex for both age groups. The YA group produced significantly less errors than the OA group. Moreover, YA-F were more likely to produce *angle-related errors* than YA-M. Thus, YA-F recall fewer correct locations than males when the rotation requires consecutive 90° body rotation in the sequence challenging their usual cognitive strategies. The body rotations demand a mental spatial cognitive map rotation update to complete a sequence which is a costly cognitive process. These results could be related to the difficulty for females to perform MR in spatial tasks (Coutrot et al., 2018; Reilly and Neumann, 2013), and to base their spatial navigation on complex allocentric processing (Lambrey and Berthoz, 2007).

However, the opposite pattern was observed in OA-M were more likely to make ARE than OA-F. These results are surprising because no other spatial measures (SPA, MRT, and VWalCT span Score) used in this study were able to show a sex effect in OA. Indeed, the sex effect in aging studies on spatial abilities seems to be relatively small (Borella et al., 2014a). Thus, it could be that even when failing more on locations following a rotation of 90° or more, OA-M are able to find alternative strategies to maintain their performances equal to OA-F.

The VWalCT is a more complex task than the classical paper-based tests because it involves a continuous updating of spatial information while navigating and changing perspective. It requires a higher level of MR abilities. It is thus coherent that this task is more discriminant at the inter-individual level than classic tasks and it allows us to find a sex effect. It seems that the differences observed in YA group which could be an advantage for males regarding spatial cognitive abilities deteriorate with the neurocognitive aspects of aging.

4.3. Strategies selection during navigation

We studied the differences in error patterns for high and low performers in VSWM (Belmonti et al., 2015c). Then, we analyzed their strategies selection according to age and sex during navigation.

4.3.1. Spatial cognitive strategies associated with the level of VSWM performances

We observed that higher performers in VSWM relied more on *place-sparing error patterns* (i.e., the participant reached the correct spatial locations in each sequence but not necessarily in the right order) whereas lower performers in VSWM produced more *path-sparing error patterns* (i.e., the participant generated a globally correct trajectory but not necessarily with the correct spatial locations).

The same pattern of results was found by investigating differences in error patterns frequencies in our YA group. However, no differences were found in OA when looking at the level of VSWM performances.

We consider that *place-sparing* strategies are based on an *allocentric* processing of space and *path-sparing* strategies are based on an *egocentric* processing of space during navigation. Indeed, Belmonti et al. (2016) observed that in children with cerebral palsy, the frequency of *path--sparing* errors increased with the extent of the right hemispheric lesion, and these errors were associated with poorer performances. As the right hippocampus has been linked with *allocentric* navigation and the left one with *egocentric* navigation (Lambrey et al., 2008) the authors suggested that right hemispheric impairments lead to the use of more *egocentric*/sequential strategies.

Here, we considered that a flexible combination of an *allocentric* and an *egocentric* processing of space favors an optimal storing of the information accessible in the long term. For instance, during the test, the participant encoded and stored the sequence according to an *egocentric perspective* but during an "optimal" recalling, the participant had to switch to an allocentric processing of space. This mental flexibility yields better VSWM performances thanks to the subsequent decrease in the working memory resources demanded during the test (Belmonti et al., 2015b; Burgess, 2006; Castilla et al., 2021).

Therefore, the VWalCT performances have been linked to executive functions because it requires the participant to inhibit an automatic response (i.e., *egocentric strategy*), switching to a more elaborated strategy (i.e., *allocentric strategy*), and monitor the performances (Kronovsek et al., 2020; Perrochon et al., 2014). We can assume that higher performers in our study may have better mental flexibility allowing them to switch more efficiently between strategies. Consequently, the VWalCT requires not exclusively VSWM but also a large panel of spatial cognitive processes such as executive functions and MR.

4.3.2. Age-related differences in navigational strategies

Regarding age-related use of strategies, the results indicated that YA relied more on an adequate combination of *Place/path-sparing strategies* presenting few *random errors*. In contrast, the OA presented significantly more *random errors* than the YA. This could be interpreted as having a lack of spatial strategy due to the VSWM being overloaded with information. These results seemed consistent with the findings of (Belmonti et al., 2015b) in which healthy YApresented few *random errors* in a WalCT task. According to the results by (Perrochon et al., 2014) random errors are present in healthy OA's responses but are still significantly lower than in participants with MCI (Stephan et al., 2012)(Stephan et al., 2012). An important number of random responses could thus be used as a pathological index when comparing healthy OA and MCI patients. In our study, the OA group has more difficulties applying an optimal combination of *ego/allocentric strategies* compared to YA.

We suggest that developmental changes in navigational strategies through aging can be interpreted in at least three ways. First, OA may have difficulties to recruit the brain areas supporting switching between strategies (*ego/allocentric*) and/or *allocentric processing* thus leading to more random responses. The neuroscientific literature describes an age-related under-recruitment of *hippocampal/parahippocampal* structures supporting allocentric processing and of the *retrosplenial cortex* assuring the conversion from *egocentric to allocentric* representations or vice-versa (Lithfous et al., 2013; Moffat, 2009). This under-recruitment may result from the observed loss of neural specialization with aging (Logan et al., 2002). These processes could already happen during the encoding of the spatial information. For example, Kronovsek et al. (2020) showed an under-activation of the dorsolateral prefrontal areas for OA during the encoding of the sequences in VWalCT. According to Baddeley (1998) (See also (Curtis and D'Esposito, 2003) this area supports executive functioning and in the context of navigation is necessary for planning, selection of relevant spatial strategies, and the ability to switch to more relevant strategies if required.

Second, it may also result from a deficit in the updating of information during the retrieval of the sequences. Lower SPA and higher ARE-r for OA tend to confirm this hypothesis. The loss of spatial data while recalling the sequence could be due to increased integration costs when updating the representation of locations after rotating. It fits with the assumptions that spatial integration happens while acting (Meilinger et al., 2011).

Finally, random errors could occur due to a higher cognitive load (i.e., amount of working memory resources) in the online switching of strategies from *egocentric to allocentric* (Harris and Wolbers, 2014). These difficulties to flexibly switch between strategies may also be linked to the age-related decline in executive functioning which is largely described as a global factor explaining the cognitive decline in aging (West, 2000).

4.3.3. Sex-related differences in navigation strategies

Our findings showed that males relied more than females on *allocentric strategies* during navigation as they produced significantly more *place-sparing errors* than *path-sparing* and *random* ones. The opposite pattern was observed for females who relied more on *egocentric strategies* as significantly more *path-sparing* errors were produced rather than *place-sparing* and *random* ones during navigation. Similar results were found in YA participants but not in OA participants for whom no preferential strategies were apparent.

This preferential use in terms of strategies can be explained by previous research indicating that during locomotor tasks, men based their strategies on space geometry and self-motion perception, whereas females based theirs with a preference on visual landmarks (Bianchini et al., 2014; Burgess et al., 2004; Lambrey and Berthoz, 2007; Saucier et al., 2002). Thus, it is possible to suggest that males tend to use an allocentric processing of spatial information which is supposed to be a higher-level strategy, or are more able to switch between egocentric to allocentric strategies.

Concerning the OA group, we did not find any preferential use of navigation strategies for males or females. It seems that aging influences VSWM and MR abilities (Borella et al., 2014a). It may be linked to a decline of the allocentric navigation capacities of spatial treatment and to the possibility of switching from one strategy to the other (Colombo et al., 2017; Harris and Wolbers, 2014).

In our study, OA-M seemed to be more affected by the rotations requested during locomotion than OA-F. It could explain the interesting observation that the OA-M compared to the YA-M appeared to lose this preferential strategy at a later age.

5. Limits and perspectives

We acknowledged some limitations and perspectives that could be taken into consideration for future research. Our sample size was not balanced relative to the male group, as unfortunately, the females outnumbered the males. Moreover, we believe that it is important to use more trials by sequence (for instance, 5 trials for each sequence) in order to explorein-depth spatial navigation strategies. Having more trials by sequence would allow us to obtain more quantitative data and propose stronger analyses.

Although the investigation of the changes in navigational strategies with age still needs to be replicated in further studies to support the presented findings. Previous research supports that the use of rehabilitation protocolsn based on virtual reality or innovative technologies help to compensate for cognitive deficits in spatial treatment observed in OA with mild cognitive impairment or dementia (Zhu et al., 2021). Moreover, it can increase the understanding when intervening in cognitive rehabilitation in patients with MCI or early stages of dementia (Borella et al., 2014a; Mitolo et al., 2017).

Although the investigation of the changes in navigational strategies with age still needs to be replicated in further studies to support the presented findings, Previous research supports that the use of rehabilitation protocols based on virtual reality or innovative technologies which can help to compensate for cognitive deficits in spatial treatment observed in OA with mild cognitive impairment or dementia (Kim et al., 2019; Kober et al., 2013; Tieri et al., 2018; Zhu et al., 2021).

It is important to take into consideration that sex-related differences in spatial navigation can be influenced by biological (e.g., sexual hormones) (Bianchini et al., 2018; Driscoll et al., 2005; Scheuringer and Pletzer, 2017), emotional (e.g., anxiety and depression) (Lawton, 1994; Munoz-Montoya et al., 2019; Wolbers and Hegarty, 2010), and personality factors (i.e., individual differences) (Coluccia and Louse, 2004; Pazzaglia et al., 2018).

Further research should explore these factors in order to identify the impact of age and sex in spatial cognition.

6. Conclusion

The current work indicated that the VWalCT is a suitable tool for assessing visuo-spatial memory, navigational strategies, and online mental rotation capacities in the near distant extra-personal locomotor space. Taken together, these results suggest that age and sex have an impact on the VSWM, cognitive strategies, and MR during navigation. We suggest that the use of this SPA can: a) be implemented as a complementary cognitive assessment and b) be used in the rehabilitation of spatial impairments.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgements

Alexander Castilla was supported by Institut de Médecine Environnementale (IME), Paris, and we thank its Director Jacques Fradin for continuous and generous support.

Declaration of competing interest

No potential conflict of interest was reported by the author(s).

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Behavioural Brain Research 398 (2021) 112981

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Age-related decline in visuo-spatial working memory is reflected by dorsolateral prefrontal activation and cognitive capabilities

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ARTICLE INFO

Keywords:
Functional near-infrared spectroscopy
Prefrontal cortex
Aging
Visuo-spatial working memory
Cognition
Executive functions

ABSTRACT

Introduction: Visuo-spatial working memory (VSWM) performances undergo a decline throughout aging and are affected by the space in which the task is performed (reaching or navigational). Cerebral oxygenation and cognitive capabilities could explain this decline. We assessed the effects of age on cerebral oxygenation of the dorsolateral prefrontal cortex (dlPFC) in VSWM tasks in reaching and navigational space. We also assessed cognitive correlates of VSWM performance in each space.

Method: Thirty-one (31) young adults (YA) and 24 healthy older adults (OA) performed a battery of neuropsychological tests and the electronic Corsi Block-tapping Test in reaching space (e-CBT) and in navigational space on the "Virtual Carpet" (VWCT). Participants were asked to memorize and recall a sequential pathway, progressively increasing from 2 to 9 blocks. Their span score reflected VSWM performance. The dlPFC oxygenation (oxyhaemoglobin: ΔO_2Hb and deoxyhaemoglobin: ΔHHb) was measured by using functional Near-Infrared Spectroscopy (fNIRS) during the encoding of the sequential pathway in both tasks.

Results: YA had higher span scores than OA in both spaces. We identified a significantly stronger decrease of ΔHHb in YA compared to OA during encoding in VWCT. OA also exhibited significantly lower cerebral oxygenation in VWCT compared to e-CBT. A decrease of ΔHHb was also associated with a better performance in VWCT. Finally, we identified the association of mental rotation and executive functions with VSWM performance in both tasks.

Conclusion: VSWM performance and cerebral oxygenation during encoding are impacted by aging. Space in which the task was performed was found to be associated with different cognitive functions and revealed differences in cerebral oxygenation.

1. Introduction

Aging is associated with spatial memory decline, including visuo-spatial working memory (VSWM) [1]. VSWM seems to be one of the major cognitive processes involved in spatial navigation and route learning [2,3]. VSWM could be involved in maintaining spatial information during navigation, the recall of previously visited locations and cognitive mapping of the environment [3].

The Corsi Block Tapping-Test (CBT) [4] is one of the most widely used clinical tests to assess VSWM in reaching space and has also been developed on a larger scale for performance in navigational space: the Walking Corsi Test [5]. This test has been further improved by computer control of both a table electronic Corsi Block Test and a computer-controlled set of light and tactile tiles: the "Magic Carpet". These have been used for navigational deficit studies in several pathologies in adult patients [6], and children (age 6 to adulthood) [7].

Abbreviations: VSWM, visuo-spatial working memory; CBT, corsi block tapping-test; e-CBT, electronic corsi block tapping-test; VWCT, virtual walking corsi task; dlPFC, dorsolateral prefrontal cortex; fNIRS, functional near-infrared spectroscopy; ΔO2Hb, oxyhaemoglobin; ΔHHb, deoxyhaemoglobin; EF, executive functions; OA, older adults; YA, young adults; CRUNCH, compensation-related utilization of neural circuits hypothesis.

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https://doi.org/10.1016/j.bbr.2020.112981
Received 1 June 2020; Received in revised form 21 October 2020; Accepted 22 October 2020
Available online 2 November 2020

Studies in aging have also shown that young adults (YA) outperformed older adults (OA) in VSWM performances in different spaces (reaching vs. navigational) [6,8–10].

Space seems to impact OA VSWM performances, since performances in reaching space appear to be superior to those in navigational space [6, 8]. These differences could be based on the fact that CBT in navigational space requires more and richer cognitive processes than in reaching space (storage of spatial information), and thus is more suited for the measure of a spatial memory closer to ecological conditions [5,9–12]. Indeed, spatial cognition is associated with various perceptual and cognitive processes, such as executive functions (EF) [3,13–16]. EF may allow individuals to maintain their goal, plan and select the appropriate strategies, manage their performance and flexibly adapt their mental state to environmental properties by maintaining relevant information and inhibiting irrelevant ones [17,18]. Anatomically, EF are known to strongly rely on the frontal lobe and especially the dorsolateral prefrontal cortex (dlPFC) [19,20]. Also, the involvement of VSWM and EF can be reflected in increased cerebral blood flow in the dlPFC during several spatial cognition tasks [3,21]. More precisely for VSWM, a fMRI study has highlighted dlPFC activation in a young population during the encoding of sequences in reaching space [22]. In another fMRI study comparing brain activation of a young population in reaching and in navigational space, authors found this time that the dlPFC, among other regions such as right lingual gyrus and calcarine sulcus, was specifically associated with encoding in navigational space [23]. The literature supposes that the differences of performances and neural basis between both spaces may be explained by the existence of two distinct VSWM systems each depending on a space [5,9–12,23]. However, the differential involvement of brain structures between spaces still needs to be substantiated.

EF are declining with age due to impairment in the functional and structural integrity of the brain, which could explain global decline in cognition in accordance to the dysexecutive hypothesis of cognitive aging [17,18,24,25]. Specifically, the dlPFC exhibits major shrinkage with age, which could explain the age-related EF decline in normal aging [17,18,26]. Associated with cognitive decline and structural changes differential neural correlates emerge between OA and YA across a wide range of cognitive tasks. In particular in the domain of working memory OA show important changes in the recruitment pattern of prefrontal regions compared with YA [27,28]. One above all has been frequently studied: an under-activation pattern of task-specific prefrontal regions in OA compared with YA [27–32]. This pattern is associated with poorer cognitive performances and has been classically linked with the brain lesion model of neurocognitive aging [17,18,26]. More recent researches also highlighted an interesting pattern of prefrontal over-activation during working memory encoding [27–32]. Current trends in neurosciences mostly relate it to compensatory processing and the maintenance of good performance in the short term. The Compensation-related Utilization of Neural Circuits Hypothesis (CRUNCH model of neurocognitive aging) was proposed to account for these patterns of overactivation and under-activation observed for older adults [31]. The overactivation pattern should occur at easy and intermediate levels (low cognitive load). As OA reach their maximal load capacity sooner than YA, they recruit more neural circuits involved in the task, a compensatory mechanism that allows age-equivalent performances. These are interpreted as strategic or neural adjustments to compensate processing inefficiency, in local or elsewhere areas of the brain. At high levels of difficulty, the under-activation pattern should occur as compensatory mechanisms for the functional deficiency in the processing mediated by the areas are no longer effective at these levels of cognitive load, as a result of reaching a resource ceiling. This under-activation might reflect poor strategy uses and the subsequent recruitment of brain structures which are inadequate for the task [27–32], and therefore may explain low performances in OA. Rather than simply occurring at a high cognitive load, Schneider-Garces, Gordon, Brumback-Peltz & Shin [32] found evidence that this under-activation pattern may be linked to individual variations in working memory span; the reaching of a resource ceiling could be associated with a subjective span.

Yet, the few studies assessing the brain activation in reaching and navigational space have only focused on a young population [22,23] and little is known about age-related compensation and the brain mechanisms supporting VSWM in both spaces.

This lack of literature is probably due to the technical limitations of neuroimaging systems in real conditions. Most of the studies assessing the age effect on neural correlates of VSWM have used fMRI systems [33, 34]. Those systems show major disadvantages, the most important being the lack of ecological validity the studies suffer from, especially the ones claiming to study spatial processes. Indeed, the participant must lie within the confines of the magnet bore which produces loud noises and the system is also very sensitive to movement artifact. Recent advances in mobile brain imaging, such as functional Near-Infrared Spectroscopy (fNIRS), allow new opportunities in spatial cognition and navigation studies [35]. fNIRS allows to measure local variations of haemoglobin concentration changes related to neuronal activity by the phenomenon of neurovascular coupling [36]. The cortical activity in stimulated area increases the oxygen demand. Oxygen is carried by the haemoglobin. Thus, the local vasculature responds by flooding the cortical area and surrounding tissue with oxygenated form of haemoglobin (ΔO_2Hb) usually accompanied with a concomitant drop in its deoxygenated form (ΔHHb). The fNIRS allows to measure cerebral oxygenation in situ with a significant temporal resolution [36]. Besides, this tool seems robust in measuring functional activity during cognitive tasks, as the result of prefrontal cortex activation is similar to magnetic resonance imaging [37]. This device is currently used to examine the neural control of gait in real walking conditions [38]. Also, fNIRS may be used to study the effect of age-related brain activity in VSWM tasks.

The main objective of this pilot-study was to assess the effect of age on cerebral oxygenation in VSWM tasks according to space (reaching or navigational). A secondary objective of this study was to determine if EF and cerebral oxygenation were involved in VSWM performance, either in reaching or navigational space. We hypothesized that: i) YA would show a better VSWM performance and therefore higher cerebral oxygenation than OA resulting in a stronger increase of ΔO_2Hb concentration and a stronger decrease in ΔHHb concentration, and ii) performances in cognitive tests would be explicative variables of VSWM performances, especially for navigational space.

2. Material and methods

2.1. Population

Fifty-five participants were recruited in this cross-sectional study, including 31 YA and 24 healthy OA. The inclusion criteria were: i) age between 18 and 35 years old for YA and over 65 for OA, ii) fluency in the French language. Exclusion criteria were: i) motor and perception (visual and auditive) disorders, ii) the presence of depressive symptoms (mini Geriatric Depression Scale (GDS) score >1), cognitive impairment (Mini Mental State Examination (MMSE) score <24), an amnesic complaint, the history or presence of neurological and/or psychiatric diseases, and the use of medications altering memory or cognitive functions. Written informed consent was obtained from each participant, and this study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki (1983).

2.2. Experimental design

The experimental protocol was divided into two phases: i) VSWM performance assessment in reaching space (i.e., e-CBT: electronic Corsi Block Tapping-test) and in navigational space (i.e., VWCT: Virtual Walking Corsi Task), ii) the administration of a battery of neuropsychological tests. The test administration order was randomized by a computed random number generator algorithm.

2.2.1. VSWM performance assessment

The e-CBT and VWCT conditions were based on Perrochon et al. [10] (Fig. 1: **A, B and C**). A main difference with the original study is that in the present study the participant performed the e-CBT while standing up. In both tests, the participant had to memorize (encoding phase) a sequence of blocks successively lighting up in red. After a computer-generated audible signal marking the end of the sequence, the participant had to reproduce (restitution phase) the sequence in the same order. The number of items gradually increased from 2 to 9. The participant had 2 trials per sequence length. If he succeeded in reproducing one of the two sequences, the sequence length increased by one item [39]. If the participant failed in both trials, the test ended and his span score was the number of items in the last sequence successfully reproduced.

In reaching space (i.e., the e-CBT), the participant stood in front of the computer screen in order to maintain the same head angle as during the encoding phase of VWCT and thus to ensure the reliability of the fNIRS measurement (Fig. 1: **B**). The computer was mounted at 700 mm on a table adjusted (min =90 cm; max =120 cm) according to the participant's height. The e-CBT sequences were displayed on a 15-inch computer screen. In this situation, the participant had to point out the blocks one after the other by touching the computer screen in order to reproduce the sequence. Although the screen was close to vertical and the floor (VWCT) was horizontal, we ensured, by the angle of the computer screen, that the participant maintained the same visual direction as much as possible (Fig. 1: **B and C**).

For navigational space (i.e., VWCT), we used the "Virtual Carpet"™ developed by A. Berthoz and M. Zaoui, previously described in Perrochon et al. [10] (Fig. 1:**A**). The participant stood on a starting point 1500 mm away from the test projection space during the encoding phase (Fig. 1: **C**). During the restitution phase, the participant had to walk on the numbered blocks in the same order as the presentation, beginning from the starting point and returning to it when finished. The projection space (W316ST Optoma® projector, Taiwan) was 3000 mm × 2400 mm (scale 1:10 in regards to the e-CBT) and reproduced the same layout as the e-CBT (Fig. 1: **D**).

Participants were wearing a fNIRS device (Portalite®, Artinis Medical, Netherlands) during VSWM tasks. The device consists of two bilateral optodes positioned on the right (Fp2) and left (Fp1) dorsolateral areas of the prefrontal lobe (EEG 10–20 system). Both optodes were connected to an independent portable battery maintained by armbands (Fig. 1). During the baseline measurements and encoding of the sequences, the participant was asked to limit head movements in order to avoid motion artifacts. In support of this, we ensured that the participant could have a global vision of the entire test layout from the starting point without having to move his head.

2.2.2. Cognitive functions assessment

The participants performed a neuropsychological test battery to measure executive functioning. We used the ZOO map test part A [40] which assesses planning abilities. The participant is asked to navigate through a zoo map while sticking to instructions on places to visit and their order, the variable was the score. We used the Trail Making Test (TMT) [41] which assesses mental flexibility (part B) and attention (part A) as well as visuo-spatial exploration. The participant must connect in ascending order circles containing numbers from 1 to 25 in part A, whereas he alternates between numbers and letters in part B. For TMT we measured time and the number of errors. We also used REY's figure [42] for planning function, attention and working memory. Participant was asked to copy a figure, without knowing he would be asked to reproduce it after a quick distraction. The score was based on the number of correct reproduced items of the figure for both copy and retrieval conditions. To measure inhibition, we used the Stroop test [43] consisting in three conditions: naming the colours of squares, reading words of colours in black ink, and naming the ink colour while inhibiting the non-congruent word reading (interference condition). We measured time for the three conditions. In addition to these executive functioning tests, we used the redrawn Mental Rotation Test (MRT) to assess mental rotation capabilities [44]. In MRT the participant is asked to determine which two of a four sample stimuli are rotated versions of a target stimulus; we measured the score on 24 items. The order of neuropsychological tests was randomized to avoid biases related to cognitive fatigue.

2.3. Outcomes

The main outcome was bilateral dlPFC activation measured by fNIRS and calculated by the change in oxygenated and deoxygenated haemoglobin relative concentration (respectively ΔO_2Hb and ΔHHb) (*Acquisition Software* – Oxysoft® version 3.0.97.1). The differential pathlength factor was calculated from the age of YA and set by default to 5 for OA [45]. A baseline was performed before e-CBT and VWCT: the participant had to stare at a red cross located in the centre of the test's layout (i.e., the screen in e-CBT and the carpet in VWCT) for a 20-second period. The baseline was done while standing in front of the screen in e-CBT and on the starting point in VWCT, in order to maintain the same angle of the head in both conditions (Fig. 1: **B and C**). We assessed dlPFC oxygenation only during the encoding of the sequences, as head motion during the restitution phase was producing significant artifacts. Since there were two sequences of encoding for the span score in each test, we computed the mean oxygenation in both sequences. We used Matlab-based scripts when needed for detection and correction of motion artifacts, and a 0.1 Hz low-pass filter was used to remove physiological and instrumental noise [46]. We obtained the relative concentration changes in oxyhaemoglobin (ΔO_2Hb) and deoxyhaemoglobin (ΔHHb) ($\mu mol.L^{-1}$) in the selected interval of the test (i.e.,

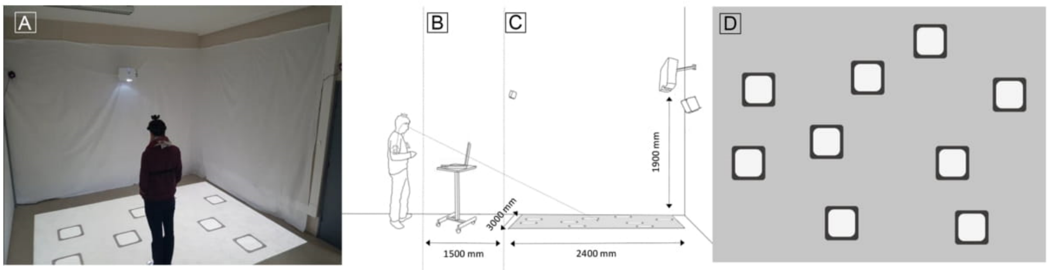

Fig. 1. Plan of the experimental conditions. The participant is wearing the fNIRS device. The experimental design was intended to maintain the same head angle during both conditions. **A)** Picture of the experimental environment, VWCT is being performed by a participant. **B)** e-CBT performed on a computer screen. **C)** VWCT performed on the projected virtual carpet. The participant is wearing two movement tracking sensors on the head and the chest connected to the two HTC base stations attached to the walls. **D)** Test layout.

the last 10 s), which were normalized by subtracting the mean values of the last 10 s of baseline from them. The failure span (span score +1) was chosen in order to assess prefrontal oxygenation during the subjective resource ceiling, in accordance with Schneider-Garces et al. [32] findings. In order to avoid any possible bias due to cognitive fatigue effect on prefrontal oxygenation during failure span encoding we also analysed prefrontal oxygenation during maximum span encoding (the span score).

The secondary outcomes were span scores in VSWM and cognitive performance. In e-CBT, the sequence validation was approved by the experimenter, while it was computerized in VWCT. During VWCT, the participant had to wear two motion trackers (HTC® Vive Tracker, HTC, Taiwan) coupled with the base stations (HTC® Vive Lighthouse). The entire device was connected to the RigidBodyViewer Software (Collège de France, Paris, France) (Fig. 1: **A and C**). For neuropsychological tests, we focused on the raw scores in MRT, ZOO, REY, Stroop and TMT.

2.4. Statistical analysis

The normality assumptions to perform parametric tests were met (Shapiro-Wilk test). Student tests were used in order to compare the socio-demographic variables and neuropsychological scores between both groups. We performed a 2*2 mixed ANOVA with the two populations (OA vs. YA) and the two spaces (VWCT vs. e-CBT) to study their effect on the VSWM span score. We also conducted 2*2 mixed ANOVAs with the two age groups (YA vs. OA) and the two spaces (VWCT vs. e-CBT) in order to study their effect on cerebral oxygenation parameters during the encoding of the maximum span and failure span. Univariable linear regressions were performed to examine relationships between cerebral oxygenation parameters and cognitive function capabilities (independent variables) and span scores in e-CBT and VWCT (dependent variable). Separate multivariable linear regressions by stepwise method were run to examine whether cognitive function variables and cerebral oxygenation parameters would explain VSWM performance in different spaces. To our knowledge, there is no literature on this subject, so it is impossible for us to estimate the number of subjects needed for this study. For all analyses, the statistical significance level was set at alpha <0.05. The statistical analysis was performed using IBM SPSS® Statistics version 22 (IBM Corp, Armonk, USA).

3. Results

55 participants were included in this pilot-study: 31 YA (22.8 ± 2.8 years; 19 female) and 24 OA (70.4 ± 3.7 years; 17 female). Socio-demographic and cognitive capabilities are presented in Table 1. We observed a decreased cognitive performance in OA (vs. YA) in all the neuropsychological tests; the MRT, ZOO, REY, TMT and STROOP ($p < 0.05$).

We also observed through the age*space ANOVA on span scores an overall effect of age, with YA showing higher span scores than OA (respectively 7.0 ± 1.5 vs. 5.1 ± 0.9; $F(1,53) = 39.657$; $p < 0.001$). We also found an overall effect of space, as participants showed better span scores in reaching space compared to navigational space (respectively 6.5 ± 1.4 vs. 5.5 ± 1.6; $F(1,53) = 55.496$; $p < 0.001$) (Fig. 2). We found no significant age*space interaction effect on VSWM span scores ($p > 0.05$).

3.1. Effects of aging on cerebral oxygenation in VSWM tasks

For the maximum span encoding, we observed overall effects of age, with YA showing higher ΔO_2Hb concentration than OA (respectively 5.3 ± 4.7 vs. 3.4 ± 2.9 μmol.L^{-1}, $F(1,53) = 8.54$; $p < 0.01$; Fig. 3: **A**) and lower ΔHHb concentration than OA (respectively -1.4 ± 1.7 vs.−0.7 ± 1.3 μmol.L^{-1}, $F(1,53) = 4.47$; $p < 0.05$; Fig. 3: **B**). We also found an overall effect of space, with participants showing higher ΔO_2Hb values in reaching space compared to navigational space (respectively 5.7 ±

Table 1
Demographic, psychologic, and cognitive characteristics of the study participants.

	Variables (unity) or [rank]	Young adults (n = 31)	Older adults (n = 24)	P value
Demographic, psychologic and cognitive characteristics	Age (years)	**22.8 ± 2.8 [19;31]**	**70.4 ± 3.7 [65;80]**	**<0.001**
	Female (%)	61.3 % (n = 19)	70.8 % (n = 17)	0.47
	Educational level	3.0 ± 0	3.3 ± 1.4	0.19
	MMSE [0–30]		28.2 ± 1.5	
	GDS [0–4]	0.1 ± 0.2	0.1 ± 0.3	0.79
	Female hormonal cycle	5.3 % (n = 1)		
Cognitive tests: Mental Rotation	MRT [0–24]	**5.9 ± 3.7**	**2.2 ± 1.5**	**<0.001**
Planning	ZOO [max 8]	**6.1 ± 2.8**	**3.9 ± 3.2**	**<0.001**
Attention. WM. Planning	REY C [0–36]	35.7 ± 0.6	35.2 ± 1.4	0.07
	REY R [0–36]	**25.9 ± 4.9**	**18.0 ± 6.2**	**<0.001**
Inhibition	STROOP D (s)	**50.6 ± 7.1**	**66.6 ± 12.9**	**<0.001**
	STROOP R (s)	**37.9 ± 5.2**	**47 ± 8.7**	**<0.001**
	STROOP I (s)	**79.6 ± 17**	**132.1 ± 30.2**	**<0.001**
	ΔSTROOP (I–D) (s)	**28.9 ± 16.4**	**65.4 ± 21**	**<0.001**
Cognitive flexibility. Visuo-spatial exploring	TMT A (s)	**22.1 ± 6.9**	**40.1 ± 14.6**	**<0.001**
	TMT B (s)	**50.5 ± 18.4**	**87.6 ± 59.2**	**<0.01**
	Δ TMTs (B-A)	28.4 ± 18.2	47.5 ± 51.4	0.06
	Errors TMT A (n.u)	0.1 ± 0.2	0.1 ± 0.3	0.45
	Errors TMT B (n.u)	1.5 ± 3.7	2.1 ± 3.4	0.49

Mean ± SD and range [minimum;maximum].
MMSE = Mini Mental State examination; GDS = Geriatric Depression Scale; MRT = Mental Rotation Test; REY C = Rey copy; REY R = Rey restitution; STROOP D = Denomination; STROOP R = Reading; STROOP I = Interference; TMT = Trail Making Test; WM = Working Memory. Data written in bold show an effect of aging on variables.

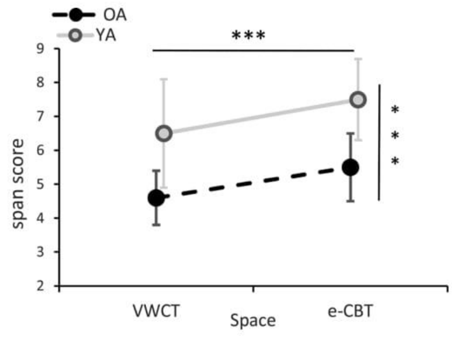

Fig. 2. Span scores means and standard deviations (represented by error bars) in VWCT and e-CBT for older adults (OA) and young adults (YA). Main effects of age (***: $p < 0.001$) and space (***: $p < 0.001$) were represented.

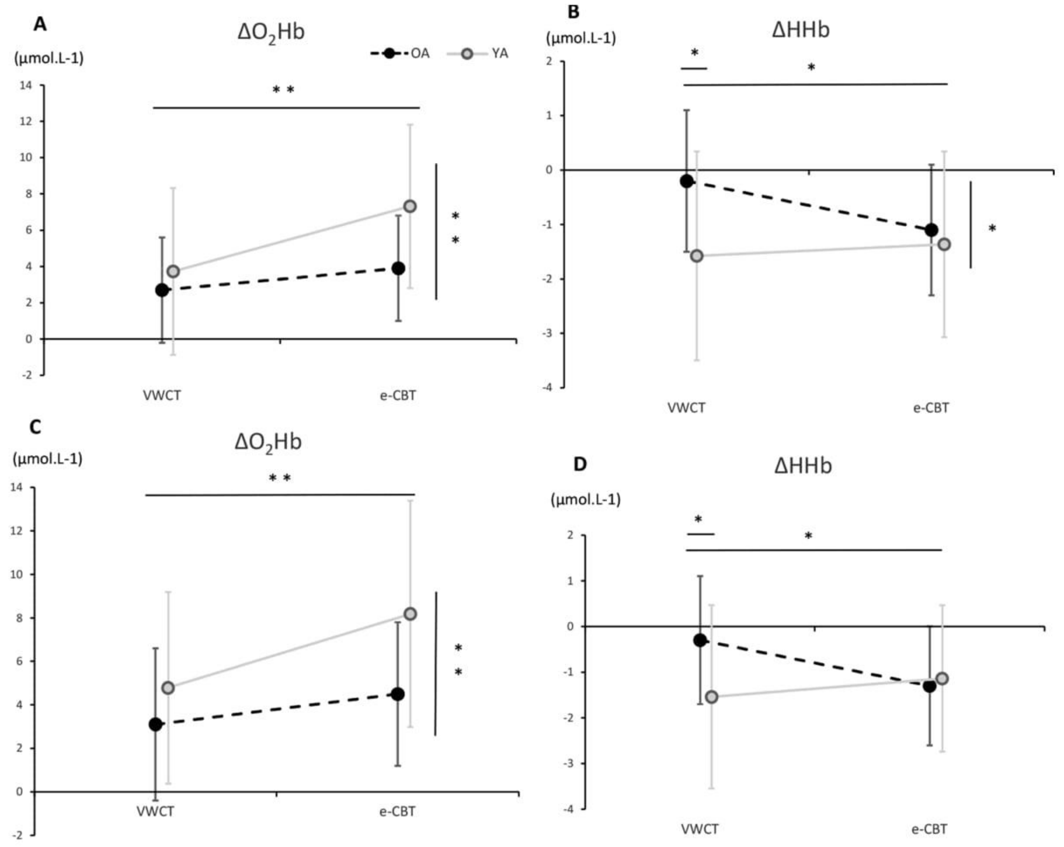

Fig. 3. dlPFC oxygenation means and standard deviations (represented by error bars) for older adults (OA) and young adults (YA) in reaching and navigational space for maximum span and failure span. **A)** ΔO_2Hb during the encoding of maximum span. Main effects of age (**: $p < 0.01$) and space (**: $p < 0.01$) are represented. **B)** ΔHHb during the encoding of maximum span. We represented differences between YA and OA in VWCT (*: $p < 0.05$), space effect for the OA group (*: $p < 0.05$) and the main effect of age on the right of the figure (*: $p < 0.05$). **C)** ΔO_2Hb during the encoding of failure span. Main effects of age (**: $p < 0.01$) and space (**: $p < 0.01$) are represented. **D)** ΔHHb during the encoding of failure span. We represented significant differences between YA and OA in VWCT (*: $p < 0.05$) and space effect for OA group (*: $p < 0.05$).

4.1 vs. 3.2 ± 3.9 µmol.L^{-1}, $F(1,53) = 8.69$; $p < 0.01$; Fig. 3: **A**). We did not find any significant age*space interaction effect on ΔO_2Hb concentration ($p > 0.05$). Finally, we found a significant age*space interaction effect on the ΔHHb concentration ($F(1,53) = 5.15$; $p < 0.05$). Post hoc analysis revealed a significant difference between groups only in navigational space, with a lower ΔHHb concentration for YA compared to OA (respectively -1.5 ± 1.7 vs. −0.2 ± 1.3 µmol.L^{-1}, $p < 0.05$, Fig. 3: **B**). Post hoc also revealed that only OA showed significant differences of ΔHHb between both spaces, with a lower value in reaching space compared to navigational space (respectively -1.2 ± 1.3 vs. −0.2 ± 1.3 µmol.L^{-1}, $p < 0.05$, Fig. 3: **B**).

For the failure span encoding, we observed an overall effect of age, with YA showing higher ΔO_2Hb concentration than OA (respectively 6.3 ± 4.9 vs. 3.8 ± 3.4 µmol.L^{-1}, $F(1,53) = 11.07$; $p < 0.01$, Fig. 3: **C**). We also found an overall effect of space, with participants showing higher ΔO_2Hb values in reaching space compared to navigational space (respectively 6.4 ± 4.6 vs. 3.9 ± 4.1 µmol.L^{-1}, $F(1,53) = 7.36$; $p < 0.01$; Fig. 3: **C**). However, we did not find any significant age*space interaction effect ($p > 0.05$). Finally, we found a significant age*space interaction effect on the ΔHHb concentration ($F(1,53) = 6.90$; $p < 0.05$). Post hoc analysis revealed a significant difference between groups only in navigational space, with a lower ΔHHb concentration for YA compared to OA (respectively -1.7 ± 2 vs. −0.3 ± 1.4 µmol.L^{-1}, $p < 0.05$, Fig. 3: **D**). Post hoc also revealed that only OA showed significant differences of ΔHHb between both spaces, with a lower value in reaching space compared to navigational space (respectively -1.3 ± 1.3 vs. −0.3 ± 1.4 µmol.L^{-1}, $p < 0.05$, Fig. 3: **D**).

3.2. Association between dlPFC activation and VSWM performance

For the e-CBT, the span score showed a positive correlation only with the dlPFC ΔO_2Hb during maximum span encoding ($r = 0.41$; $p < 0.01$) and failure span encoding ($r = 0.32$; $p < 0.05$, Table 2). For the VWCT, the span score was associated with more oxygenation parameters such as ΔHHb concentration during the maximum span encoding and failure span encoding ($r = -0.52$; $p < 0.01$, $r = -0.50$; $p < 0.001$ respectively) and with the dlPFC ΔO_2Hb during the maximum span encoding ($r = 0.29$; $p < 0.05$) and during the failure span encoding ($r = 0.31$; $p < 0.05$).

3.3. Cognitive functions associated with VSWM according to space

Most of the neuropsychological tests, such as MRT ($r = 0.64$; $p < 0.001$), ZOO ($r = 0.45$; $p < 0.001$), REY R ($r = 0.60$; $p < 0.001$), STROOP I ($r = -0.63$; $p < 0.001$), TMT A ($r = -0.54$; $p < 0.001$), TMT B ($r = -0.40$; $p < 0.01$) and ΔTMTs ($r = -0.28$; $p < 0.05$) were associated with the span score in reaching space (Table 2). Similarly, MRT ($r = 0.68$; $p < 0.001$), ZOO ($r = 0.34$; $p < 0.05$), REY R ($r = 0.59$; $p < 0.001$), STROOP I ($r = -0.54$; $p < 0.001$), TMT A ($r = -0.49$; $p < 0.001$) and TMT B ($r = -0.33$; $p < 0.05$) were associated with the span score in navigational space.

Table 2
Correlations between raw scores in cognitive tests, VSWM tasks and oxygenation parameters in maximum span and failure span encoding.

Cognitive domain	Psychological tests	e-CBT r value	e-CBT P value	VWCT r value	VWCT P value
Mental Rotation	MRT	**0.64**	**<0.001**	**0.68**	**<0.001**
Planning	ZOO	**0.45**	**<0.001**	**0.34**	**<0.05**
Attention. WM. Planning	REY R	**0.60**	**<0.001**	**0.59**	**<0.001**
Inhibition	STROOP I	**−0.63**	**<0.001**	**−0.54**	**<0.001**
Cognitive flexibility. Visuo-spatial exploring	TMT A	**−0.54**	**<0.001**	**−0.49**	**<0.001**
	TMT B	**−0.40**	**<0.01**	**−0.33**	**<0.05**
	Δ TMTs (B-A)	**−0.28**	**<0.05**	−0.21	0.116
Span level	**Oxygenation parameters**				
Maximum span	ΔO_2Hb	**0.41**	**<0.01**	**0.29**	**<0.05**
	ΔHHb	−0.15	0.26	**−0.52**	**<0.01**
Failure span	ΔO_2Hb	**0.32**	**<0.05**	**0.31**	**<0.05**
	ΔHHb	−0.11	0.43	**−0.50**	**<0.001**

r = correlation coefficient (Bravais-Pearson). Data written in bold show a significant relation between raw scores in cognitive tests and span score.

3.4. Stepwise regression model

By performing stepwise regression, including age, level of education, sex, MRT, ZOO, REY R, STROOP I, TMT B and dlPFC oxygenation parameters, we found associations between the span score and age ($p < 0.05$), MRT ($p < 0.01$) and ZOO ($p < 0.05$) performance in reaching space (Table 3). Furthermore, we observed additional associations between the span score and dlPFC oxygenation during failure span encoding (ΔHHb: $p < 0.05$), MRT ($p < 0.001$) and REY ($p < 0.05$) scores in navigational space (Table 3). The total variance accounted for these models was strong, while these variables explained 67 % of VSWM performance in reaching space and 63 % of VSWM performance in navigational space (Table 3).

4. Discussion

This is the first study assessing the age-related effect on cerebral oxygenation in VWSM and the association of cognitive capabilities with VSWM according to space. We observed a significant difference of cerebral oxygenation depending on age, with higher dlPFC activation (i.e., decreased ΔHHb) for YA compared to OA when the participant was encoding the subsequent task in navigational space. dlPFC activation seems to be associated with VSWM performance, specifically in the navigational task. Finally, different EF (i.e., planning capabilities, attention) and mental rotation are associated with VSWM performance according to space.

4.1. Effect of aging on cerebral oxygenation in VSWM

First, we observed an effect of aging on VSWM performance, as YA outperformed OA. These results match findings of other studies, which demonstrated age-related deficits in VSWM performances in similar paradigms [6,8–10].

We found a global effect of age on ΔO_2Hb concentration with a stronger increase for YA. In navigational space, we found that YA showed a stronger dlPFC activation (i.e., decrease of ΔHHb) compared to OA during the encoding phase in navigational space (maximum span and failure span in VWCT). The increase of ΔO_2Hb and the decrease of ΔHHb is a typical intravascular oxygenation response to brain activity [47–49]. Thus, in our framework, OA showed an under-activation of dlPFC compared to YA.

Overall, ΔHHb was more affected by age-related effects and associated with VSWM performance in navigational space. ΔHHb is more affected by oxygen consumption than ΔO_2Hb, and therefore is a better indicator of activation than ΔO_2Hb [48]. However, ΔO_2Hb is often described as a more reliable indicator for functional brain activity because of its higher amplitude, and is less sensitive to noise [50,51]. Still, ΔHHb is a reliable indicator of functional activation, and we followed the Fishburn et al. [46] correction method to remove noise effects from the signal. Most of the recommended guidelines, from the design of the protocol to fNIRS instrumentation and analysis approaches to avoid false positives/negatives, were followed [52].

This prefrontal under-activation pattern is a well-known neural correlate of age-related decline in cognition [27–32]. It has been linked with a more global model of neurocognitive aging of the lesioned brain that links structural and functional changes in prefrontal cortex with age-related decline in cognition [17,18,26]. It is frequently observed in memory tasks which requires intentional encoding and the spontaneous production of encoding strategies [53].

Indeed, the age-related under-activation pattern during encoding could be linked to poorer cognitive strategies use by OA to encode the stimuli in memory and to plan restitution, hence leading to the recruitment of inaccurate cerebral areas [28,29]. OA often fail to use controlled and costly processing strategies to support their performance. As a support to this assumption authors have shown that training and providing strategies can reverse this pattern with a possible functional recovery of specialized brain regions which were under-used for the encoding [28,29]. This poorer strategy use is likely to be linked with decline in EF. Indeed, EF are required in acquiring new skills, selecting appropriate strategies, planning the execution of the task, monitoring behavioural responses and finding alternative strategies if the selected one is not efficient [17].

Table 3
Regression analysis for the variables identified as correlated to VSWM tasks.

Variables	e-CBT ($R = 0.81$; $R^2 = 0.67$) B value	P value	95 % CI Lower bound	Upper bound	VWCT ($R = 0.80$; $R^2 = 0.63$) B value	P value	95 % CI Lower bound	Upper bound
Age	**−0.3**	**<0.05**	−0.023	0.014	0.1	0.280	−0.027	0.008
Level of education	0.1	0.324	−0.144	0.426	−0.01	0.871	−0.336	0.285
Sex	−0.2	0.235	−0.022	0.902	−0.1	0.271	−1.034	0.297
ΔHHb (failure span)					−0.2	**<0.05**	−0.322	−0.005
MRT	**0.3**	**<0.01**	0.045	0.223	**0.4**	**<0.001**	0.091	0.303
REY					**0.3**	**<0.05**	0.008	0.129
ZOO	**0.2**	**<0.05**	0.019	0.187				

B = regression coefficient. **CI** = confidence interval. **R** = correlation coefficient. $\mathbf{R^2}$ = coefficient of determination. Data written in bold show a significant relation between raw scores in cognitive tests and span score.

This under-activation pattern may also be due to neural recruitment mechanisms changes within the older brain. OA tend to recruit regions not specified as specialized in the chosen task in a control young population [29]. The VWCT mobilises a wide neural network from visual occipital to parietal to prefrontal regions [23]. In particular, the parietal cortex is presumed to support the processing of self-generated locomotor movements in parallel of the encoding [23,54]. Its pattern of activation should be investigated and compared to prefrontal sites under-activation in further neuro-imaging studies. Except its role in executive functioning and VSWM, the dlPFC may finally also be implied in processing the movement along a learned route in a navigational environment and supporting strategy related to motor imagery [23,54].

For working memory, the CRUNCH model predicts that age differences in neural recruitment should vary with the level of task demand and subjective working memory load [31,32]. OA should recruit more neural and executive resources than YA at low cognitive load to support working memory and maintain equivalent performances. However, at higher levels of cognitive loads we should observe a prefrontal under-activation for OA as their processing capacity limits are reached, and compensatory mechanisms may no longer be effective. Thus, in our framework the results corroborate partly with the CRUNCH model, since we observed a prefrontal under-activation for OA compared to YA at high levels of cognitive load.

We can hypothesize that at lower spans (<4) the results should be consistent with the CRUNCH model and an over-activation could be observed for OA as frontally mediated executive processes may be recruited to support working memory performance [31]. However, we only focused on high cognitive load as dlPFC oxygenation measurements in low loads (<4th span) were not available. Indeed, a systematic methodology-focused study have enlightened a certain delay (≈ 6 s) between stimulus presentation and cortical haemodynamic response [55]. In addition, we need the last 10 s of the encoding phase for signal analysis. For this reason, we cannot analyse span 3 or lower (14 s duration).

Age differences in cerebral activation were particularly observed in navigational space. Since dlPFC has been specifically linked with navigational space and not reaching space [23] we can assume that it may explains why dlPFC oxygenation differences between our populations is only discriminated in VWCT. However, we found an overall effect of space on ΔO_2Hb, with higher concentration values in reaching space compared to navigational space during high span encoding. Thus, dlPFC oxygenation seems to be stronger in reaching space. It may be load-dependent, since reaching space allows better performances for both our populations than navigational space, which is known to be more complex and requires more resources [56]. Nevertheless, we did not find ΔO_2Hb to be linked with VSWM performance. While Nemmi et al. [23] linked dlPFC with navigational space, we found that ΔHHb was different between spaces for OA, with a stronger decrease in reaching space compared to navigational space. However, the observations of Nemmi et al. [23] were only done in a study of a young adult population (mean age 24.7 ± 4.5), and we cannot state that tests in both spaces lie on a distinct neural basis exactly in the same way as in the OA population. Thus, dlPFC may play a role in better performances of OA in reaching space compared to navigational space.

4.2. Cognitive correlates of space

We had assumed that raw scores on cognitive tests would be more associated with VSWM performance in navigational space because of the more active and complex nature of this task compared to the VSWM task in reaching space [5,9,11,12]. Our results would not allow us to confirm this hypothesis, as we observed that both spaces imply distinct cognitive processes (see R^2 values in Table 3) as well as common processes. Nonetheless, these results highlight the major association of mental rotation with VSWM performances [57]. Mental rotation may support the updating and mental manipulation of spatial information as the participant is orientating and moving through the environment [5,56, 57]. On one hand, the ZOO test [40] evidenced that planning ability was one of the EF associated with VSWM performance in reaching space. On the other hand, the analyses of the Rey figure [42] confirmed the strong association between executive functioning, in the maintenance of spatial information, the selection of appropriate strategies, the control of performance and mental flexibility and VSWM performance in navigational space. Our results allowed us to demonstrate a clear link between higher executive functioning and VSWM performances in different space. As we observed age-related deficits in all of these cognitive tests (Table 1), we could suppose that the decline of EF could partly explain the poorer VSWM performance in aging through their potential role in strategy production and especially in navigational space. In such case it would support the dysexecutive hypothesis of cognitive aging, that age-related memory differences and global decline in cognition may be mediated by the prefrontal area deterioration and executive dysfunction [17,18,26].

To summarise, VSWM performances in navigational space were associated with prefrontal ΔHHb concentration during the encoding of sequences, and appear to be associated with aging, mental rotation abilities, working memory, planning and attention, whereas reaching space VSWM performances were associated with mental rotation abilities and planning ability.

4.3. Limitations

Several limitations should be considered in future studies. First, fNIRS acquisition could only be done during the encoding phase of the sequences, due to the great number of head rotations and movements during the restitution phase in navigational space that induced large motion artifacts in the signal. Nevertheless, it has been demonstrated by means of EEG power analysis that encoding of visuo-spatial information is more cognitively challenging than retrieval because it requires more cerebral activation [58]. Moreover, as being said fNIRS analysis could not be done for low spans ($<$ 4th span) and thus they still need to be studied to demonstrate if age-related differences in patterns of cerebral activation really fit with CRUNCH model. Second, despite its important temporal resolution, fNIRS cannot be used to investigate deep brain structures involved in spatial memory, such as the hippocampus [3,21, 59]. We were also limited to two optodes in this study thus, we could not assess the lateralization effect. Since our device was not a multi-channel fNIRS, we were not able to investigate the involvement of the parietal cortex, which is a key structure in spatial working memory [23,54,60]. Furthermore, because of the switch of engaged brain areas due to aging from posterior to more anterior structures (PASA model) [61], it would be relevant in future studies to investigate the effects of age on parietal cortex activation. Third, cognitive tests allowed us to identify several implied cognitive functions such as mental rotation and EF in VSWM tasks, but this work remains to be conducted with more varied cognitive tests, as we limited them to avoid cognitive fatigue.

4.4. Perspectives

This research takes part in the investigation of brain mechanisms that tend to decline in aging and may be essential factors of age-related deficits in VSWM. VWCT could be used in the early detection of spatial memory impairment, such as in the dementias [1]. This study could be reproduced in those with neurological pathologies such as stroke, in which brain damage leads to different haemodynamic responses [62]. Finally, fNIRS could be used in complex navigation tests [63,64] to reflect the involvement of EF in these tasks.

5. Conclusion

This pilot-study demonstrated that healthy OA seem to have less activation of their dlPFC compared to YA in VSWM tasks. This dlPFC activation seems to be associated with VSWM performance, particularly in navigational space. Finally, we identified the association of some cognitive functions, such as mental rotation and EF with VSWM performance in reaching and navigational spaces.

Author contributions

TK: Conceptualization and methodology, data acquisition and analysis, manuscript drafting; EH: Methodology, formal analysis, and manuscript review; AB: Conceptualization, software and manuscript review; AC and MGG : Methodology and manuscript review; JCD: Resources, conceptualization, manuscript review; AP: Conceptualization and methodology, data analysis, supervision, resources, manuscript drafting.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors report no declarations of interest.

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III.2. Replanning following target shift during locomotion in children diagnosed with cerebral palsy (CP).

In the second thematic, we aimed to study *replanning following target shift during locomotion in children diagnosed with cerebral palsy (CP).* For this, we conducted a research entitled: Goal-oriented locomotion in children with spastic diplegia: Anticipatory orienting strategies and trajectory formation (Castilla, Berthoz, Cioni, et al., 2022a). Three main research questions are posed:

1) Can we detect disorders of anticipatory orientation and/or trajectory formation in subjects with spastic diplegic CP?

2) Are navigation skills distinctively impaired in spastic diplegic CP, independently from gait disorders?

3) In contrast to independent locomotion, does accompanied locomotion help subjects with spastic diplegic CP cope with their perceptual and balance disorders, allowing them to generate better trajectories?

In this study, it was hypothesized that:

i. Subjects with CP split into at least two categories: those with typical head anticipation and trajectory formation, despite gait disorders, and those presenting navigation abnormalities.
ii. goal-oriented locomotion as an intrinsically double motor control task: navigation, on one hand, and gait control on the other.

DEVELOPMENTAL NEUROREHABILITATION
https://doi.org/10.1080/17518423.2022.2047122

Goal-oriented locomotion in children with spastic diplegia: Anticipatory orienting strategies and trajectory formation

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ABSTRACT
Goal-oriented locomotion (GOL) is a complex task integrating navigation and gait control. To our knowledge, this is the first study of GOL in subjects with Cerebral Palsy (CP). Thirteen subjects with spastic diplegia and 26 with typical development were enrolled in the study. Subjects performed a GOL task to reach luminous targets. Within-subject trajectory variability, maximal head deviation from trajectory and mean head anticipation over trajectory were analyzed. While all subjects showed gait impairment, only 8 of 13 subjects also showed navigation abnormalities as revealed by either: a) abnormal head orientation *and* trajectory formation, or b) abnormal head orientation with normal trajectory formation. Abnormal gait patterns do not account for and can be distinguished from navigation disorders in spastic diplegic CP. This distinction has important implications for novel rehabilitation methods that should specifically address navigation, not only gait.

ARTICLE HISTORY
Received May 22, 2021
Revised October 26, 2021
Accepted February 23, 2022

KEYWORDS
Navigation; cerebral palsy; development; motor control; head anticipation; rehabilitation

Introduction

When studying locomotion, a crucial distinction should be made between two sub-functions: gait (i.e., the manner or style of walking, usually done by observing the individual walking naturally in a straight line), and navigation (i.e., body orientation and displacement in external space). Goal-oriented locomotion has been identified as a simple, yet powerful paradigm for the study of navigation in adults[1–4] and children.[5] In the present work we study, for the first time, goal-oriented locomotion in Cerebral Palsy (CP).

Gait and Navigation in Cerebral Palsy

Cerebral Palsy (CP) is a complex neurodevelopmental condition due to early, non-progressive brain injury, encompassing postural and motor disorders as well as perceptual, cognitive and emotional difficulties.[6] In this study, the spastic diplegic form of CP is investigated, because it is frequent (29% of all CP's,[7]) characterized by invalidating locomotor disorders and by a recurrent pattern of brain damage consisting of periventricular white-matter lesions.[8] Studies of locomotion in CP are almost entirely confined to gait. Several classifications of abnormal gait patterns in spastic diplegia are based on lower-limb joint angles on the sagittal plane while the subjects are walking in a straight line.[9,10] The Gross Motor Function Classification System (GMFCS) grades severity into 5 levels according to locomotor ability.[11] Ferrari et al.[12] identified 4 forms of spastic diplegia and described the so-called *perceptual disorders*, i.e., disorders of the sense of motion and balance.[13] No CP classification has addressed navigation, so far. Visual-spatial disorders are prominent in spastic CP,[14] but they are assessed only by means of table-top tests that exclude locomotion. Only recently, a novel navigation paradigm, the Magic Carpet, has been applied to CP, showing specific deficits related to the anatomy of brain lesions.[15] It is therefore likely that children with CP experiencenot only gait issues, but also issues related to navigation, which should affect goal-oriented locomotion as well.

Development of Goal-oriented Locomotion

Two consistent adult behaviors in goal-oriented locomotion are *head stabilization* and *head anticipation*. Head stabilization refers to the minimization of head movement relative to the horizontal plane.[16] Head anticipation refers to the constant lead of head orientation on walking direction while turning.[3,17] This cephalocaudal orienting organization is thought to align gaze and vestibula with a reference frame centered on the upcoming walking direction, thus allowing anticipatory control on body kinematics.[15,18,19]

Another behavioral signature of mature anticipatory control is the generation of *optimal* locomotor trajectories, characterized by low curvature, high smoothness and low variability across trials toward the same target.[9] Adult trajectory formation, similarly to hand movements, abides by a maximum-smoothness law minimizing the total jerk produced.[20,21] This law is consistent with a feed-forward (anticipatory) control loop regulating the whole trajectory from the start.[21]

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Recent research has investigated the typical development of anticipatory orienting strategies and trajectory formation in goal-oriented locomotion by means of kinematic analyses and it appears that children attain an adult level of anticipatory orienting strategies and trajectory formation between 11 and 13 years.[5] This developmental sequence puts the development of these skills much later than the maturation of gait.[22,23]

Purpose of the Present Study

This study is devoted to the investigation of goal-oriented locomotion in subjects with spastic diplegic CP. The same methods previously employed in typical development[5] have been applied. Three main research questions are posed: 1) Can we detect disorders of anticipatory orientation and/or trajectory formation in subjects with spastic diplegic CP?, 2) Are navigation skills distinctively impaired in spastic diplegic CP, independently from *gait disorders?* Our hypothesis is that subjects with CP split into at least two categories: those with typical head anticipation and trajectory formation, despite gait disorders, and those presenting navigation abnormalities, and 3) In contrast to independent locomotion, does accompanied locomotion help subjects with spastic diplegic CP cope with their perceptual and balance disorders,[13] allowing them to generate better trajectories?

Materials and Methods

Participants

13 subjects (aged 5 to 23 years) with spastic diplegic CP and 26 subjects (aged 4 to 35 years) without CP (i.e., assumed typical development) were included in the study. Patients admitted to IRCCS Stella Maris (Calambrone, Pisa, Italy) were screened for the following inclusion criteria: diagnosis of spastic bilateral CP, clinically defined according to Rosenbaum et al.,[6] due to periventricular leukomalacia, documented and scored by brain MRI,[24] ability to walk without assistance or with mild use of sticks (GMFCS levels I–III), and total IQ>50 (WISC IV or V). The presence of a perceptual disorder was ascertained by means of Ferrari's 6 clinical signs and judged as positive if at least 4 out of 6 signs were detected.[13] Control data were taken from a previous study published in 2013.[5] The main characteristics of subjects and controls are reported in Table 1. All parents and children gave written, informed consent and assent, respectively. The study was approved by the local ethic committee at the University of Pisa and carried out in accordance with the declaration of Helsinki.[25]

Experimental Set-up

The experiment took place in a room (12.0 × 5.0 × 2.2 m) and it was arranged exclusively for the 'locomotor reaching' task.[5] The layout included a starting point (Start), a visual corridor and three targets (Central, left and right) (see Figure 1). Each target was represented by a round plastic lamp adapted with a speaker (30 cm in diameter) placed on a table. A light or visual start signal was presented one at a time accompanied by an acoustic start signal (beep) by a programmable controller. Additionally, this programmable controller gave the output to the motion capture system. The central target was placed on a small table (50 l × 730 w × 70 h cm) in front of the subjects' starting position (Start) at a distance of 3.8 m. The left and the right targets were positioned at a distance of 4.20 m (i.e., 3.3 m on either side and 2.6 m in front of Start). Both targets (Left and Right) lied on two larger tables (250 l × 7,120 w × 90 h cm) evenly positioned laterally to Start, with their long axes facing each other. All 3 tables were completely covered with a white cloth. A 0.96 m wide, 1.4 m long visual corridor, made from two white lines on the ground, departed from Start toward Center, to force an initially straight walking direction (see Figure 1 for all details). Kinematic information was recorded and quantified by means of an optoelectronic motion capture system (SMART-D, BTS, Milan) equipped with 12 infrared cameras sampling at 140 Hz. For the present study, we calibrated a volume of approximately 6.0 × 3.5 × 1.8 m before each session (accepted mean error ≤0.3.6 mm). Each subject was equipped with 15 markers: 3 on the head, then shoulders, sternum, hips, sacrum, knees, heels, and toes. All measures were made in a laboratory-fixed reference system having its origin at the end of the corridor (midpoint between the two stripe ends), the Y-axis lying on the line from Start to Center and pointing forward, the X-axis perpendicular to the previous one on the horizontal plane and pointing to the right, and the Z-axis perpendicular to the XY plane and pointing upward.

Procedure

The subjects were given instructions on how to perform the experiment beforehand and were guided to begin the trial standing at the Start, facing the Central target. The subjects were reminded to walk at self-paced speed and walk naturally. In case of a trail not being performed according to the instructions, the subject was invited to repeat the trail. Safe stopping was ensured by placing the targets on tables which the subjects could lean on. Two walking conditions were studied: *Independent Locomotion (IL)* and *Accompanied Locomotion (AL)*. In IL, the subject walked alone, the experimenter remained at Start. In AL, an experimenter followed the subject throughout the trial, walking behind them without touching them. For each walking condition, there were 5 left, 5 right and 3 center trials (the latter used only for offsets), for a total of 26 trials per subject. Four additional training trials were not analyzed.

Data Analysis

All analyses were carried out with open-source software (Python 2.6 for Linux, www.python.org with NumPy 1.0, numpy.scipy.org). Raw displacement signals were interpolated and filtered with a cubic splines function and a 6.5 Hz Butterworth low-pass filter. Body center was defined as the midpoint between sternum, right and left shoulders. Lab-referenced displacement signals, orientation angles of body segments and of the walking direction (heading) on the horizontal (yaw) plane were extracted. The following parameters, relative to each trial, were computed (single-trial parameters, see Figure 2):

Table 1. Clinical characteristics of the sample and mean values (Averaged Within Each Subject) of gait and navigation parameters. On the bottom: average values of the control sub-groups.

Subject No.	Age (years)	Gender	Height (m)	GMFCS	Walking aids	Ferrari Classification	Perceptual Disorder	Navigation sub-group	Mean step length (m)	Mean velocity (m/s)	Curvature index (%)	HHD max (deg)	HHD max location (%)	Head Ant (s)	ATD (m)
1	5	F	1.06	II	no	IV	no	1	0.34	0.82	23.7	25	44.6	0.26	0.13
2	6.5	F	1.04	II	no	IV	no	2	0.37	1.09	22.1	25.1	21.36	0.31	0.09
3	6.92	M	1.1	III	sticks	III	yes	3	0.22	0.6	34.2	36.4	59	0.2	0.24
4	7.66	M	1.21	II	no	IV	no	2	0.43	0.94	22.4	46	13.7	0.1	0.11
5	7.83	F	1.13	II	no	III	yes	2	0.4	1.02	28.4	45.3	39.2	0.34	0.12
6	9.33	F	1.2	II	no	IV	no	2	0.46	0.92	25.1	36.7	8.3	−0.12	0.11
7	9.83	F	1.37	II	no	IV	no	1	0.47	0.92	25	24.2	35.7	0.2	0.08
8	10.75	M	1.36	III	sticks	I	yes	3	0.35	0.81	27.7	37	48.9	0.16	0.15
9	11.5	F	1.34	II	no	II	no	1	0.4	0.77	26.6	26.2	35.9	0.26	0.08
10	12.5	M	1.52	II	no	IV	no	2	0.6	1.19	22.2	13.8	48.4	−0.14	0.08
11	13.42	M	1.41	III	no	III	yes	3	0.2	0.33	26.6	53.5	31.7	1.49	0.2
12	19.83	F	1.5	II	no	III	yes	3	0.32	0.63	32.6	38.5	19.2	0.5	0.15
13	23	F	1.63	II	no	IV	no	1	0.45	0.88	21.8	20.4	29.5	0.24	0.05
Control sub-group															
N = 14	4–11	9 M	1.24	N.A.	N.A.	N.A.	N.A.	N.A.	0.55 (±0.05)	1.15 (±0.09)	26.8 (±4.4)	23.2 (±7.5)	42.5 (±11.9)	0.18 (±0.20)	0.11 (±0.03)
N = 6	12–18	3 M	1.59	N.A.	N.A.	N.A.	N.A.	N.A.	0.63 (±0.02)	1.22 (±0.11)	22.7 (±2.1)	19.0 (±5.0)	40.0 (±8.8)	0.15 (±0.07)	0.06 (±0.02)
N = 6	>18	3 M	1.65	N.A.	N.A.	N.A.	N.A.	N.A.	0.63 (±0.04)	1.18 (±0.10)	23.0 (±3.4)	22.7 (±5.5)	39.0 (±9.3)	0.21 (±0.07)	0.05 (±0.01)

Note. GMFCS = Gross Motor Function Classification System; HHD = Head-Heading Deviation; ATD = Average Trajectory Deviation; Head Ant = Head anticipation. The symbol ± indicates the standard deviation among controls.

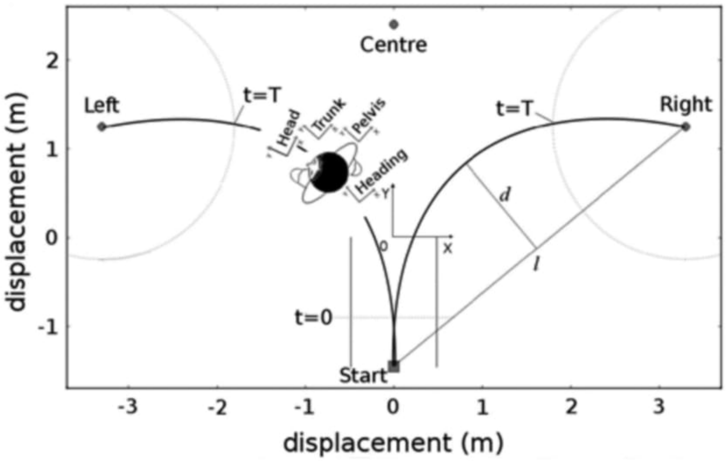

Figure 1. The representation of the spatial layout on the yaw plane (horizontal plane) (Belmonti et al., 2013). Start indicates the starting position. Left, Center and Right designate the three luminous targets. The two vertical bold gray lines depicts the corridor constraining initial walking direction. Time-normalization was computed using the point of t = 0 and t = T. l represents the length of the ideal straight trajectory from Start to target (Right in the example). d represents the maximum orthogonal distance reached along the real trajectory (depicted as a bold black line) from the ideal straight trajectory. The four moving coordinate systems for head, trunk, pelvis and heading are also displayed.

Curvature Index (CI)

Ratio (in percentage) between the maximal distance reached from the straight Start-to-target line (i.e., the shortest possible trajectory), and the length of that line.

Anticipation Time (AT)

For each pair of orientation signals (i.e., head over heading, head over trunk, etc.): it is given by cross-correlation[4,5] and is positive if the first signal leads (anticipation), negative if the first signal lags (delay).

Maximal Head-Heading Deviation (Hhd_{max})

Maximal difference between head and heading orientation angles in the direction of turning (head rotation).

HHD_{max} Location

Distance from Start, in percentage of the total trajectory length, where HHD_{max} was detected. In addition, within-subject trajectory variability was computed.

Average Trajectory Deviation (ATD)

Average spatial dispersion of body trajectory was analyzed across trials toward the same target.

Statistical Analysis

To answer the three research questions, all navigation parameters were checked for differences between subjects and controls first, and then between the IL and AL conditions. Finally, to further investigate the relationship between navigation and motor impairment, and to check our hypothesis that a dissociation between the two exists, correlations between navigation parameters, gross-motor function and lesion extension were checked.

Subjects and controls were sub-grouped into three age-ranges : 8 children aged 4 to 11 years (total 208 trials), 3 adolescents 12–18 years (78 trials), and 2 adults (52 trials). This sub-grouping was aimed at comparing subjects' with CP trials with controls without CP and therefore was identical to that of Belmonti et al.[5] Each single-trial parameter was first studied among all subjects with a Kruskal–Wallis test to check for the presence of any significant between-subject differences. Parameters were then compared between each subject and the sub-group of controls in the same age-range. Finally, parameters were compared at group level, between all subjects and controls within each age range. Mann–Whitney tests were used for all comparisons, as normal distribution could not be assumed. Within-subject effects of target direction (Right vs. Left) and walking condition (IL vs. AL) on each parameter were studied by means of Mann–Whitney tests as well. All parameters were then tested for correlation with GMFCS level and lesion extension as defined by Fiori et al.[24] by means of Spearman's test.

Results

The clinical characteristics of the sample are reported in Table 1, along with the main experimental measures. The findings for each of the navigation parameters studied are presented below, with particular regard to the differences between subjects with CP and control subjects without CP, and between IL and AL.

Curvature Index (CI)

Figure 3 shows the distribution of CI in each subject of the sample and in controls. Individual differences were large, as confirmed by the Kruskal–Wallis test (χ^2 = 111.63, p < .0001). CI was found to be lower than normal in two subjects (S2: W = 1179.5, p = .0002; S4: W = 1263, p = .0002), whereas it was higher than normal in other two subjects (S3: W = 2887.5, p = .0009; S12: W = 2152, p < .0001). Overall, CI did not significantly differ between subjects and controls (W = 55008, p = .093). Significant differences could be found, however, within age-ranges: in children, CI was lower than normal (W = 16682, p = .032); in adolescents, CI did not

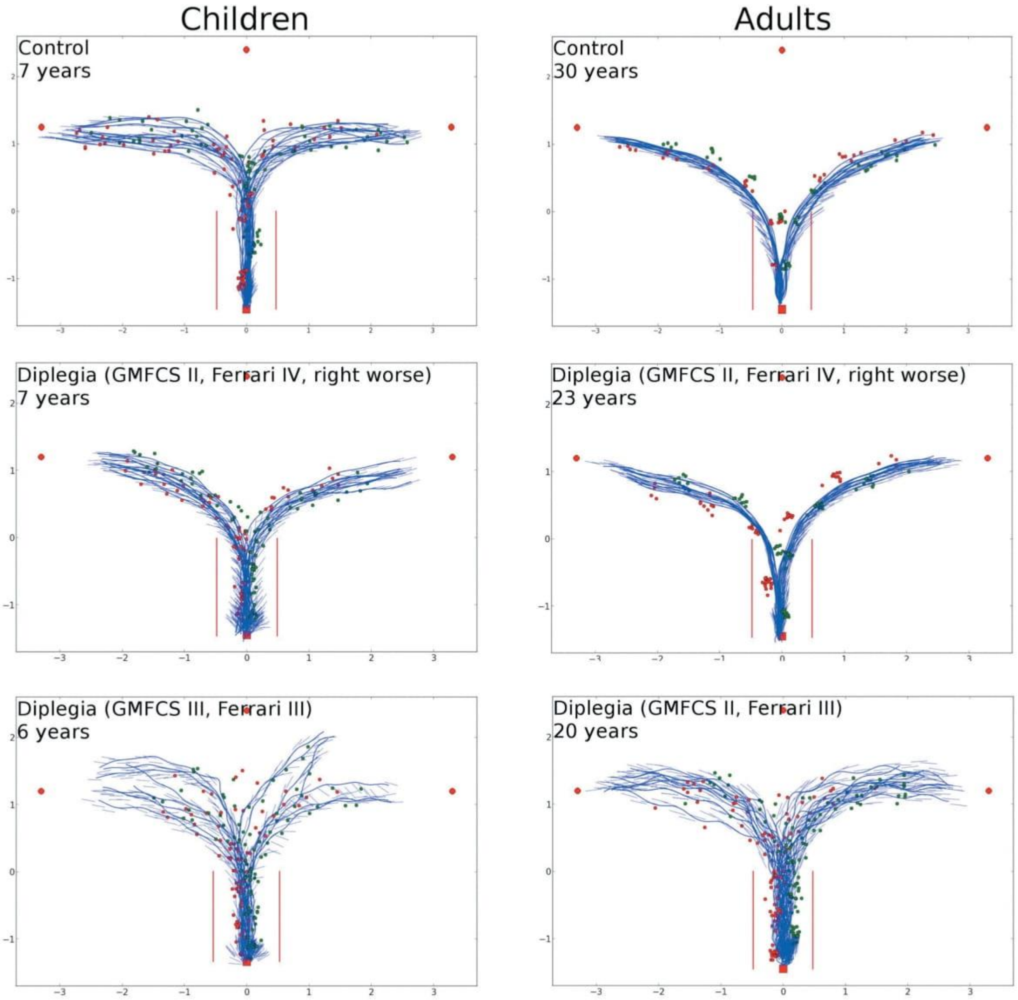

Figure 2. Trajectories plots, head orientations and foot placements of six representative subjects. Black lines represent the locomotor trajectories generated on the yaw plane by each subject toward left and right targets. Short gray segments departing from trajectories represent head orientation sampled at fixed time-intervals. Dots are foot placements: the left ones in dark gray and the right ones in light gray. Note the changes in trajectory geometry and the reduction of spatial variability from childhood to adulthood in controls (top-most graphs). Subjects with diplegia without perceptual disorders made trajectories similar to those of age-matched controls (middle graphs), while those with perceptual disorders showed less smooth and more curved trajectories (bottom graphs).

differ from normal values ($W = 1167$, $p = .746$); in adults, CI was higher than normal ($W = 3097.5$, $p = .0006$). Thus, CI seems to follow a different developmental trend in spastic diplegia than in typical development, starting low in childhood and increasing faster than normal with age.

Anticipation Time (AT)

AT showed a large variability, both between and within subjects. The Kruskal–Wallis test revealed the presence of significant individual differences ($\chi^2 = 27.74$, $p = .006$). Mean AT was positive in all subjects except two (S6 and S10). AT significantly differed from controls in S6 ($W = 1876.5$, $p = .049$), S10 ($W = 655$, $p = .0036$), S11 ($W = 222$, $p = .016$), and S12 ($W = 1582.5$, $p = .0052$). It should be noted that a negative AT (i.e., head lag) is not surprising in children with CP, being also found in control subjects without CP under 12 years. As far as age subgroups are concerned, AT was shorter in adolescents with CP than controls ($W = 877$, $p = .037$), whereas it was longer in adults with CP than controls ($W = 2837$, $p = .0183$).

Maximal Head-Heading Deviation (Hhd_{max})

HHD_{max}, shown in Figure 4, ranged in the whole sample from 7.12 deg to 98.6 deg (mean = 31.3, SD = 15.6). HHD_{max} varied more between-than within-subject, as revealed by the Kruskal–Wallis test ($W = 113.75$, $p < .0001$). Mean HHD_{max}, averaged by subject, ranged from 13.8 deg (S10) to 53.5 deg (S11). Mann-Whitney showed a significantly wider HHD_{max}, relative to age-matched controls, in S3 ($W = 3173$, $p < .0001$), S4 ($W = 4370$, $p < .0001$), S5 ($W = 3987$, $p < .0001$), S6 ($W = 4054$, $p < .0001$), S8 ($W = 2162$, $p = .0002$), S11 ($W = 222$, $p = .016$), S12 ($W = 2110$, $p < .0001$). HHD_{max} was significantly smaller than normal only in S10 ($W = 556$, $p = .0004$). HHD_{max} was on average larger than normal in each

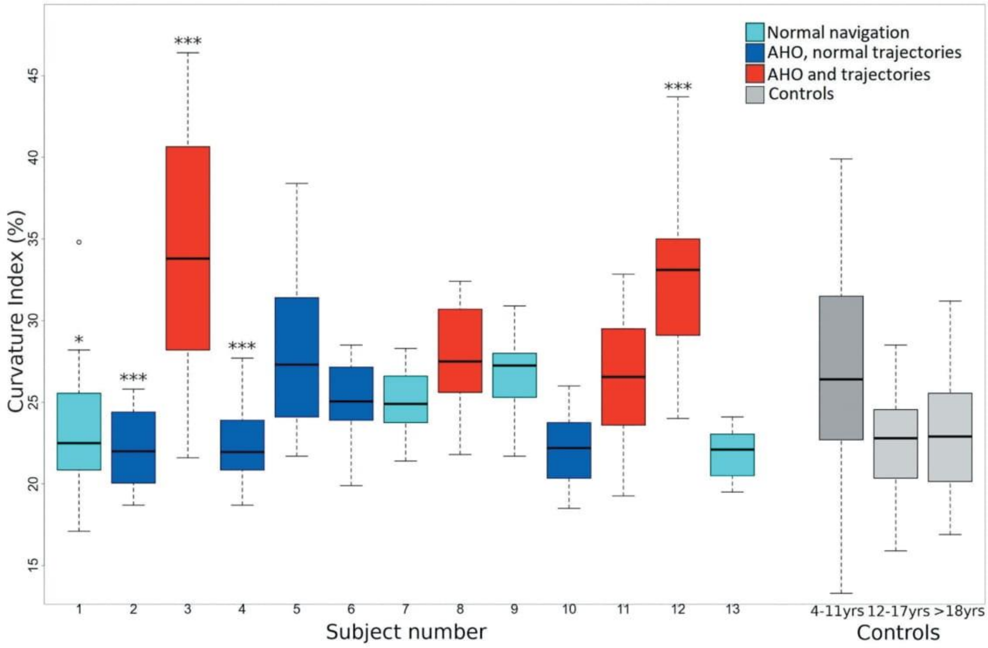

Figure 3. Barplot of the Curvature Index (CI) in subjects with CP (colored bars) and in controls (gray bars). Each colored bar represents one subject, while each gray bar represents an entire age-range within the control group. The light blue turquoise color represents the normal navigation, the dark blue color represents Abnormal Head Orientation (AHO) with normal trajectories, the red color represents Abnormal Head Orientation (AHO) with abnormal trajectories. Colors represent navigation sub-groups (Navigation sub-groups are explained in the Discussion. The asterisks indicate subjects whose values significantly differ from controls within the respective age-range.

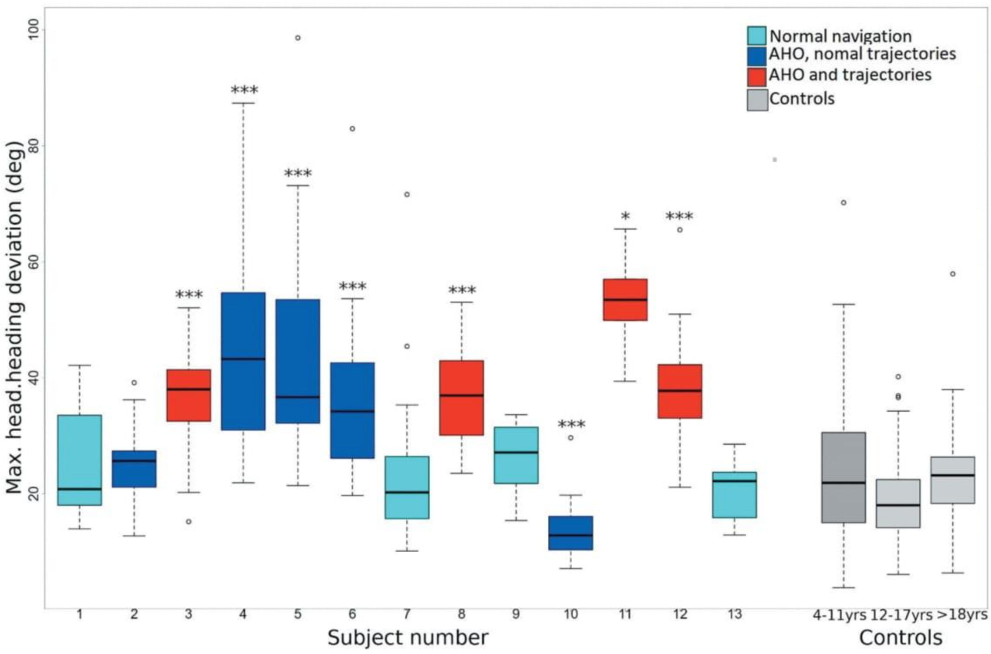

Figure 4. Barplot of Maximal Head-Heading Deviation (HHDmax) in subjects with CP (colored bars) and in controls (gray bars). Each colored bar represents one subject, while each gray bar represents an entire age-range within the control. The light blue turquoise color represents the normal navigation, the dark blue color represents Abnormal Head Orientation (AHO) with normal trajectories, the red color represents Abnormal Head Orientation (AHO) with abnormal trajectories. Each colored bar represents one subject, while each gray bar represents an entire age-range within the control group. Colors represent navigation sub-groups (see legend). Navigation sub-groups are explained in the Discussion. The asterisks indicate subjects whose values significantly differ from controls within the respective age-range.

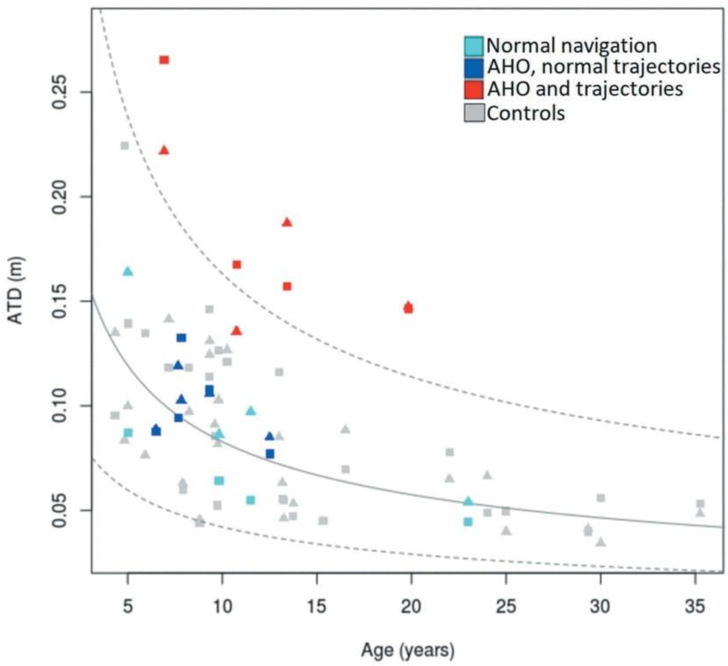

Figure 5. Average Trajectory Deviation (ATD) by age (years) in subjects with CP and controls. Each marker represents the ATD of one subject across trials toward either the Left (triangles) or the Right (squares) target. The light blue turquoise color represents the normal navigation, the dark blue color represents Abnormal Head Orientation (AHO) with normal trajectories, the red color represents Abnormal Head Orientation (AHO) with abnormal trajectories. Colors represent the navigation sub-groups (see legend). The gray lines are generated by the best-fitting logarithmic regression model of ATD through age, with dashed lines indicating the 95% prediction interval of the model.

age sub-group: children ($W = 27247$, $p < .0001$), adolescents ($W = 778$, $p = .007$), and adults ($W = 2991.5$, $p = .003$). HHD_{max} thus proved a hallmark of individual behavior and was typically larger in CP than in controls apart from one exception (S10).

HHD_{max} Location

HHD_{max} location ranged from 0% to 100% of the trajectory, i.e., maximal head deviation from trajectory could occur anywhere. In only one case HHD_{max} location occurred later than normal: S3 ($W = 1262$, $p = .009$), whereas in other subjects it occurred significantly earlier than in age-matched controls: S2 (W1145.5, $p = .0001$), S4 ($W = 802$, $p < .0001$), S6 ($W = 526.5$, $p < .0001$), S12 ($W = 470$, $p < .0001$), S13 ($W = 607$, $p = .003$). HHD_{max} location occurred significantly earlier than normal in children ($W = 13668$, $p < .0001$), and in adults ($W = 1190$, $p < .0001$), while the difference did not reach significance in adolescents ($W = 1385.5$, $p = .32$).

Trajectory Variability

Average Trajectory Deviation (ATD) is shown for each subject in Figure 5. As it clearly appears, most of the subjects with CP fall within the normal range and abide by the typical logarithmic law in relation to age, as fitted on control data.[5] Four subjects, however, were over the upper limit of the normal range (i.e., the range of values expected with a 95% confidence interval), either in left or right-directed trials: S3, S8, S11 and S12. These four subjects with CP showed high ATD values andtheir within-subject trajectory variability was important, contrary to both controls without CP and the other nine subjects with CP. As a whole group, subjects with CP had a larger ATD than controls ($W = 858$, $p = .009$). No significant difference was found between age-matched sub-groups of subjects and controls.

Effects of Accompanied versus Independent Locomotion (AL Vs. IL)

No statistically significant difference was found between AL and IL, for none of the parameters studied, according to the Mann–Whitney test. However, a sole subject with CP demonstrated behavior that varied between the two walking conditions. This subject could walk only when accompanied; when unaccompanied he remained frozen, unable to start. As shown in Table 1, he walked at slow speed, head anticipation was early and wide (long AT and wide HHDmax), while trajectory curvature (CI) was normal. This subject was a 13.4-year-old male with a mild intellectual disability and a prominent perceptual disorder. MRI indicated extensive bilateral periventricular leukomalacia involving mostly the parietal and frontal lobes, associated with bilateral damage to the thalami and the posterior limb of the internal capsule (PLIC).

Correlation with GMFCS and Lesion Extension

None of the studied parameters proved to be correlated with either GMFCS or lesion extension, as measured by Fiori et al. Global score, according to Spearman's test ($p > .05$).

Table 2. Navigation profiles are identified by abnormalities of either head or trajectory parameters, or of both.

Trajectory Parameters	Normal head parameters	Abnormal head parameters
Normal	S1, S2, S7, S9, S13	S4, S5, S6, S10
Abnormal	none	S3, S8, S11, S12

Discussion

Though flawed by some significant limitations includingthe small sample size and the large age range of the participants, the present study is the first account of disorders of trajectory formation and anticipatory orientation in CP. Having applied the same methodology of our previous study on typical development, we are now able to identify quantitative deviations from the normal range and to interpret them in a coherent framework, providing preliminary answers to the research questions posed in the introduction.

Behavioral Characterization

In the CP group, at least three behavioral patterns can be distinguished based on navigation parameters. Five subjects (S1, S2, S7, S9 and S13) fell within the normal range of all five major parameters (no navigation disorders). Four other subjects (S4, S5, S6 and S10) showed abnormalities of head orientation, but generated normal trajectories with an age adequate ATD (abnormal head orientation with normal trajectory formation). Whereas four subjects (S3, S8, S11, S12) showed major difficulties in both head orientation and trajectory formation. Each subject's performance was characterized by wide HHD_{max}, high CI and high ATD (see Table 2).

It is noteworthy that *all* subjects with CP had major gait disorders. The preservation of trajectory formation in most subjects with CP is an important finding. Eight subjects even adhere to the logarithmic law relating trajectory variability (ATD) to age, observed in typical development.[5] So, it seems that trajectory formation can develop normally despite major gait disorders. S2, a young female, performed even better (low curvature and early anticipation) than controls without CP.

On the other hand, several deviations from the norms were also found. The picture is made complex by high intersubjective variability, which is not surprising in neurological disorders. Although we restricted our investigation to one type of brain lesion, periventricular leukomalacia, its extension varied within the sample, and out limited sample size did not allow for analysis using multiple regression. However, *none* of the parameters studied were related either to measures of lesion extension or to GMFCS levels. Moreover, each navigation parameter showed a different distribution within the sample, raising the need for specific, subject-wise interpretation.

The abnormalities found point to the presence of major disorders of navigation in a subpopulation of children with spastic diplegia CP, represented by the third subgroup of our sample, which is characterized by abnormalities of both head orientation and trajectories. Their large head deviation can be interpreted as a sign of exaggerated feedback control aimed to balance a lack of anticipatory locomotor control. In other words, these subjects probably had to look continuously at the target to adjust for steering errors. So, in this context, a large head deviation in individuals with CP does not have the same meaning as in typical development, as it is exaggerated and associated with altered trajectories.

In the subjects showing abnormal head behavior with normal trajectories, different patterns of head orientation abnormalities were found. One subject (S5) exaggerated head deviation-like sub-group 3 but generated normal trajectories. Two subjects (S4 and S6) were characterized by a wide and early HHD_{max} with little, if any, head anticipation (zero or negative AT). Curvature was low and trajectory variability was age adequate. These two subjects seemed to adopt a mixed feedback strategy: they started walking while looking at the target (feedback navigation), but then shifted gaze from the target to their own feet. Looking at one's own feet is a specific feedback strategy subserving gait control while turning.[26] S10 showed very little head deviation and negative head anticipation associated with well-shaped trajectories. In the videos, he was observed looking continuously at his feet, but, contrarily to S4 and S6, never looked at the target. It can be assumed that navigation was preplanned and he used visual feedback only for gait control.

Finally, S11 is the first case ever described in which locomotion strictly required accompaniment without contact. In all other cases, accompaniment did not determine any significant difference, while in this case it determined access to locomotion. We can now assume that accompaniment has an all-or-nothing effect (i.e., it can allow a subject to walk, but does not affect trajectory formation). It can be hypothesized that some people with CP, like S11, cannot exert any anticipatory control, neither on trajectories nor on gait, and therefore need perceptual feedback for both.

In this limited number of subjects, our findings support the modeling of goal-oriented locomotion as an intrinsically double motor control task: navigation, on one hand, and gait control on the other. Either component can be primarily accomplished by means of feedback or feed-forward mechanisms, with the latter progressively integrating the former throughout development. In typical development, feed-forward control seems to take care of gait first and only afterward of navigation. In spastic diplegia, this ontogenetic course might be altered by numerous disorders, especially lower-limb spasticity and musculoskeletal problems. Navigation, in its turn, might develop normally or not, depending on top-down factors.

None of the commonly used classifications of spastic diplegia or of spastic gait patterns accounts for the presence of navigation abnormalities. The only clinical feature that match to some extent our analysis is the presence of a perceptual sense-of-motion disorder[13,27] according to Ferrari's classification.[12,13] In fact, all four subjects showing abnormalities of both head orientation and trajectories, proved to also have a perceptual disorder. Further studies, including detailed brain imaging scoring and neurophysiological investigations, are needed to clarify the

nature of this disorder in CP and its relationship with navigation.

Conclusion

This study is the first research to examine behavioral signatures of anticipatory control in locomotor navigation subjects with spastic bilateral CP. It has allowed us to detect the presence or absence of minor and major navigation disorders. The results of this research support the idea that modeling of goal-oriented locomotion is an intrinsically double motor control task that distinguishes between navigation and gait control. Further research, in a larger group of participants with CP, should be undertaken to explore the relationship between motor behavior to spatial cognition, kinematic data to neural modeling.

Acknowledgments

Alexander Castilla was supported by Institut de Médecine Environnementale (IME), Paris, and we thank its Director Jacques Fradin for continuous and generous support.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

Funding

This research was partially supported by Current Research funds by the Italian Ministry of Health and by 5 for 1000 Funds to IRCCS Fondazione Stella Maris.

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III.3. Exploration of the inhibitory control and cognitive flexibility by the means of a visuo-spatial locomotor task.

The third thematic is related to the exploration of the *inhibitory control and cognitive flexibility by the means of a visuo-spatial locomotor task*. Here, we will present two studies, one published, and one draft. The first study is named: A New Paradigm for the Study of Cognitive Flexibility in Children and Adolescents: The “Virtual House Locomotor Maze” (VHLM) was published in Frontier (Castilla et al., 2021a). This study presents a new protocol for assessing the capacities of planning and replanning trajectories and to study inhibition and CF using a spatio-temporal index. We measured kinematic behavior (i.e., trajectories, tangential velocity, and head direction) during spatial navigation in typical children. This study proposed the next hypothesis:

i. In the re-planning trial, subjects need to inhibit the overlearned path and re-explore and exploit a new path.
ii. Due to the task’s temporal constraints, behaviors can manifest in three different forms: departure without inhibition or impulsive responses, in the impulsive online planning, and in the anticipatory- planning,

The second paper is a draft of an additional article which discussed the *executive functions and the role of inhibition involved in spatial navigation in typical and psychiatric children, adolescents, and adults* using the VHLM. This paper is being drafted and is expected to be submitted by the end of 2022. The objective of this article was to assess the development of IC and CF in a near extrapersonal space using a negative prime paradigm.

i. We hypothesized that we would observe a negative priming effect comparing the performance in the VHLM, more specifically.
    a. that the IC is confirmed when an overlearned shortest path that was ignored or inhibited after a blocking.
    b. that when the inhibited shortest path was unblocked, we expected the subsequent trajectories requiring the shortest path to be affected by the previous inhibition.
ii. We predicted that a disruption in the performance decreased velocity, increased latency and increased exploration (head-chest-yaw). Indeed, we anticipated that the difference between head-chest included more movement in terms of exploration and reconfiguration. The inhibition capacities are closely related to

cognitive development and therefore we expected the cognitive inhibition process to be modulated according to the different types of age groups and pathologies.

iii. In addition, we expected to observe behavioral evidence of different developmental trajectories in the manifestation of IC and CF.

frontiers in Psychiatry

BRIEF RESEARCH REPORT
published: 23 September 2021
doi: 10.3389/fpsyt.2021.708378

A New Paradigm for the Study of Cognitive Flexibility in Children and Adolescents: The "Virtual House Locomotor Maze" (VHLM)

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Classical neuropsychological assessments are designed to explore cognitive brain functions using paper-and-pencil or digital tests. The purpose of this study was to design and to test a new protocol named the "Virtual House Locomotor Maze" (VHLM) for studying inhibitory control as well as mental flexibility using a visuo-spatial locomotor memory test. The VHLM is a simple maze including six houses using the technology of the Virtual Carpet Paradigm^{TM}. Ten typical development children (TD) were enrolled in this study. The participants were instructed to reach a target house as quickly as possible and to bear in mind the experimental instructions. We examined their planning and replanning abilities to take the shortest path to reach a target house. In order to study the cognitive processes during navigation, we implemented a spatio-temporal index based on the measure of kinematics behaviors (i.e., trajectories, tangential velocity and head direction). Replanning was tested by first repeating a path chosen by the subject to reach a given house. After learning this path, it was blocked imposing that the subject inhibited the learned trajectory and designed a new trajectory to reach the same house. We measured the latency of the departure after the presentation of each house and the initial direction of the trajectory. The results suggest that several strategies are used by the subjects for replanning and our measures could be used as an index of impulsivity.

Keywords: replanning, spatial navigation, executive functions, cognitive control, locomotor protocol, visuospatial abilities

OPEN ACCESS

Edited by:
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Reviewed by:
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Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: *11 May 2021*
Accepted: *26 August 2021*
Published: *23 September 2021*

Citation:
Castilla A, Borst G, Cohen D, Fradin J, Lefrançois C, Houdé O, Zaoui M and Berthoz A (2021) A New Paradigm for the Study of Cognitive Flexibility in Children and Adolescents: The "Virtual House Locomotor Maze" (VHLM). Front. Psychiatry 12:708378. doi: 10.3389/fpsyt.2021.708378

INTRODUCTION

The human brain combines many cognitive processes to understand the world around us and to enable us to adapt to different situations in a vicarious way (i.e., brain capacity for finding different solutions for a given problem) (1). This adaptation requires that learned associations to solve specific problems are sometimes challenged by new events needing different strategies. Spatial navigation abilities such as planning, replanning, visuo-spatial working memory and inhibition are crucial for everyday activity. For instance, inhibitory mechanisms allow the brain to perform these changes in strategies and to develop in children during ontogeny (2–4). Inhibitory processes can be observed during the very early timing for the initiation of an action, or when a re-planning is required. In that case, a delay is caused by the time necessary for the brain to (a) inhibit the learned process, and (b) elaborate the new strategy (5–7). Numerous psychological and neuropsychological tasks using paper-and-pencil assessment have documented this cognitive delay. We suppose here that such a delay also appears during a spatial navigation task in which subjects must re-organize a memorized locomotor trajectory.

Throughout typical cognitive development (TD), inhibitory control is actively involved during selective attention when irrelevant information needs to be ignored or inhibited, and during the production of optimal behavioral response (e.g., stop an action or avoiding reacting). Children are always confronted to a choice between using automatic strategies (i.e., intuitive system or so called "heuristics"), or substituting strategies based on logical algorithms (i.e., analytical system) in order to accomplish a goal in specific contexts (3, 8, 9). Concerning neurodevelopmental disorders, the inhibition process is particularly affected in the attention deficit disorder with or without hyperactivity (ADHD) that is characterized by above-normal levels of hyperactive and impulsive behaviors and below-normal levels of attention (DSM-V) (10). In ADHD, attention deficit and impulsiveness due to poor inhibition processes can lead to academic learning impairments (11) and difficulties in planning adequate behavior (12).

Previc (13) puts forward a neuropsychological model based on the egocentric space segmentation linked with the motor capacities and perceptual integration. His model proposes a division of space in four key behavioral "realms" in addition to body space: the peripersonal space (PPS) (i.e., the reaching space), the focal extrapersonal space (FE), the action extrapersonal space (ES) and the ambient extrapersonal space (AES). This corresponds to what neurologists had identified long ago, from observing pathological deficits following brain lesions, as body space, peripersonal space, near distant action space and environmental action space (14, 15). The extrapersonal space serves to navigate and to orientate oneself toward objects that are situated beyond the near-body space. Recently, it has been suggested that this segmentation of space is based on a modular organization of the brain networks in which each type of action space requires specific geometries. These types of geometries are composed of Euclidean and Non-Euclidean geometries and they are regrouped in a general geometry called Topos (4, 16). The understanding of the different brain networks for different action spaces is an essential factor to consider during the assessment of spatial navigation. For instance, spatial navigation abilities have been extensively tested using the mobile-app-based cognitive task (Sea Hero Quest) assessing planning-replanning and inhibition (17). However, specialized cognitive navigational tasks involving the locomotor space could reveal complementary information concerning spatial navigation abilities. The present specifical designed protocol concerns only the "near distant extrapersonal locomotor space" which is described as walking around a room.

Piccardi et al. (18) suggested adapting a classical table spatial memory test, the table Corsi test, to the locomotor space, and proposing an initial version of the paradigm. They designed a test with tiles on the floor. The experimenter walks on these tiles in a sequence and asks the subject to observe, memorize and repeat the sequence by walking on the tiles. A span from one to nine tiles was used. Overall, normal subjects can successfully repeat up to five tiles, and exceptionally up to seven tiles depending on the difficulty of the path. This paradigm was called the Waking Corsi Test(WalCT). Subsequently, Alain Berthoz and his team developed the "Magic Carpet" which is a computerized version of the previous WalCT test. It uses translucent tiles equipped with lights for presenting the sequences and allowing the tactile sensors to record the timing. These flexible features provide accurate measurements of the subjects' performance. Several studies were conducted using this design on normal children and adults (19, 20). A difference in cognitive performance was observed in children and adults in the visuo-manual space (VMS) and visuo-locomotor space (VLS) (named by the authors "micro and macro spaces").

By comparing the memory span in children using the walking Corsi test (WalCT) for the locomotor space vs the classical Corsi block tapping test (CBT) (21), the participants were asked to reproduce a series of sequences in a specific order. The results indicated that the youngest children presented no difference in the memory span in either test. However, a clear difference was observed from 5 to 6 years old characterized by a better performance in the classical Corsi block tapping test. The authors suggest that children develop spatial memory in the reaching space sooner than in the navigational space. In addition, the analysis of the performance in the WalCT revealed the existence of gender differences in spatial memory (22). Moreover, the adaptation of the classical cognitive test (i.e., Stroop Test) to spatial tasks facilitated the detection of an early cognitive impairment compared to the standard neuropsychological test (20, 23).

A similar study confirmed that the working memory span in the CBT is significantly greater than in the WalCT and that it improves in both tests during development (CBT and WalCT) (19). The results demonstrate an improved performance in boys aged 10 to 11 in the navigational space but found a significant distinction between the CBT and the WalCT. These findings provide clear indications that a cognitive performance is somehow modulated by space. In addition, it was used in children with Cerebral Palsy (24), and in adults with mild cognitive deficits (MCD), hippocampal lesions, cortical, or cerebellar deficits (20, 25).

From a scientific perspective of brain spatial modularity (i.e., reaching space and locomotor space) and given the lack of tools to explore human cognition during navigation, especially cognitive control and regarding that re-planning a learned task is an effective paradigm for studying executive functions and the role of inhibition during navigation. We devised a new protocol and a methodology to study behavioral indices of cognitive control during locomotion.

To our knowledge, no study has addressed the question of replanning and inhibition with a specifically designed protocol using a visuo-spatial locomotor memory test. The objective of the current study was to design and to test a new protocol named the "Virtual House Locomotor Maze" (VHLM). It allowed us to study cognitive control during navigation throughout neurocognitive development based on the Virtual Carpet paradigm. We explored the capacities of planning and replanning trajectories to study inhibition and mental flexibility using a spatio-temporal index by the means of measuring kinematic behavior (i.e., trajectories, tangential velocity and head direction) during spatial navigation. We concentrated our analysis on : (a) comparing the departure's latency (delays) of the overlearned paths and the new replanned path, (b) analyzing directional locomotor trajectories during replanning, and (c) exploring age and cognitive performance. This idea is built on the typical developmental studies based on the walking Corsi or Magic Carpet, which have shown that the development of spatial cognition plays an important role in the switching of cognitive strategies (26).

METHODS

Participants

The experiment was carried out following the ethical standards established by the Declaration of Helsinki (27) and approved by Paris University's ethical committee (n° 2019-26-CASTILLA-COHEN). Ten children with typical development (TD) (six boys and four girls) aged from 9 to 16 years (mean = 10.72, SD = 2.45) were included in the pilot study (See **Table 1**). The parents or participant's legal representative signed an informed consent document before participating in the pilot study. Young participants gave their consent orally. Each participant was assessed individually. The study took place in the department of child and adolescent psychiatry at the Hospital Pitié Salpêtrière Paris, FranceAll TD children were relatives of the staff members of the department. All TD children had normal or corrected-to-normal vision and did not present any neurological or neuropsychological disorders nor exhibited any motor difficulties in gait.

Experimental Setup

The Virtual Carpet™ Paradigm

The experimental set-up used was the Virtual Carpet™ paradigm (24) that combines two computers, one video projector and one HTC Vive (HTC® Vive, Taiwan) for the experimentation. The first computer is connected to a video projector for projecting the navigational space and the stimuli over the floor. The second computer is connected with the HTC Vive and it runs the Basic Trajectory Software version 1 (BTS) to track the participant's trajectory and the navigational space's configuration.

The HTC Vive is a virtual reality system equipped with two infrared cameras, two handheld three-dimensional space (3D) motion sensors and one virtual reality headset. The two infrared cameras are placed 5 meters (16.4 feet) apart diagonally to cover the room in order to record the position of the two handheld 3D sensors (**Figure 1A**). The two handheld 3D sensors are used as motion-trackers during the experimentation. The first handheld 3D motion sensor (i.e., controller) is adapted to a bike helmet and is worn on the participant's head. The second handheld 3D is attached to the belt which is worn on the participant's waist (**Figure 1B**). Both motion sensors provide respectively 3D motion information from the head and the waist. The headset was only used during the calibration procedure to determine the navigational space in 3D coordinates system.

The Virtual House Locomotor Maze Protocol (VHLM™)

With the "Virtual carpet"™, we projected on the floor a virtual maze named the "Virtual House Locomotor Maze" (VHLM™) which allowed us to study the behavior and cognitive control during locomotion. The VHLM™ is composed of 6 houses placed about in a simplified labyrinth delimited by walls created using Microsoft PowerPoint software 2016 (**Figure 2**). Each house can be identified as a target for the subject by a green dot appearing on the house and surrounding it by a green light square. A beep sound is launched simultaneously to the lighting of the house to increase the attentional focus of subjects on the target house. The projection on the floor delimited the navigational space environment (3.5 x 2.5m). This maze deals with spatial memory of the images of a simplified labyrinth with houses projected on the floor. It requires that the participant generates mental representations of the array, stores them and can recall them. When the participant has to navigate in the virtual labyrinth redirecting himself to the departure point, the process can even engage mental rotation processes (28, 29). This paradigm allows us to also study changes in perspectives during spatial navigation (26). Our paradigm is therefore very adequate for replanning procedures because of the diversity of the brain strategies dealing with space. It offers a large repertoire of choices that participants can use and that we can evaluate in order to understand the basic mechanisms of executive functions and the role of inhibition in the locomotor space.

TABLE 1 | Subjects characteristics of the sample.

Subject no.	Age (years)	Gender	Height (m)	Hand dominance	Mean tangential velocity (Cm/s)
1	9	M	1.26	Right	90.2
2	16	M	1.70	Left	93.7
3	9	M	1.23	Right	91.9
4	9	F	1.11	Right	82.6
5	10	M	1.23	Right	78.6
6	10	F	1.48	Right	89.5
7	14	M	1.57	Right	81.9
8	9	F	1.06	Right	87.5
9	10	F	1.34	Right	79.5
10	9	M	1.10	Right	88.7

Procedure

The experimental design was divided into two assessments: (a) the visual-spatial assessment (VSA) and (b) the goal-oriented locomotion task (GOLT) on the Virtual House Locomotor Maze (VHLM).

Visual-Spatial Assessment (VSA)

The visual-spatial assessment was implemented as a control in order to test the visual perception of the stimuli presented in the navigational space and to introduce or familiarize the participant with the VHLM. Every house was presented five times

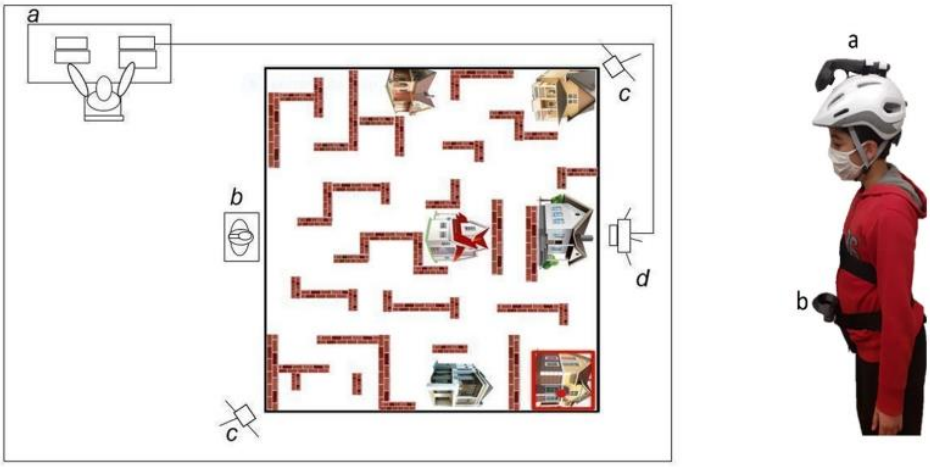

FIGURE 1 | (A) The representation of the experimental setup: (a) control desk location where the experimenter runs the experiment, (b) departure point, (c) two HTC Vive cameras, (d) the video projector. **(B)** 3D motion sensors motion-tracker. (a) one handheld 3D motion sensor is adapted to a bike helmet and is worn on the participant's head and (b) the second handheld 3D motion sensor is attached to the belt which worn on the participant's waist.

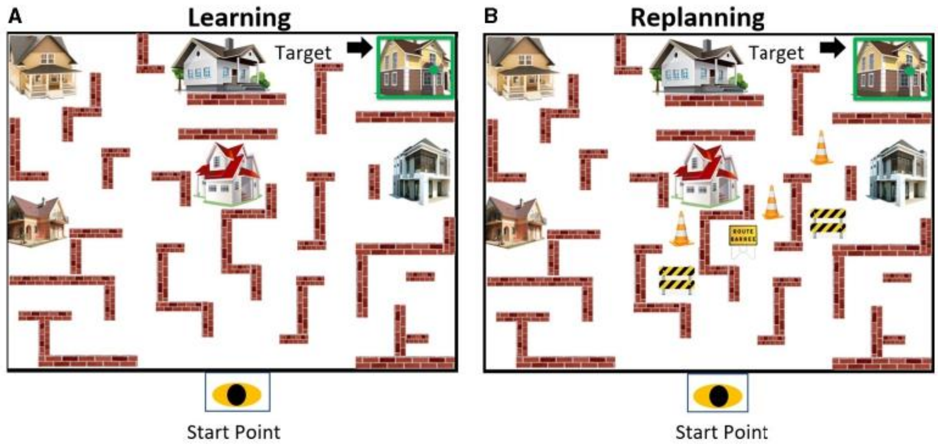

FIGURE 2 | The Virtual Maze layout. **(A)** The left image shows a target house highlighted in green. The same house was shown 5 times for inducing an overlearned trajectory. **(B)** The right image shows a target house highlighted in green and the obstacles blocking access to the house by the shortest paths. This induced the necessity to replan the overlearned trajectory.

in a random order for a period of 1 s with an interval of 1 s between each stimulus (23, 30). The participant's task was to point to the house that was previously highlighted in green without making any sound. The experimenter supervised whether the participant pointed to the right house in order to include or exclude the participant from the experiment. Following the VSA, the participants performed the goal-oriented locomotion task (GOLT).

The Goal-Oriented Locomotion Task (GOLT)

The GOLT was divided into two conditions, (a) the learning condition and (b) the replanning condition where participants are asked to walk on the VHLM to reach the house target presented randomly. In both conditions, the participant always starts each trial at the start point location. The participant was asked to reach a target house highlighted in green accompanied simultaneously by a sound (i.e., beep). They were instructed to reach the target as fast as possible by selecting the shortest path. They were instructed to avoid crossing any walls or obstacles and returning to the start-point while waiting for another trial to begin. Additionally, the participant is also instructed to avoid any possible obstacle that blocks his path to reach a house. The same target house is presented in the learning conditions and in the replanning condition (**Figure 2**).

Learning Condition

In the learning condition, each house is presented five times (i.e., five trials) encouraging the participant to learn and automatize his/her trajectory plan.

Replanning Condition

After the learning condition, the participant performs the replanning condition. In this condition, the same target house is presented but the shortest path is permanently blocked. The participant is then required to replan a new trajectory in order to reach the target and return to the start-point.

Data Acquisition

The Virtual Carpet^{TM} paradigm includes a software (the Basic Trajectory Software (BTS) for recording kinematic information occurring during locomotion. It uses the drives of the HTC Vive: (a) to generate the target positions (i.e., the houses) in the virtual environment known as the calibration procedure, and (b) to record the trajectories of the participant during navigation. This information is saved in two different files: the first file contains the X-axis and the Y-axis coordinates for the locations and the second file contains the participant's locomotion information.

The calibration procedure enables us: (i) to configure the global navigational array; (ii) to mark the four reference corners of the array; and (iii) to set the target's (houses) positions in a Cartesian coordinate system by triggering the 3D motion sensor (**Figure 3**). The calibration procedure is performed by the participant by placing himself over each target house following a standard order.

Locomotion is recorded during the experimental sessions using the HTC Vive handheld 3D motion sensors to track the participant navigation. Two HTC cameras detected the handheld 3D motion sensors in the navigational space, which registered their positions. Each trajectory trial is saved individually as a TXT file: column 1 contains the time span for each participant's trail (ms). Time zero corresponds to the moment when the experimenter launched the recording. The columns 2, 3, 6, and 7 represent the participant's head and waist position named PosX, PosY in meters (m). Columns 4, 5, 8 and 9 (i.e., Pitch head and waist and Yaw head and waist) indicate rotation angles with respect to the X and Y- axis direction (**Supplementary Table 1**). For the purpose of the present study, only the horizontal component of the 3D motions sensors was measured.

The raw data was treated using the Matlab 2019 programming language. Initially, an automatized script read the trajectory file and the targets position file was generated by the BTS. The corporal adjustments (i.e., artifacts) in the standing position at the start point prior to the stimulus presentation were deleted for each trial. The data were filtered using an averaging filter of 2-by-2 neighborhood algorithm. We conducted: (a) a trajectory and head direction qualitative behavioral analysis, and (b) tangential velocity (cm/sec) and latency quantitative analysis.

The Trajectory and Head Direction Analysis

By using the trajectory locomotor analysis and the head direction in the horizontal plane, it was possible to identify: (i) the kinematic behavior during the planning and replanning phase, (ii) the behavior during the initial segment of trajectory (**Figures 4A,C**).

The Tangential Velocity (cm/sec)

It is the velocity produced during the trajectory (see formula below) (**Figures 4B,D**). Thereafter, the latency or departure time cm/s (DT) was computed from the tangential velocities. The latency corresponds to the delay between the presentation of the target house (i.e., "GO" signal, house lit and beep), the initiation of the locomotor departure and once his tangential velocity reached above the threshold of 30 cm/s (**Figure 5**). This threshold is arbitrary but considering that standard average walking velocity is 125 cm/s, this represent a 24 % threshold (31).

$$v(t) = \sqrt{\dot{x}(t)^2 + \dot{y}(t)^2} \quad (1)$$

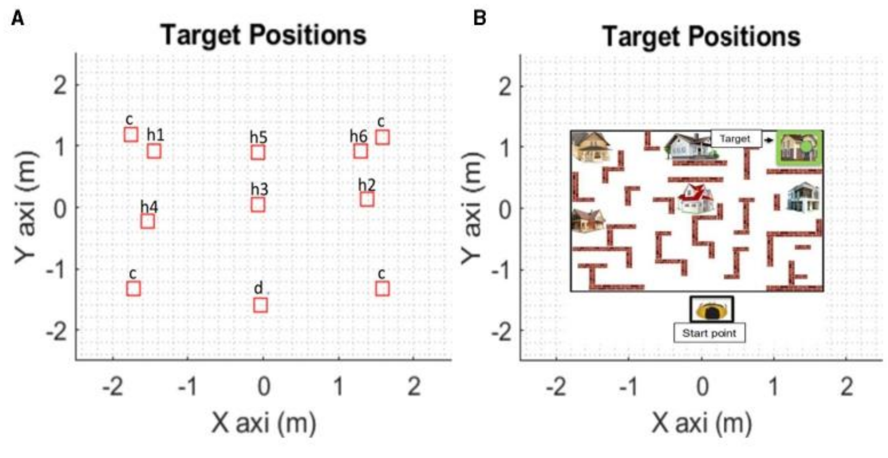

FIGURE 3 | The global navigational array in the X and Y- axis coordinates. **(A)** The "c" represents de corners, the "h1", "h2", "h3", etc. represent the house order presented to the participant and the "d" represents de Start point. **(B)** Representation of the projection on the floor including the houses and the start point.

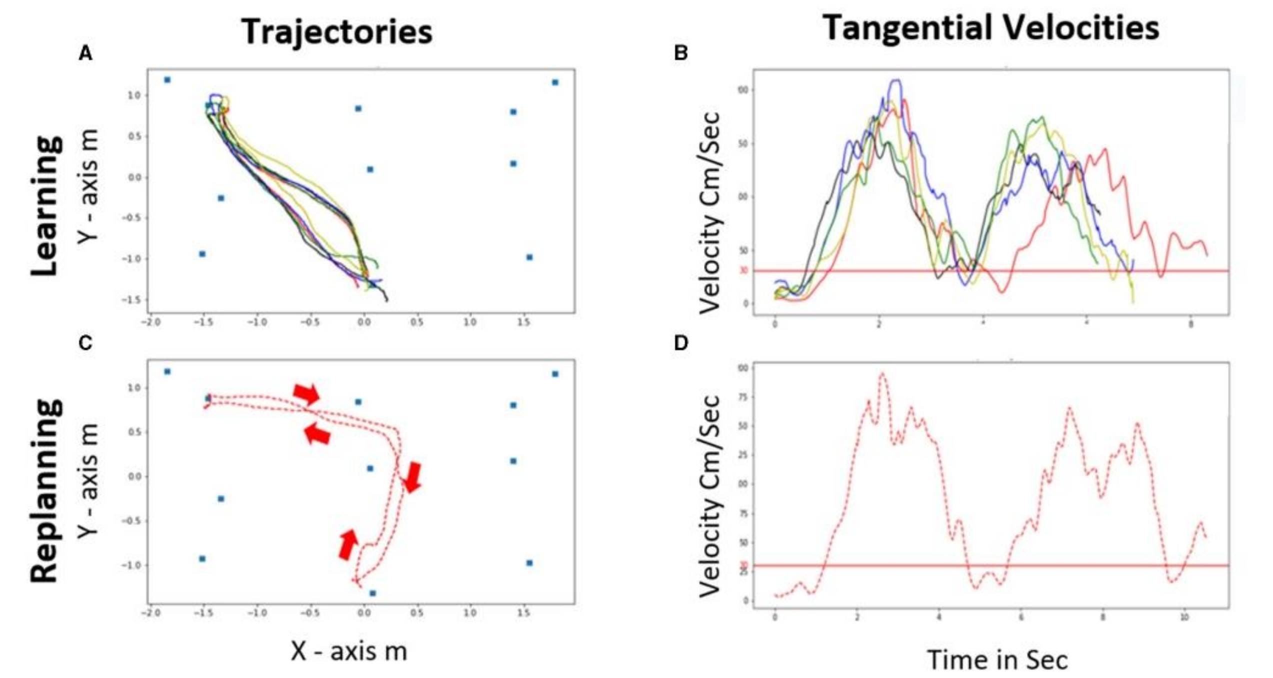

FIGURE 4 | Representation of the Learning and the Replanning phase for a single participant : **(A)** Trajectories and **(B)** tangential velocities for the learning. **(C)** Trajectory and **(D)** tangential velocity for the replanning phase for the first house. The red arrows represent the direction of the trajectories for the replanning phase showing a *new direction* (ND) adapted reconfiguration during the replanning.

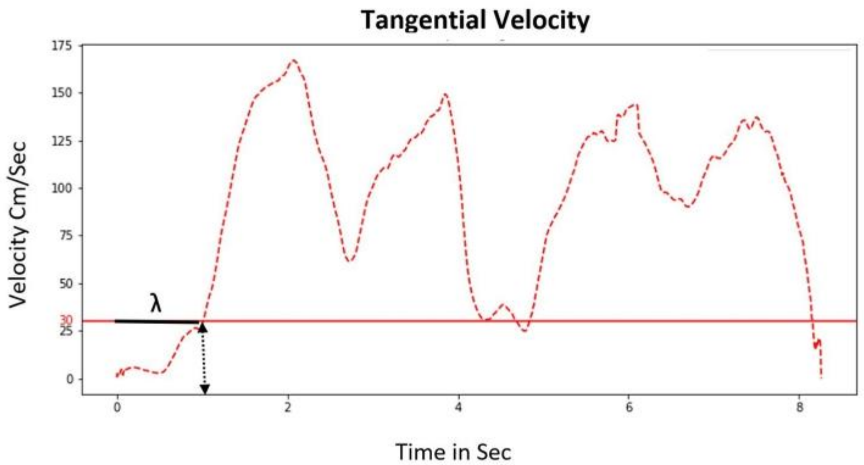

FIGURE 5 | Representation of the computing tangential velocity and latency (Lambda, **λ**) of one participant during a trail in the Learning phase. In the X-axis, the zero corresponds to the moment when the house was lit on the ground indicating "GO" signal. The time of real departure of the subject was computed when the tangential velocity was above the threshold of 30 cm/sec. The "**λ**" is the delay between the "GO" signal and the velocity exceeding the threshold.

Statistical Analysis

All statistical analyses were performed using the open-source statistical software R version 4.0.3. for Windows (www. R-project.org). The collected data were analyzed using descriptive statistics. Given the sample size, these are only exploratory statistics.

RESULTS

Tangential Velocities and Latencies for Each Trial

The main results are shown in **Tables 2**, **3** and **Figure 6**. During the learning phase, from the first trial to the fifth trial the tangential velocities' means increased and it decreased again during the replanning trial. The means of the latencies between target presentation and initiation of locomotion decreased from first trial to the fifth trial. However, the latency increased again during the replanning phase.

TABLE 2 | Means (M) and Standard Deviations (SD) of tangential velocity and latency in sec by trials.

	Tangential Velocity		Latency	
Trial	**M**	**SD**	**M**	**SD**
1	81.7	13.6	0.88	0.25
2	85.4	15.5	0.72	0.19
3	87.5	13.0	0.70	0.20
4	89.9	14.2	0.66	0.18
5	90.0	16.7	0.65	0.19
Replanning	82.3	10.9	0.90	0.35

Kinematic Behavior During Learning Phase

Figure 7A shows an example of the recorded trajectories and head direction during the learning phase. The blue line represents the head trajectory in the horizontal plane for the head 3D motion-sensor (but a similar graph could be draw for the trunk trajectories). The red arrows indicate the head direction with respect to the experimental room. From this graph, it was possible to identify two behavioral interesting features: (a) overall, subjects went to the target house using the shortest path; (b) once subjects had chosen a trajectory, they generally repeated it with small or rare variations in the trajectories.

Kinematic Behavior During the Replanning Phase

When the learned path was blocked, as shown on **Figure 7B**, the subjects chose a new path. We concentrated our analysis on two features of the initial response of the subjects behavior, namely the initial segment of trajectory. Often, the subject started immediately walking in the pre-learned direction (PLD) instead of walking in the direction of a new path (**Figure 8A**). Then, they could either stop and reorganize the path or continuously

TABLE 3 | Median and range quartile (Q1–Q3) of the tangential velocity and the latencies by trials. (*n*) represent the number of observations.

Dependent variable	**Trial 1 (*n* = 62) median value [Q1;Q3]**	**Trial 2 (*n* = 56) median value [Q1;Q3]**	**Trial 3 (*n* = 55) median value [Q1;Q3]**	**Trial 4 (*n* = 57) median value [Q1;Q3]**	**Trial 5 (*n* = 58) median value [Q1;Q3]**	**Trial replanning (*n* = 58) Median Value [Q1;Q3]**
Tangential Velocity Cm/Sec	81.8 [73.8; 91.0]	84.6 [73.8; 95.5]	86.6 [78.6; 95.8]	86.1 [81.0; 99.8]	88.5 [78.0; 96.1]	83.81 [77.4; 88.1]
Latency (Sec)	0.89 [0.71; 1.04]	0.73 [0.60; 0.89]	0.69 [0.54; 0.84]	0.68 [0.56; 0.77]	0.66 [0.56; 0.78]	0.94 [0.64; 1.14]

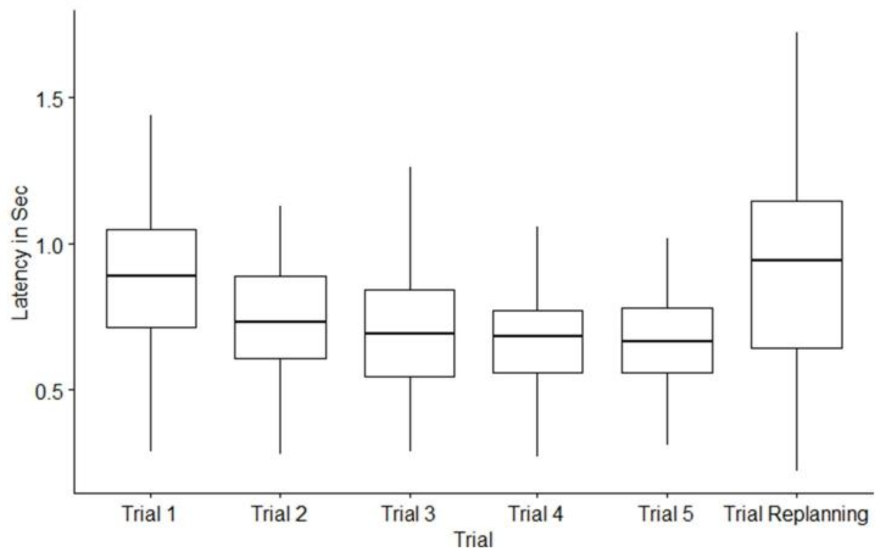

FIGURE 6 | Boxplot of latency in Sec by trials (Leaning and replanning). Box = 25th and 75th Percentiles; bars = min and max values.

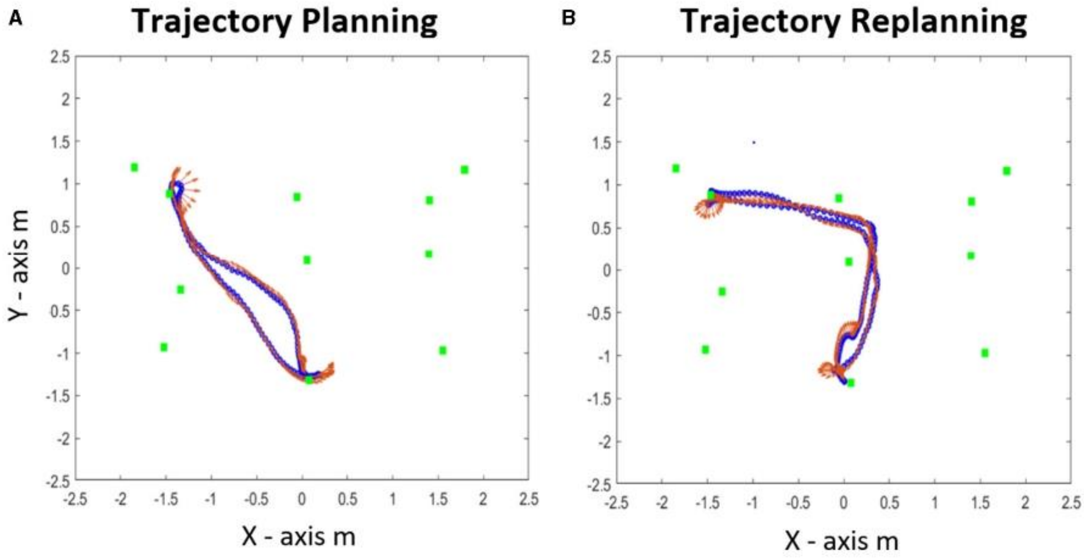

FIGURE 7 | (A) An example of a trajectory for the learning phase. **(B)** An example of a trajectory for the replanning phase. The red arrows represent the head direction of the trajectories for each phase.

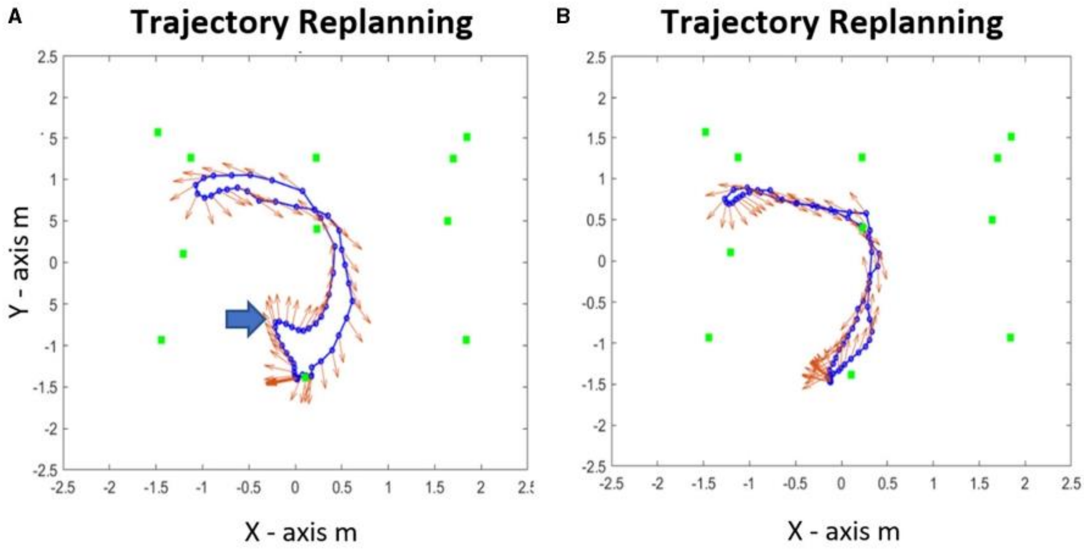

FIGURE 8 | Trajectories replanning examples. **(A)** Departure to *previous learned direction* (PLD) during replanning before the treatment. **(B)** Departure to a *new direction* (ND) after the treatment. The red arrows represent the head direction of the trajectories during the replanning phase.

redirect the locomotion toward a new goal. In many cases however, the subject would immediately start in the replanned new direction (ND) because they have mentally planned a new trajectory while waiting at the departure point. This can be observed both from the trajectory, and from the head direction vectors in red (**Figure 8B**). Such a variety of strategies had been observed in a virtual maze paradigm (32). We have named these three behaviors: *the impulsive response with stop, the impulsive response with online planning,* and *the anticipatory- planning.*

Age Differences

We made two observations concerning the age differences based on the trajectories and the head rotation that suggest further exploration of age differences. Firstly, we found that two very young children (7–8 years old) made a great number of head direction changes during both the learning phase and the replanning phase, and that the oldest subjects did not show this behavior. Secondly, very young children in our sample made more impulsive responses with starts in the wrong direction. It is also know that a progressive maturation of executive functions occurs in the age range of this study from 5 years old to adolescence. Finally, it has been shown that this acquisition of cognitive flexibility is related to the progressive use of inhibition allowing a shift of automatic heuristics to new strategies (6).

DISCUSSION

The objective of the current study was to design and to test a new protocol named the "Virtual House Locomotor Maze" (VHLM). It allowed us to study cognitive control during navigation throughout neurocognitive development based on the Virtual Carpet paradigm. We explored the capacities of planning and replanning trajectories to study inhibition and mental flexibility using a spatio-temporal index by the means of measuring kinematic behavior (i.e., trajectories, tangential velocity and head direction) during spatial navigation. We concentrated our analysis on : (a) comparing the departure's latency (delays) of the overlearned paths and the new replanned path, (b) analyzing directional locomotor trajectories during replanning, and (c) exploring age and cognitive performance.

During the learning phase, we found a decrease in latency after the repetition of the same target which indicates that there is an ongoing learning and automatization process of the locomotor trajectory. The duration of this initial delay is about 1 s. This delay is compatible with a complex reaction time (about 300 ms), with an additional 600–800 ms time for initiation of gait under cognitive control of a spatial task (33–35). We observed thatbetween the second to the fifth learning trial there is a rapid optimization of the trajectory following the first learning trial throughout the initial trials. In addition, we observed that in the learning condition, the generation of locomotor trajectories follow a kinematic stereotypy (i.e., repetition of the same trajectory) which has already been proven by previous research (36, 37).

The latency (λ) differs between the last (5th) learning trial and the replanning trial by about 0.48 s, reflecting the existence of a delay caused by the inhibition process of the overlearned path. This is observed, in general, when an automatic response (i.e., heuristic) needs to be replaced by a new one with an inhibition process (8). Interestingly, the mean latencies from the first learning trial and the replanning trial are similar, suggesting that the production of a "new" locomotor trajectory engages similar cognitive strategies.

Another interesting observation is the large variability of initiation latencies for the replanning. This variability may reflect the differences of cognitive processes occurring in different subjects depending upon several factors. For example, the encoding of the spatial array of houses may differ according to attentional differences or oculomotor strategies. It is also know from previous work using the magic carpet that children from ages 5 to 12 differ in their use of spatial reference frames (allocentric or egocentric) (26). Also, oculomotor strategies have been found to influence the performance in the planning of a visuo-spatial locomotor task (38).

In our experiment, the learning process is modulated by the task rules, the target spatial location and the temporal constraints ("as fast as possible"). The subject needs to acquire the information about the environment and tries a first path in the virtual labyrinth. This process has been named the "*exploration phase*" (39). In the following trials, this first attempt is used to confirm or modify the "shortest path" chosen by the subject to reach the target house. It has been called the "*exploitation phase*". A clear distinction of brain activation is identified in the animal model in both phases. The cortical areas and striatum are involved in the *exploration phase* and the hippocampus and cerebellum are involved in the *exploitation phase* (40). In addition, it has been also suggested that the human posterior hippocampus (PH) invigorates exploration while the anterior hippocampus (AH) supports the transition to exploitation on a reinforcement learning task with a spatially structured reward function (41). Thus, our findings are aligned with neuroscience literature suggesting that after repeating the same behavior (i.e., a path), this process induces a shift of neural activity from the prefrontal cortex areas to the basal ganglia cerebellar circuits that "automatizes" the behavior for a faster responses (42, 43). Hence, when the chosen overlearned path is blocked, it will require from the subject to create a new alternative path involving inhibition of the previous path. The prefrontal cortex is reactivated for adapting to this situation and accomplishing the given task (44–46). Thus, prefrontal regions may contribute to spatial navigation involving cognitive processes such as decision-making, goal tracking, and planning (47).

Strategy Selection and Neurodevelopment

We consider that the combination of locomotor initiation latency and start toward the pre-learned direction should be a good index of impulsivity. Regarding the learning phase, it would be interesting for further research to consider two types of cognitive strategies which could be adopted within the experimental design. The first type of learning relates to a sequential selection of the path (i.e., trial by trial). However, the subject can also anticipate the blocking of the path and adapt their behavior. In addition, an optimal strategy needs to deal with a tradeoff between faster responses and correct responses (for instance, avoiding to go through the virtual walls of the labyrinth) which is a good indicator of cognitive control during neurodevelopment (48).

In the re-planning trial, subjects need to inhibit the overlearned path and re-explore and exploit a new path. We observed that, due to the task's temporal constraints, behaviors can manifest in three different forms:

(a) *Departure without inhibition or impulsive responses:* the subject starts walking toward the target but in the wrong direction (i.e., good target- through the blocked path), then stops and changes the trajectory. We speculate that in this case the subjects are mentally operating in an egocentric frame. Spatial locations are encoded relative to the body (49) without the use of an allocentric global representation of the whole array. Thus, after the blocking of the learned path, the subjects need more time to process spatial information and to plan a new path because they have to shift from the egocentric to the allocentric frame (26).

(b) In the *impulsive online planning*, the subject starts walking toward the target with the learned trajectory and changes the trajectory without completely stopping but instead reduces velocity. In this case, the performance requires a more continuous switching in strategies from egocentric to allocentric treatment. This switching of strategies has been previously reported in children, associated with the maturation of executive functions during the spatial treatment (26). The tangential velocities along the trajectory are somewhat slower as the subject performs on line correction of their trajectory.

(c) In the *anticipatory- planning*, the subject waits at the start point and selects the alternative path avoiding going to the wrong pre-learned direction. In this case, the subject inhibited the automatic response to replan a new trajectory using allocentric encoding before starting the locomotion. It can be associated with longer latencies before the initiation of the locomotion but once a new path has been identified, a higher velocity and amplitude in the tangential velocity is distinguished. We consider that these navigational capacities are acquired throughout child development process and achieved in early adolescence (50).

These results indicated that the VHLM is a suitable tool for assessing visuo-spatial memory, inhibition and cognitive flexibility in the near distant extra-personal locomotor space. The VHLM differs from existing protocols which can assess the behavioral strategies involved during the replanning of a new trajectory by implementing behavioral strategies using navigational arrays. They could also be a good index for development of spatial abilities from childhood to adult.

Limits and Perspectives

This study has, however, several limits which at the same time encourages further studies: Firstly the small number of subjects could not allow us to jump to conclusions (51). However, we hope that our navigational protocol encourages further extensive research in visuo-spatial memory and replanning including not only children with atypical development such as ADHD and autistic spectrum disorder (ASD) patients but also adults.

Secondly, future research could incorporate new measurements such as the head direction and the difference of head direction with trunk direction (Gaze control Parameter in the absence of eye movements measurements). If a subject who plans, and executes a path with an egocentric sequential set of body movements will make a small number of gaze direction movement. A subject with attentional disorders, or who has difficulties in encoding correctly the array and the location of the target house, or the spatial distribution and geometry of the "streets" in the labyrinth will make more head orientation movement during the replanning phase. For this, it is important to include very light head mounted eye movement devices in order to have precise measurement of gaze direction as was done in Bernardin et and Authié (52–55). However one has to avoid loading the head of children with equipment as this may cause modifications or the behavior.

We will also adapt the negative priming paradigm of O. Houdé and G. Borst group to the VHLM for studying the inhibition process during navigation in typical and atypical development such as ADHD, motor coordination disorder and/or autism spectrum disorder (56). This protocol can also be used to evaluate the contribution of the different action spaces and it is therefore of high interest to better understand complex cases (e.g., multidimensionally impaired) (57).

This paradigm could be used to analyze also non pathological dimensions of personality. For example the possible correlation between different dimensions of the Gregarious Positioning (e.g., Submission and Dominance) (58, 59) and the navigational pattern during the performance in the VHLM. Submission is generally associated with a tendency to remain egocentric and locked on rules and learned behaviors, dominance is generally linked with more global allocentric encoding and an easier capacity to escape rules and find new solutions.

Lastly this protocol could be used in elderly patients, and in particular with Alzheimer patients for testing not only their spatial memory but their spatial cognitive flexibility. It could also be attempted to use is as remediation training for these pathologies.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Paris University's ethical committee - 2019-26-CASTILLA-COHEN. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

AB, JF, CL, MZ, and AC designed the study. AC collected and analyzed the data. AB, DC, and AC interpreted the results and wrote the manuscript. OH and GB supervised and helped with the revision. All authors contributed to the article and approved the submitted version.

FUNDING

AC was supported by a CDI grant from Institute de Médecine Environmental (IME).

ACKNOWLEDGMENTS

We want to acknowledge and thank Dr. Julie Brunelle, Ingrid Zammouri, and Hugues Pellerin for their help regarding the recruitment of participants and their constant support concerning the statistics. We also heartily thank the staff from the department of Pedopsychiatry (Director Pr DC) at Hospital la Salpétrière who contributed to the technical and administrative support of the experiments. The clinicians of this department kindly helped with the recruitment of the subjects and provided valuable information on the clinical evaluation of the patient.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.708378/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

III.3.1. Article in preparation (drafting)

Title: Inhibitory control and cognitive flexibility for replanning in a visuo-spatial memory task. A study in typical children and children with neurodevelopmental disorders

The identification and the selection of relevant information is a key feature for adapting to a rapidly changing environment. This selection of information involves the suppression of irrelevant or pertinent information. As previously stated in the introduction, the IC is responsible for the filtering of the appropriated information. One way to experimentally demonstrate the IC is using the negative priming paradigm which is commonly used in neuropsychology and cognitive neurosciences to test the suppression of irrelevant information (Borst, Moutier, et al., 2013; Neill et al., 1995; Tipper, 1985). The main idea of the negative prime paradigm consists of when a stimulus (e.g., item) that was previously suppressed or ignored, the next cognitive treatment of the same stimulus will be disrupted leading to less accurate responses or a slower reaction time in the cognitive processing (Borst, Poirel, et al., 2013; Houdé & Guichart, 2001; Tipper, 2001). The classical negative prime paradigm consists of the association between stimulus *prime* and *probe*. The first stimulus presented is the *prime* followed by the presentation of a *probe*. During the test-probe condition, the prime is a distractor (e.g., stimulus to be inhibited) followed by the presentation of the probe target. In the control-probes, the prime does not share any relation with the stimulus presented. The negative prime is measured by measuring the differences between the test-probes condition and the control-probes condition. Thus, the presentation of a prime (stimulus that is being ignored or inhibited) influences the performance when this previous information is required in the probe (Tipper,1985). An example of the negative priming effect can be observed during the performance of the classical Stroop test. In the Stroop test, the task is to read the color of the ink and to avoid reading the color name (e.g., Green, color text is Red). The negative priming effect is observed when the name of the word previously inhibited needed to be generated as a response causing a slower reaction time (e.g., Blue, Color text is Green)(Dalrymple-Alford & Budayr, 1966).

It is important to take in consideration the findings mentioned earlier and to bear in mind the conventional assessment employed in neuropsychology and cognitive neurosciences to explore inhibition control which is limited to the peripersonal space. The objective of this article was to assess the development of IC in a near extrapersonal space using a negative prime paradigm.

To our knowledge, this is the first experimental research paper that investigates IC in near extrapersonal space in a goal-oriented locomotion task. We hypothesized that we would observe a negative priming effect compared to the performance in the VHLM, more specifically. IC will be observed comparing the performances of the test-probe (T3) where the trajectory needed to be inhibited and the control-probe (T6) where a new maze was presented and not related to the original maze. Thus, we predicted that the latencies for the departure will be smaller for T6 compared to T3 where the overlearned was inhibited. Additionally, head movement before the start will be smaller in T6 compared to T3.

We predicted that the inhibition of the path by blocking the trajectory will be increased latency and increased exploration (head-chest-yaw). Indeed, we anticipated that the difference between head-chest included more movement in terms of exploration and reconfiguration. The inhibition capacities are closely related to cognitive development and therefore we expected the cognitive inhibition process to be modulated according to the different types of age groups and pathologies. In addition, we expected to observe behavioral evidence of different developmental trajectories in the manifestation of IC and CF.

The main idea was to combine the negative priming protocol with a goal-oriented navigational task in a new simplified maze named the "Virtual House Locomotor Maze (VHLM)"(Castilla et al., 2021a). The VHLM is based upon the technology of the Virtual Carpet Paradigm™ which is used for exploring IC in both the peripersonal and the near navigational extrapersonal space. An adaptation of the negative prime protocol was created to assess the inhibition process during the trajectory replanning in children, adolescents, and adults. The experimental design is a behavioral task based on a non-correlational paradigm in order to study cognitive control during the reconfiguration of an alternative trajectory.

III.3.1.1. **Methods**

III.3.1.1.1. Participants

One hundred and nine participants were enrolled in the study (Table 7). The parents or participant's legal representative were provided a detailed explanation by the experimenter and then signed an informed consent document before participating in the study. Additionally, they were given a document to take home which summarized the experiment. The study took place in the department of child and adolescent psychiatry at the Hospital Pitié Salpêtrière Paris, France. Young participants gave their consent orally and each participant was assessed individually. All TD children and adults had normal or corrected-to-normal vision and did not present any neurological or neuropsychological disorders nor exhibited any motor difficulties in gait. The experiment was carried out following the ethical standards established by the Declaration of Helsinki and approved by Paris Cité University's ethical committee (n° 2019-26-CASTILLA-COHEN).

Table 7. Category of participants and diagnoses

Group	Male	Female	Total	Mean Age and SD
TD Children	32	10	42	11.12 (3.13)
TD Adults	10	22	32	24 (2.3)
ADHD Children	17	2	19	10.8(2.6)
ASD Children	8	1	9	11.5(3.2)
DCD	6	1	7	12(2.06)
Total participants	**73**	**36**	**109**	

III.3.1.1.2. Experimental setup

We used the "Virtual House Locomotor Maze" (VHLM) based on the technology of the virtual carpet paradigm (Castilla et al., 2021a). The VHLM is composed of a simplified labyrinth of 6 houses where a series of path blocking trajectories are programmed to change the participant's trajectory (Figure 45).

Figure 45. The Virtual House Maze. Representation of the navigational space. The participant is positioned on the start point.

III.3.1.2. **Procedure**

The experiment was divided into a) *visual-spatial assessment (VSA), b) negative prime condition, and c) control condition.*

III.3.1.2.1. The visual-spatial assessment

The VSA was implemented as a control to test the visual perception of the stimuli in the navigational space and to familiarize the participant with the VHLM. Each house was presented five times in a random order for a period of 1 second with an interval of 1 second between each stimulus. The participant was asked to point to the house that was previously highlighted in green. If the participant pointed correctly and achieved higher than 80 %, they were invited to continue with the experiment. Once the VSA was completed, the participants performed the goal-oriented locomotion tasks (negative prime and control condition).

In the experiment, the participants performed a goal-oriented locomotion tasks to reach a house (i.e., target) which was located in a maze and highlighted in green. The participant is asked to navigate on the maze which was projected on the floor and to reach a target as fast as possible while avoiding crossing any walls. In each trial, the participant began at the start-point placed in front of the maze. The departure signal was announced simultaneously by a sound and with the target's apparition. For each trial of the experiment, the participants were instructed to select the shortest path and to reach the target as soon it appeared. After reaching the highlighted house, the participant was required to return to the start-point and waited for another trial to begin.

III.3.1.2.2. The experimental design of the negative priming condition

The experimental design was validated under the supervision of Professor Olivier Houdé and Professor Gregoire Borst. The negative priming condition was developed to assess IC during the locomotion in children, adolescents, and adults. This task is an adaptation of the classical negative prime paradigm and was modified to take place in the navigational space. It follows the identical methodology presenting prime and probe during the experimentation.

The experimental design is divided into two conditions: 1) the negative priming condition and 2) the control condition. Each condition is subdivided into three phases: a) the learning phase, b) the prime trial, and c) the probe trial. These conditions are presented in a fixed order to the participant during the experiment: first the experimental condition followed by the control (See Figure 46).

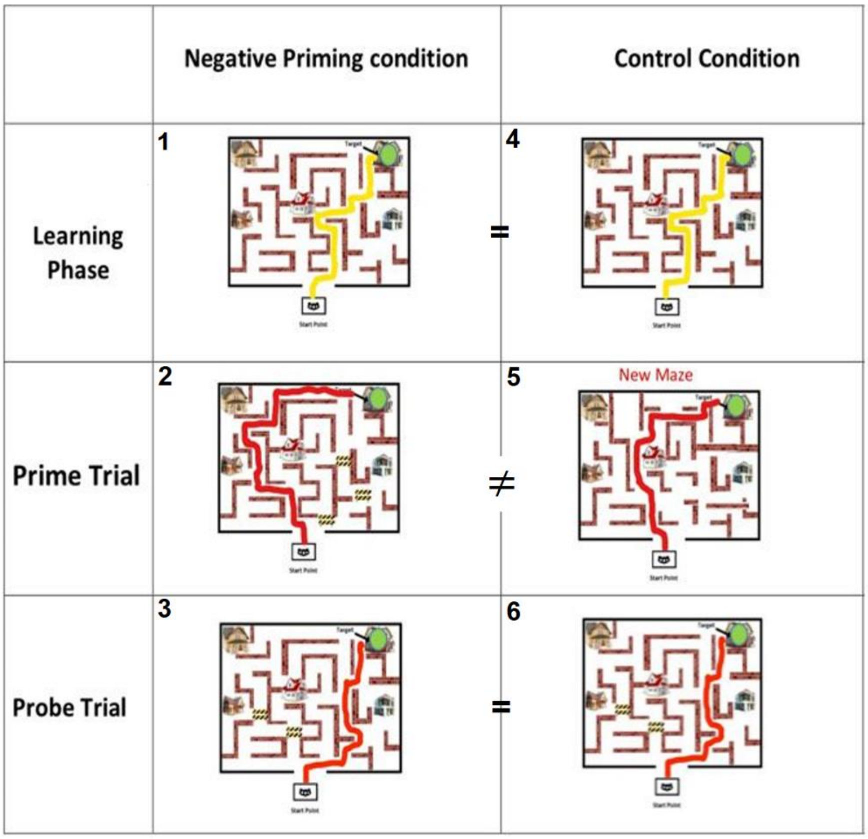

Figure 46. Experimental design representation. The yellow and red lines depict the possible trajectories performed by the participant during the experimental and control condition. The numbers correspond to the order of the experimentation.

III.3.1.2.3. Learning phase trials

In the learning phase or phase (T1), the participant was instructed to select the shortest path in the maze to reach a target. The departure signal was announced simultaneously by a sound and with the apparition of the target (i.e., house highlight in green). After the presentation and selection of the shortest path, the participant moved through the maze to reach a specific target as soon as it appeared. This procedure was repeated five times.

III.3.1.2.4. Prime trial (Inhibition and Replanning)

After the learning phase, the participant performs the prime trial or phase (T2), During this phase, the target is presented in the same position as in the learning phase. The departure signal was announced simultaneously by a sound and with the apparition of the target. After the presentation of the target, the shortest path was blocked indefinitely. During the blocking of the path, the participant was required to replan a new trajectory in order to reach the target and then return to the start-point.

III.3.1.2.5. Probe trial

During the probe trial or phase (T3), the participants were instructed to reach the same target as quickly as possible. The trial began with the presentation of the target and the departure signal. Simultaneously, the alternative path to reach the target was blocked forcing the participant to choose between the path memorized in the learning phase or an alternative trajectory.

III.3.1.2.6. The control condition

The control condition included a learning phase (phase T4), a Prime trial (phase T5), and a Probe trial (phase T6). The learning phase was identical to the negative priming condition (i.e., the shortest path is repeated five times). During the prime trial or phase 5, a new maze was presented to the participant. This new maze was characterized by a different configuration of the walls and the paths in order to reach the targets. The target, however, was placed at the same position as in the learning phase. In the probe trial, The participant was able to take the same path that they memorized in the learning phase or choose another path.

III.3.1.3. **Data analysis**

To observe if the behavioral inhibition was manifested during the experiment, we used the same conventional method used in the classical negative prime paradigm. It compared the probes trial's (phase 3) performance of the negative prime condition versus the probe trial in the control condition (phase 6). Comparing phase 3 and phase 6, the probes indicated a difference in the performance because the prime trial in the control condition is not related with the probe trial. Moreover, further analysis can be implemented in this protocol for studying the executive functions.

III.3.1.4. **Parameters of measurement**

Based on data recorded during the trajectories generated by the participants, we measured and analyzed the following parameters: *a) the tangential velocity, b) the latencies of the departure time* (Lambda λ), *c) the differences between the head-chest angles of rotations* in the Yaw Axis (Epsilon ε) before and during locomotion.

The tangential velocity (cm/sec) is the velocity produced during the trajectory (see formula below) (Figure 47). We computed the *tangential velocity*'s mean and standard deviation during the locomotion to arrival on the target. This parameter allowed us to compare the difference between the experimental condition and the control condition.

$$v(t) = \sqrt{\dot{x}(t)^2 + \dot{y}(t)^2}$$

b) The *latencies of the departure time (cm/sec) or* Lambda λ. Based on the *tangential velocity,* we computed λ which is the interval between the presentation of the target (i.e., "GO" signal, house lit and beep), the locomotor initiation (i.e., departure) and the *tangential velocity* reaching above the threshold of 30 cm/sec, (Figure 48). λ is an index of impulsivity or lack of inhibition control(Figure 49).

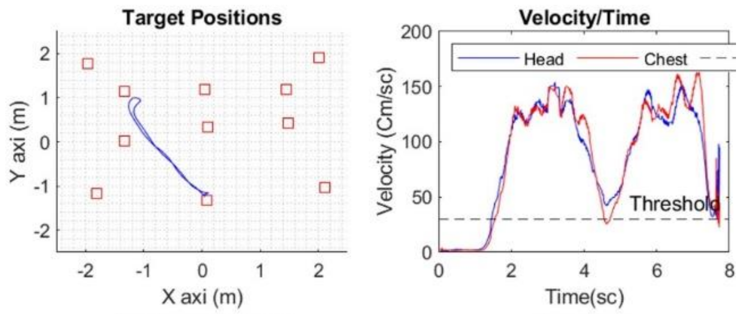

Figure 47. Plots of the spatiotemporal parameters: the trajectories during the trials, the tangential velocity (cm/sec) for the head and chest, the acceleration (cm/sec) and the curvature (1/cm).

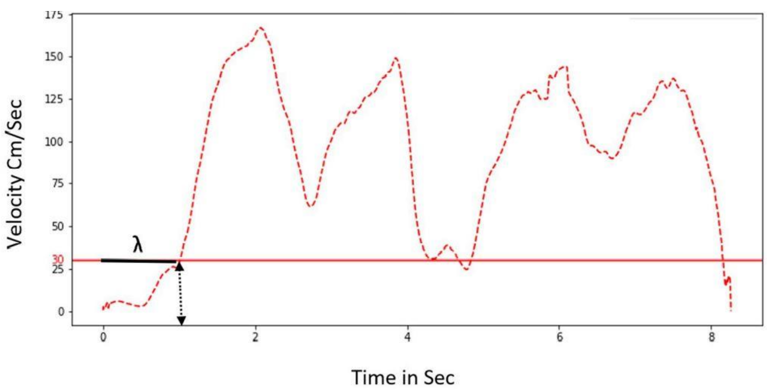

Figure 48. Representation of the latency (Lambda λ). λ is the delay between the 'go' signal and the tangential velocity exceeding the threshold 30 cm/sec.

c) Differences between Head-Chest angles of rotations in Yaw axis (Epsilon ε) before and during the locomotion (Figure 49). Using the head and chest rotations (in degrees) in the horizontal plane (Yaw Axis), it was possible to identify ε which is a kinematic index of behavior exploration before the locomotion and during the spatial navigation (see Figure 50, 51, 52).

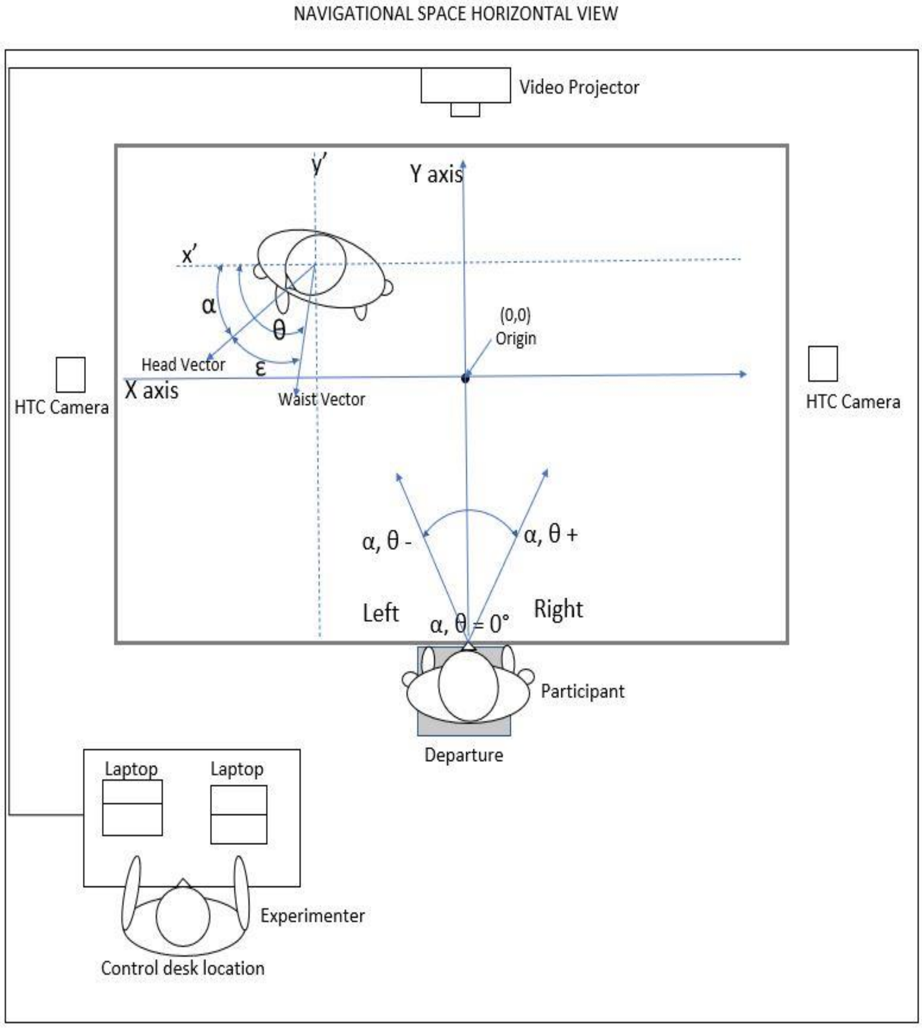

Figure 49. Representation of the navigational space from a horizontal view (Yaw axis). The head rotation (deg) in the horizontal axis is represented by Alpha symbol (α)-, whereas the chest rotation (deg) in the horizontal axis is represented by Theta symbol (θ). The difference between head and chest rotations in degrees is represented by an epsilon symbol (ε) with respect to the X-axis of the experimental room.

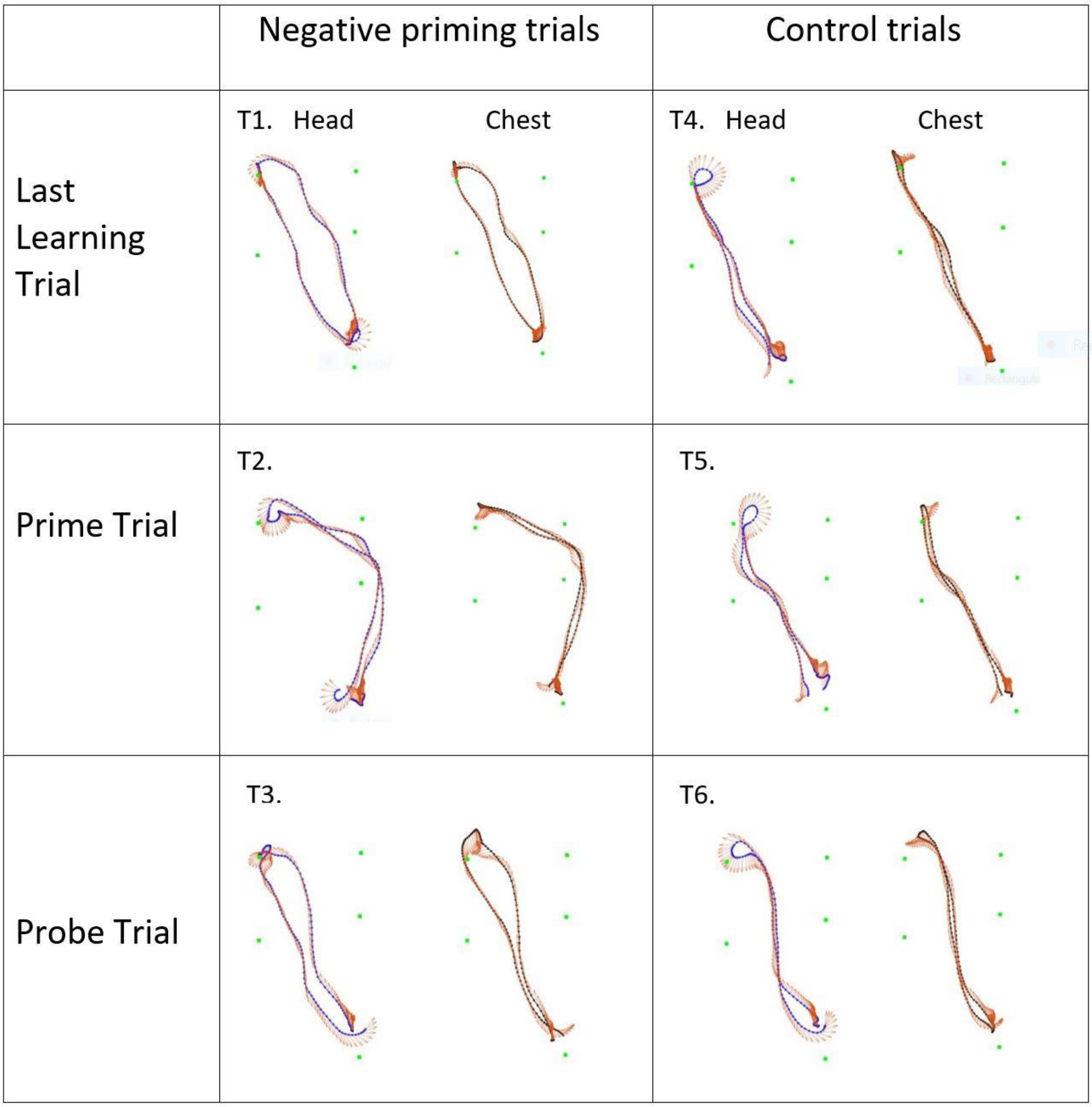

Figure 50. Trajectories and head-chest orientations for a typical child 10 years old in Negative prime and control trials. The red arrows represent the head and chest direction during the trajectory and the blue and black dots represent the trajectories. The green squares represent the 6 houses, the start point and the references corners.

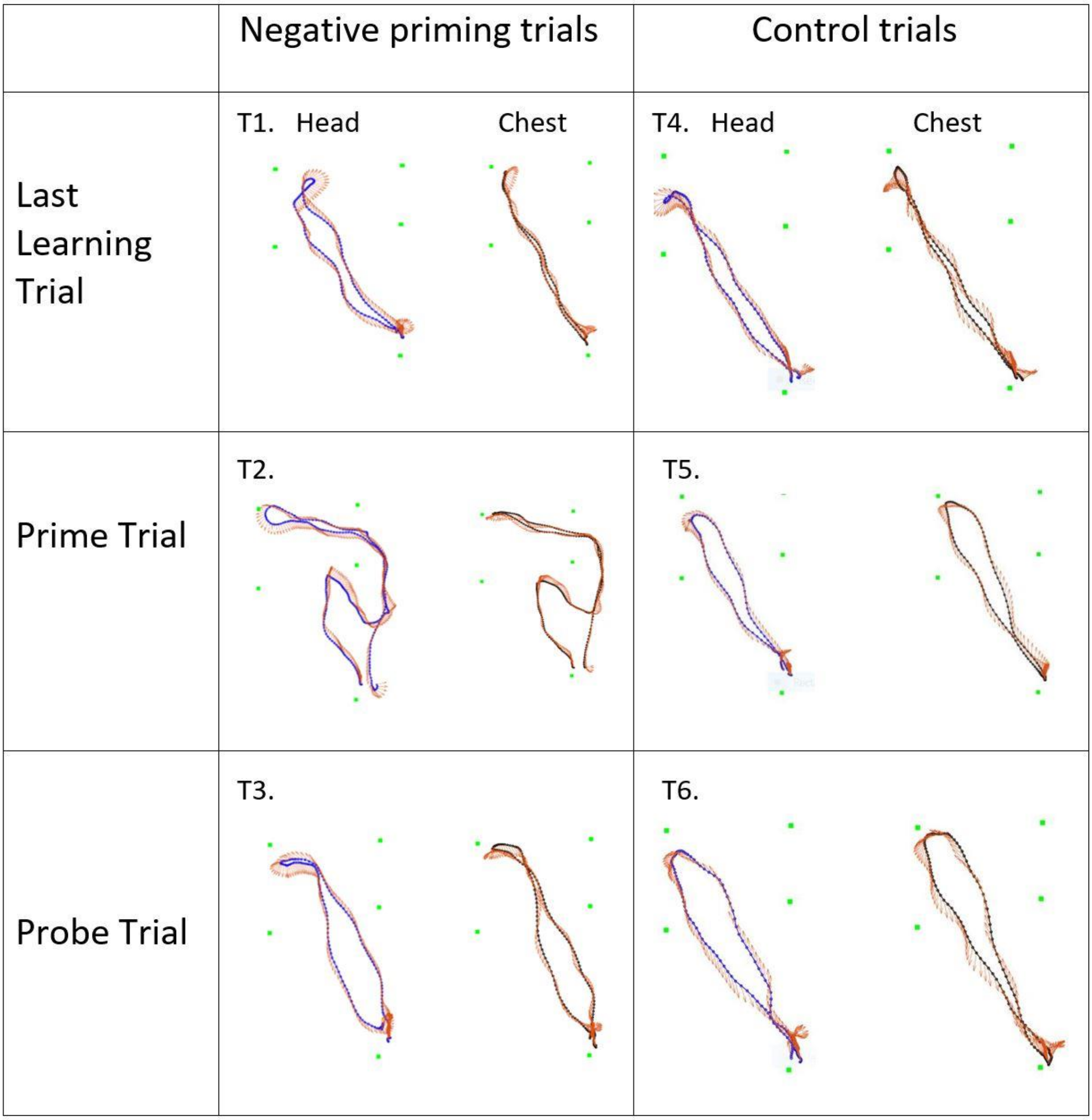

Figure 51. Trajectories and head-chest orientations for an ADHD child 10 years old in Negative prime and control trials. The red arrows represent the head and chest direction during the trajectory and the blue an black dots represent the trajectories. The green squares represent the 6 houses, the start point and the references corners.

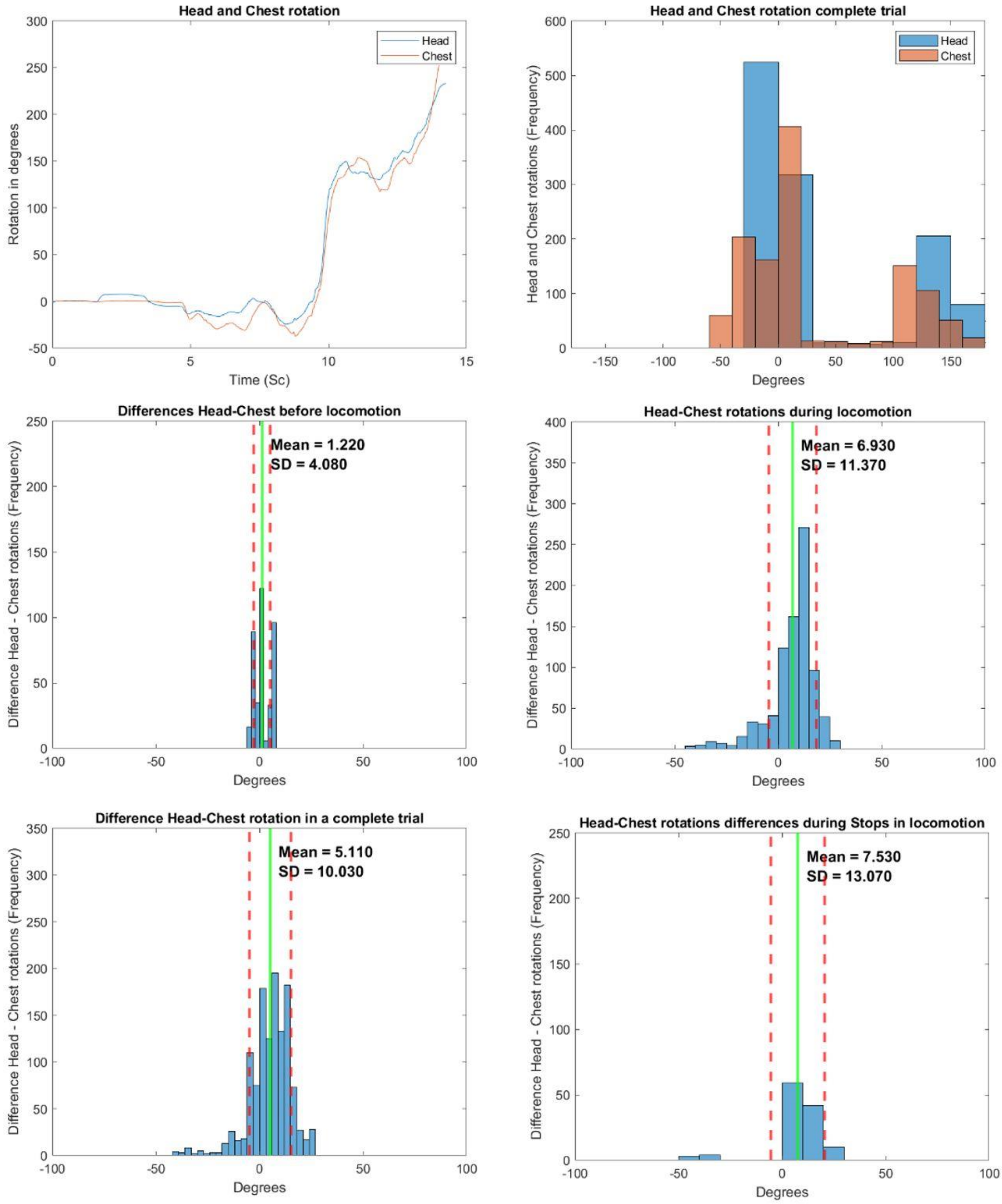

Figure 52. Plot and histograms of head-chest orientations for a typical child 10 years during locomotion.

PART IV: DISCUSSION

In this section, we will discuss the main results and findings of the experimentation, the future perspective of possible research as well as the ongoing projects. The aim of this thesis was to study IC, CF, and VSWM involved in typical and atypical neurodevelopment. We mainly explored brain processes involved in the capacity to choose appropriate behavior during the resolution of visuo-spatial locomotor tasks using behavioral paradigms. We focused on a) the memorization and generation of sequences of visuospatial targets, b) the planning and the adjusting of trajectories when faced with unpredicted changes when reaching a goal, and c) the inhibition and replanning of previously over perfected learned paths.

We conducted five studies grouped in three thematics: a) developmental exploration of spatial cognitive capacities and brain activity in healthy adults using the WalCT, b) replanning following target shift during locomotion using the goal-oriented navigational task, and c) inhibitory and CF in the visuo-spatial locomotor task.

IV.1. Developmental exploration of spatial cognitive capacities and brain activity in healthy adults using the WalCT.

In the first thematic, we included two studies aiming to examine the neurocognitive performances in young (YA) and older adults (OA) using the WalCT. First, we conducted a behavioral study to assess VSWM, MR, and cognitive strategies during navigation (Castilla, Berthoz, Urukalo, et al., 2022). We recorded locomotor trajectories during the performance of the WalCT. Additionally, the participants performed cognitive tests such as MR, planning, visual memory, IC , and visuospatial exploring tests. The VSWM performances were analyzed using the classical span score and a new method named the score point attribution (SPA). In the SPA, each correct retrieval of the stimulus received 2 points, if the target was reached during the trial but was recalled in the wrong order, the participants would obtain 1 point, if the stimulus was not recalled, 0 points. Furthermore, we analyzed the error patterns to determine the cognitive strategies used during the performance of the WalCT used in previous studies (Belmonti, Cioni, et al., 2015; Perrochon et al., 2014). Three categories of error patterns were distinguished: *Place-sparing errors patterns, Path-sparing error patterns, and Random/minimal error patterns errors*. In the *Place-sparing error patterns,* the participant reached the correct targets in each sequence but not necessarily in the right order (i.e., preserving targets' location). In the *Path-sparing error patterns,* the participant generated a globally correct trajectory but not necessarily with the correct targets (i.e., preserving the targets' order). *Random/minimal error patterns errors* is considered to be a total disorientation without any specific or identifiable strategy. Additionally, we took in consideration the body rotation during the WalCT. We examined the results according to a) VSWM performances, b) MR performances, and c) strategies during the navigation.

IV.1.1. VSWM performances

We analyzed VSWM performances using the classical span score and the SPA. In both analysis we found that YA outperformed OA in VSWM capacities. However, only the SPA method showed sex differences concerning the YA. Concerning age differences, these results are consistent with previous findings that suggested an age-related cognitive decline in older adults when performing visuospatial locomotor tasks (Iachini et al., 2009; Perrochon et al., 2014; Perrochon, Mandigout, et al., 2018; Piccardi, Bianchini, et al., 2014; Piccardi et al., 2011). This age-related cognitive decline has been previously reported in healthy adults of around 47 years old (Piccardi, Palermo, et al., 2014). Moreover, poor performances by OA in visuospatial locomotor tasks such as WalCT have been linked to spatial disorientation, MCI, and early detection of Alzheimer's disease not observed in classical cognitive assessment (Bianchini et al., 2014; Iachini et al., 2009; Perrochon et al., 2014).

In the SPA, we observed that YA-M performed better than YA-F in the WalCT. These results are also consistent with scientific literature that suggest that there are sex differences in spatial navigation tasks (Driscoll et al., 2005; Lambrey & Berthoz, 2007; Lawton, 1994).

IV.1.2. Mental rotation abilities

We assessed MR capacities by means of the Mental Rotation Test (MRT) and we found that YA perform better in MRT than OA group. However, the MRT do not show any differences regarding sex. The online MR of the remembered array suggested that both groups (OA and YA) were affected by the sequences that required more body rotation during navigation. We considered that during the presentation of the stimuli, the participants encoded and memorized the sequences according to their own point of view (i.e., egocentric reference frame) whereas during locomotion, there they were required to update their spatial map. However, this update became increasingly difficult in sequences that demanded more body rotations. Only analysis of the rotation during locomotion revealed age and sex differences in which the YA-M group presented less errors related to body rotation of more than 90° in comparison to the YA-F group. These results are in line with previous reports that suggest that females presented difficulties to perform MR during spatial tasks (Coutrot et al., 2018; D. Reilly & Neumann, 2013). Interestingly, the OA group presented a different pattern where OA-M presented more errors concerning the spatial updating than OA-F. Research linking impact of sex effect in aging seemed to be relatively rare (Borella et al., 2014)

IV.1.3. Strategies during the navigation.

Concerning spatial cognitive strategies, first we grouped VSWM scores into high and low performers during the navigation. Then, we examined their strategies according to sex and age. We identified that higher performers in the WalCT relied more on *place-sparing strategies* (i.e., preserving the locations), whereas lower performers relied more on *path-sparing strategies* (i.e., preserving the order). We considered that *place-sparing strategies* are based on an allocentric processing of space and *path-sparing strategi*es are based on an egocentric processing of space during navigation.

We found age related differences in navigational strategies. YA relied more on both strategies (*place and path sparing*) presenting few random errors in comparison to OA. According to Belmonti et al., (2015), YA presented a lower number of random errors during the WalCT mainly basing their performances in place or path sparing strategies. In healthy OA, random errors are considered as an indicator of cognitive decline related to age. However, comparing the performances between healthy OA and MCI participants in WalCT random errors are a considered as a pathological index for the detection of MCI (Perrochon et al., 2014; Stephan et al., 2012).

Regarding sex-related differences in navigation strategies, we found that YA-M relied more on allocentric strategies than YA-F, producing more place-sparing errors. The OA did not present any sex difference in regard to the use of strategies. Sex-related differences during the spatial processing suggested that YA-M based their strategies on space geometry and self-motion perception, whereas YA-F based their performance on visual spatial landmarks (Bianchini et al., 2014; N. Burgess et al., 2004; Lambrey & Berthoz, 2007; Saucier et al., 2002). These results suggested that YA-M employed more allocentric strategies for spatial processing and memorizing the sequences during the WalCT. Taking together the results, we considered a flexible combination of allo/egocentric strategies in the performance of the WalCT. In the task of the automatic presentation of the stimuli, the participants encoded and memorized the sequence according to their viewpoint or egocentrically. Then, during the locomotor reproduction of the sequence, the participant was required to switch from an egocentric to allocentric strategy. These switching in strategies was possible thanks to the inhibition of a referential frame to activate another, in this case the egocentric needed to be inhibit to active the allocentric referential frame (Berthoz, 2020a). Thus, the inhibition process of the egocentric frame allows them to switch between strategies. We considered that the WalCT also involved

EFs processing not only temporarily storing the spatial information (VSWM) but also in CF during the selection of the strategies. This CF is possible due to the inhibition of the heuristic treatment of space allowing the participant to have a more adequate processing of space. This idea is supported by the theory of third system proposed by Oliver Houdé (see I.1.4 introduction).

In the second study, we recorded neurophysiological activity using the functional near-infrared spectroscopy (fNIRS) to assess the effect of age on cerebral oxygenation in VSWM tasks depending on the space (reaching or navigational). We also used the fNIRS to determine if EFs and cerebral oxygenation were involved in VSWM performance, either in reaching or navigational space. We hypothesized that YA would show a better VSWM performance and therefore higher cerebral oxygenation than OA resulting in a stronger increase of oxygenated form of hemoglobin (ΔO2Hb) concentration and a stronger decrease in deoxygenated form hemoglobin (ΔHHb) concentration. Healthy OA and YA participated in the study and all participants performed the WalCT and electronic Corsi Block-tapping Test (e-CBT). As expected, YA outperformed OA in both assessments. The results found a significant decrease in ΔHHb in YA during the encoding in WalCT in comparison to the OA group. Additionally, OA presented significantly lower levels of oxygenation in the WalCT than in the e-CBT. Higher scores in the WalCT were related to a decrease of deoxygenated form hemoglobin. Moreover, EFs assessment and MR capacities were linked to the performance in both tasks. YA presented higher activation of the dorsolateral prefrontal cortex than OA when the participant encoded sequences in the WalCT. The activation of the dorsolateral prefrontal cortex correlated with the performances in VSWM in the locomotor space. These results suggested that age affects VSWM and cerebral oxygenation during the encoding of visuospatial targets. Moreover, cerebral oxygenation and performances were modulated by the type of space (near space and far space) and related to different cognitive functions.

Taken together, these results suggested that the spatial cognitive assessment in the WalCT involved a dynamic neurocognitive processing related to EFs. We identified that poor cognitive strategies (*place or path sparing strategies*) in OA could be related to age-related dorsolateral prefrontal cortex under-activation during the encoding of visuospatial targets. This difficulty to encode stimuli in memory in OAs is associated with the recruitment of others brain structures to compensate the aging of the brain (J. M. Logan et al., 2002; Reuter-Lorenz & Lustig, 2005). Thus, poor cognitive strategies evidenced by random errors in OA are linked to a decline in EFs. To choose the right strategy among various alternatives, planning and keeping in mind information requiring high level demand in brain capacities often decreased with age (West, 1996).

IV.2. Replanning following target shift during locomotion

In the second thematic, we aimed to examine behavioral signatures of anticipatory control in locomotor navigation subjects with spastic bilateral CP. It important to indicate that visual-spatial impairments are frequent in CP. However, they are measured only by means of table-top assessment that exclude locomotion or navigational space. Even though behavioral signatures of anticipatory control in locomotor navigation are well described in adults and across typical development, they have never been studied in CP. What is not yet clear is if patients with spastic diplegic CP suffer only from disorders of gait patterns, or if they also show disorders of anticipatory control over locomotor navigation. To answer this question, a descriptive cross-sectional study on 13 patients with spastic diplegia aged 5 to 23 years was conducted. Control data were obtained from a previous study on typical development. Subjects performed a GOLT to reach luminous targets. Whole-body trajectories and orientation of body segments were extracted from 15 reflective markers. We analyzed parameters comprised: within-subject trajectory variability, maximal head deviation from trajectory and mean head anticipation over trajectory. We compared these kinematic parameters between CP subjects and controls of the same age, and between each subject and age-matched controls. The results suggested the major impairments for both head orientation and trajectories in a subpopulation of children with CP. Based on the analysis, we identified three sub-groups of patients: a) participants that presented major navigation disorders characterized by high trajectory variability and abnormal head orientation profiles, b) participants that showed minor navigation abnormalities generating consistent trajectories, and c) those who did not differ from controls in any navigation parameter, despite their gait. We considered that goal-oriented locomotion is an intrinsically double task integrating navigation and gait control. Abnormal gait patterns do not account for and can be distinguished from navigation disorders in spastic diplegia. This classification has important implications for implementing rehabilitation and should therefore address navigation, not only gait.

It is very innovative as well as useful to clinicians who want to envisage novel, integrative rehabilitation protocols, going beyond the traditional divide between motion and cognition. Our model allows us to distinguish locomotor anomalies due to purely motor problems (spasticity and lever arm dysfunction) from control problems due to poor integration of spatial information and spatial reference frames. This is an original perspective, linking motor behavior to spatial cognition, and kinematic data.

IV.3. Inhibitory control and cognitive flexibility in the visuo-spatial locomotor task

In the third thematic we focused on studying the development of IC and CF in children and adolescents with typical and neurodevelopment disorder. In the first study, we designed the VHLM to assess IC and CF during the navigation in the near extrapersonal space using the VC paradigm (Castilla et al., 2021b). We implemented a spatio-temporal index based on the measure of kinematics behaviors such as trajectories, tangential velocity, and head direction. This is an original perspective, linking motor behavior to spatial cognition, kinematic data to IC and CF. We examined mainly a) delays or departure’s latency for the overlearned path and the replanning of a new path, b) directional locomotor trajectories, and c) age and cognitive performance.

Regarding the learning phase, we observed that the latencies decreased across the trials indicating automatization of the locomotor trajectory. Additionally, the locomotor trajectories evidenced a kinematic stereotype by repeating the same kind of trajectory to automatize. The initial delay for the departure was about 1 second. This is possible due to a complex reaction time to generate a planning plus additional 600-800 sec for the initiation of gait under cognitive control of a spatial task (Bayot et al., 2018; Deblock-Bellamy et al., 2021; Yogev-Seligmann et al., 2008). Comparing the latencies during the replanning and the first trial of the learning phase, we observed that the latencies were similar suggesting that during the plan of the first trajectory and the replanning a new trajectory similar cognitive processing were required. However, a greater variability in the replanning suggests additional cognitive processes for different participant. This variability can be explained according to development of spatial cognition capacities in children. For instance, using the Magic Carpet paradigm, children between 5 to 12 years old differed in the application of spatial referential frames (allocentric or egocentric). Moreover, differences in the oculomotor strategies have been found during the planning of a visou-spatial locomotor task (Demichelis et al., 2013).

Our experimental protocol was designed to require of the participant explore and exploit the spatial information in a short period of time. In the exploration phase, the participant was expected to figure out the shortest path and avoid obstacles during the locomotion. During the exploitation phase, we use the information already gathered to confirm or modify the previous selections (Kaplan & Friston, 2018). Contracting our findings to the neuroscientific literature, we considered that the repetition of a trajectory can induce a shifting in the activation of the brain structures and more precisely for the prefrontal cortex to the basal ganglia and cerebral structures (Babayan et al., 2017; Seitz & Roland, 1992). Interestingly, when the shifting of the prefrontal cortex to basal ganglia are considered established, the blocking demanding a replan a new trajectory may induce a reactivation of the prefrontal cortex involved in the planification of an alternative path (Patai & Spiers, 2021).

IV.3.1. Strategy Selection and Neurodevelopment

We considered that during the replanning phase the participant need to inhibit a prelearned direction in order to generate a new trajectory. We observed three behavioral responses during the replanning phase: a) Departure without inhibition or impulsive responses, b) impulsive online planning, and c) anticipatory – planning.

a) Departure without inhibition or impulsive responses: the participant starts a trajectory towards the target; however the participant hastens the responses without considering the eventual change (blocking the path). Then, they had to stop and plan a new trajectory. We speculated that in this scenario, the participant was required to shift between strategies in order to navigate and reach the target (Belmonti, Cioni, et al., 2015).

b) Impulsive online planning: the participant walked to the target and changed trajectory without stopping. This impulsive online planning is related to a more ease shifting in trajectories. The relative rapid change from one path to another is possible to developing of inhibition and CF processes but not fully accomplished.

c) Anticipatory – planning, the participant inhibits the go signal while waiting and planning before starting a new optimal trajectory. This behavior can be linked to longer latencies and faster tangential velocities. This strategy is established during child development and fully achieved in adolescence (Belmonti et al., 2013).

This study provided four main contributions to the scientific field: first, a new experimental paradigm for testing visuo-spatial locomotor memory during navigation for normal children and adults. Second, a new test to studying executive functions deficits in a variety of psychiatric or neurological patients such as ADHD, DCD, ASD and CP. Third, a potentially useful index for the evaluation of impulsivity during locomotion. And fourth, a possible useful tool for the rehabilitation of planning deficits and EFs in children with neurodevelopmental disorders.

IV.3.2. Assessment of inhibitory control and cognitive flexibility during spatial navigation in typical and psychiatric children, adolescents, and adults.

We present a draft of an article which discussed the evaluation of EFs during spatial navigation in typical and psychiatric children, adolescents, and adults using the VHLM. The objective of this article was to assess the development of IC and CF in a near extrapersonal space by means of the negative prime paradigm. We recorded locomotor trajectories using the VC paradigm of 109 participants divided into 6 groups: typical (children, adolescents and adults) and neurodevelopmental disorders (ADHD, ASD, and DCD). We hypothesized that a negative priming effect can be observed comparing the performance in the VHLM, more specifically: IC will be observed when comparing the performances of the test-probe (T3) where the trajectory needed to be inhibited and the control-probe (T6) where a new maze was presented and not related to the original maze. Thus, we predicted that the latencies for the departure will be smaller for T6 compared to T3 where the overlearned was inhibited. Additionally, head movement before the start will be smaller in T6 compared to T3.

We predicted that the inhibition of the path by blocking the trajectory will cause an increased latency and increased exploration (head-chest yaw). Indeed, we anticipated that the difference between head-chest included more movement in terms of exploration and reconfiguration. The inhibition capacities are closely related to cognitive development and therefore we expected the cognitive inhibition process to be modulated according to the different types of age groups and pathologies. In addition, we expected to observe behavioral evidence of different developmental trajectories in the manifestation of IC and CF such as a rapid adaption to the repetitions of the same trajectories.

IV.4. Ongoing research projects

In this section, we will present the five ongoing projects which are related to the results of the thesis: a) A study of visuo-spatial memory deficits in ADHD children using the "Virtual City paradigm" in Pisa, Italy, b) An electroencephalography study for assessing brain activity during locomotor replanning with the VHLM in Brussels, Belgium, c) Visuo-spatial memory in vestibular and vertiginous patients using the WalCT in a clinical setting in Paris, France d) Artificial intelligence methods for quantification of data analysis, in Oujda, Morocco and e) Exploring Gregarious Positioning behavior, CF and IC using the VHLM in Hospital Salpêtrière, Paris, France.

IV.4.1. A study of visuo-spatial memory deficits in ADHD children using the "Virtual City paradigm" in Pisa, Italy.

Traditionally, spatial navigation has been assessed by means of paper mazes, in the reaching space, not requiring any locomotion. However, recent evidence indicated that different processing of spatial data is required during navigation space compared to peri-personal space. While during a reaching space task the object position is processed according to an egocentric strategy that leads to the creation of body-centered representations, based on subject-to-object relation, during a navigational task, more options are available: updating egocentric locations or switching to an allocentric reference frame. The latter one leads to a representation independent from the subject's point of view and based on object-to-object relation and acquired later in life, requiring the maturation of specific neuronal networks.

The VC^{TM} paradigm, which evolved from more recent Magic Carpet tasks, was created to enable the assessment of cognitive strategies in navigation. The paradigm simulated skills needed in real-life scenarios which include complex neuropsychological functions beyond spatial memory as complex executive functions, frequently impaired in children diagnosed with neurodevelopmental disorders, such as ADHD.

The aim of the study was to create a new ecological and motivating task to assess real locomotor navigation in a controlled laboratory space and under specific experimental conditions, tapping degree of task difficulty and cognitive processes believed to underlie this task, namely EFs and visuo-spatial memory. A feasibility analysis of navigation transferred to the VC™ paradigm was conducted in a group of school-aged children diagnosed with ADHD. To test the construct validity of the paradigm, performance of the children with ADHD on the VC™ was compared with performances on classical neuropsychological tasks measuring EFs such as inhibition, visuo-spatial working memory, planning and short-term memory as visuo-spatial short-term memory. This approach could shed light on the cognitive strategies and neuropsychological processes involved in the navigation task. Furthermore, if suitable for children with neurodevelopmental disorders, this navigation task could potentially be highly informative for understanding these functions which are specifically challenging for these children, especially when they have to be recruited together as is the case in real-life situations. With respect to other navigation tasks, the computerized motion capture system of the VC™ allowed for direct assessment of how the child approaches the task, yielding preliminary data on cognitive strategies, such as egocentric and allocentric reference frames, necessary for successful completion of the locomotor navigation task. The comparison of performances of children with ADHD with a small matched-for-age control group provided preliminary evidence on patterns of behavior characterizing the clinical population across age groups as well as the typically developing children.

IV.4.2. An electroencephalography study for assessing brain activity during locomotor replanning with the VHLM in Brussels, Belgium

The purpose of this preliminary study was to investigate cognitive brain function approached by the electroencephalogram (EEG) brain oscillations focusing on IC and CF during active navigation in the “Virtual House Locomotor Maze” (VHLM)(Castilla et al., 2021b) (Figure 53). The VHLM tested replanning by first asking the participant to repeat five times a self-chosen path to reach a given house in the maze. After having learned it, the path was blocked on the 6th navigation, imposing the subject to inhibit the learned trajectory and to design a new one.

Brain oscillations underlie brain function and characterize brain states (Buzsáki & Draguhn, 2004). The EEG technique offered the possibility to directly (but not invasively) have access to the real global electrical brain activity underlying brain function. EEG brain rhythms have been proposed to represent “universal codes” based on which communication is established in the central nervous system by local-global communication that considers pre-existent endogenous ongoing constraints. From a more technical point of view, EEG dynamics modulations can be characterized by specific mathematical measures developed in the last decade as the power spectral and phase variations of the EEG oscillations (Delorme et al., 2002).

Theta oscillations (4 – 7 Hz) are recognized as an essential mechanism underlying head orientation computation of spatial coding in grid cell models in actively orienting rodents (Brandon et al., 2011; Winter et al., 2015). However, it has been discovered only very recently that theta EEG oscillations in humans during active spatial navigation have been demonstrated for the first time (Do et al., 2021). In this study, besides theta power spectrum increasing in active navigation, it was also found that theta oscillations were more prominent in the retrosplenial cortex while computing direction changes, irrespectively of the length of the total path walked (Do et al., 2021).

In accordance with the recent study of Do et al., (2021) first, we expected to confirm that the EEG power spectrum increases in the theta rhythm during active navigation while performing the VHLM tests. Secondly, we hypothesized that theta EEG oscillation power increase characterizing active navigation will be localized in the prefrontal cortex in the 6^{th} trial underlying intentional inhibition and replanning processes in comparison to the preceding trials. 64 EEG signals were being recorded on young (age range 18 – 29 years) healthy participants with EEG TM sports EEG system (LE-200, ANT Neuro, The Netherlands, 2048 Hz sampling rate) while performing the VHLM protocol. In addition to EEG, two electromyogram signals were recorded on both left and right tibialis anterior muscles with the same amplificator.

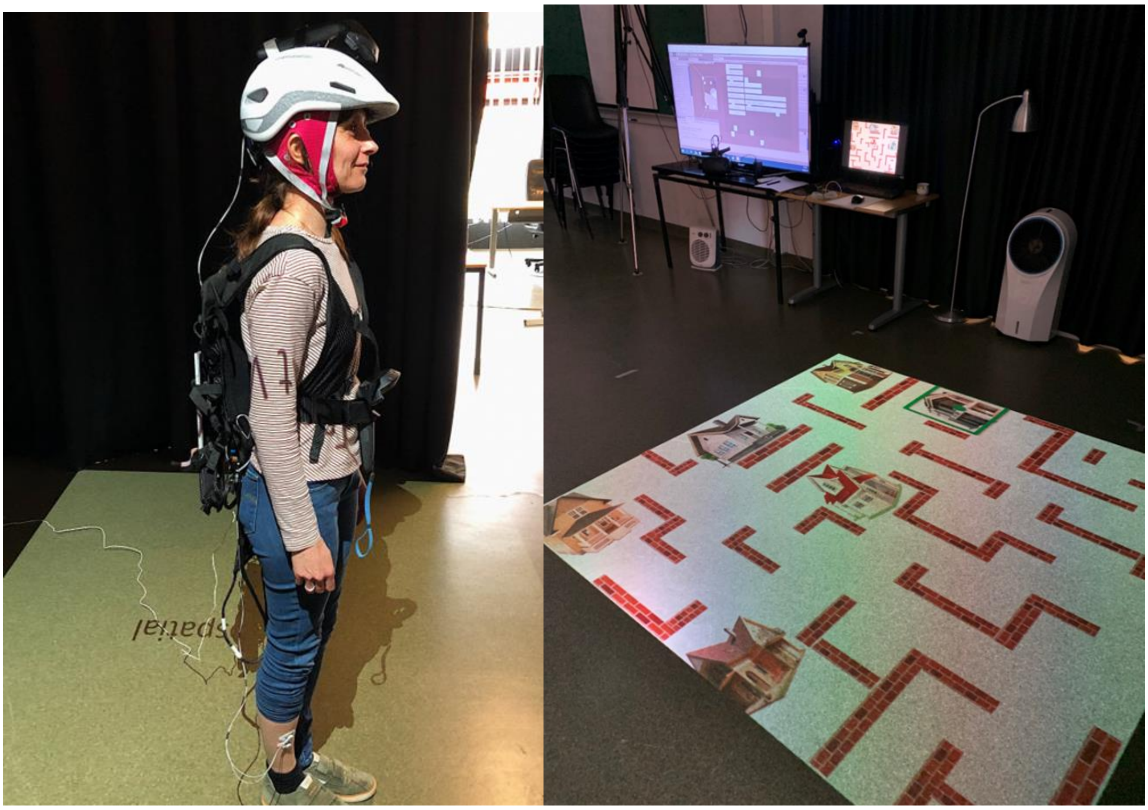

Figure 53. Illustrating the EEG and EMG equipment installed on one participant before and after the specific VHLM equipment and scenario.

Off-line, data treatment, and statistics were being performed by means of EEGLAB software (Delorme & Makeig, 2004) and the ASA software (ANT Neuro, The Netherlands) .Initially, a 200 Hz low pass and a 0.1 Hz high pass filters were applied on EEG signals. Then, any artefactual portion of the EEG data was rejected by visual inspection. Synchronous or partially synchronous artefactual activity (mostly blinks) was detected and rejected by independent component analysis (ICA). The baseline-normalized spectrograms or event-related spectral perturbation (ERSP in dB) were calculated with respect to the house target's event (1 sec before to 4.5 sec after the house target's event. Figure 54 illustrates an ERSP spectrogram (frequency bands in Hz in the X axe; time in ms. where 0 ms. correspond to the house target's event) for one EEG electrode (CP3, central-parietal position over the scalp, on the left) for one participant. An increase of the power spectrum starting at around 700 ms. with a duration longer than 1000 ms. in the theta frequency band (around 5 Hz) was illustrated by the dark red colored cloud in the spectrogram. This observation was in line with our first expectation of the theta rhythm during active navigation.

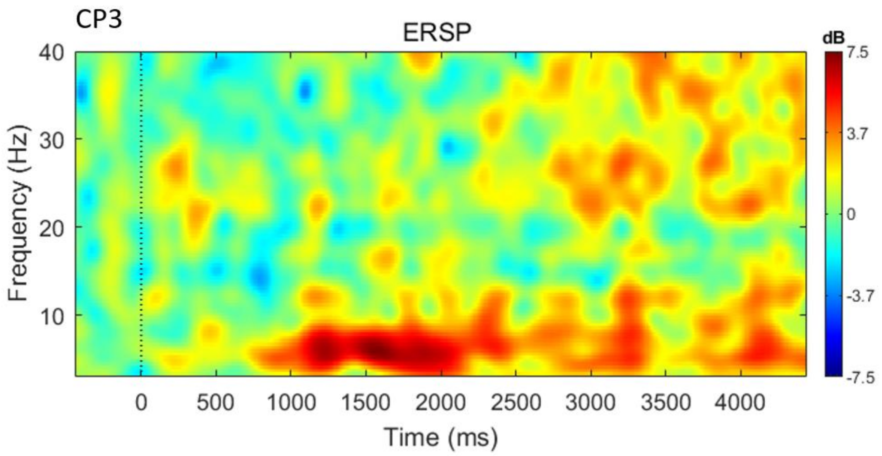

Figure 54. Event related spectral perturbation template for one EEG electrode (CP3). 0 ms. time correspond to the house target's event. Note the red colored cluster illustrating theta power increase.

To avoid the pitfalls occurring when focusing on the power spectrum topographies at the scalp level, associated with the mixing of multiple cortical processes by volume conduction, we were modelling the brain sources of the power spectrum variations using the swLORETA method (Cebolla et al., 2017) during the VHLM tests. Figure 55 illustrates very preliminary observations of the brain generators related to the 1st, the 5th, and the 6th navigation (this last corresponding to navigating when the path has been blocked. In this analysis, frequency band distinction has not yet been performed, nor any statistical comparison between the 1st, the 5th, and the 6th navigations.

Preliminary observations suggested that frontal Brodmann areas were implicated in the three navigations. Statistical contrasts between navigations in the whole population will be applied to assess the hypothetical stronger contribution of the prefrontal cortex in the 6th trial underlying intentional inhibition and replanning processes in comparison to the preceding trials that we proposed, suggesting the involvement of these areas in the inhibition of the learned trajectory and the replanning of the new one.

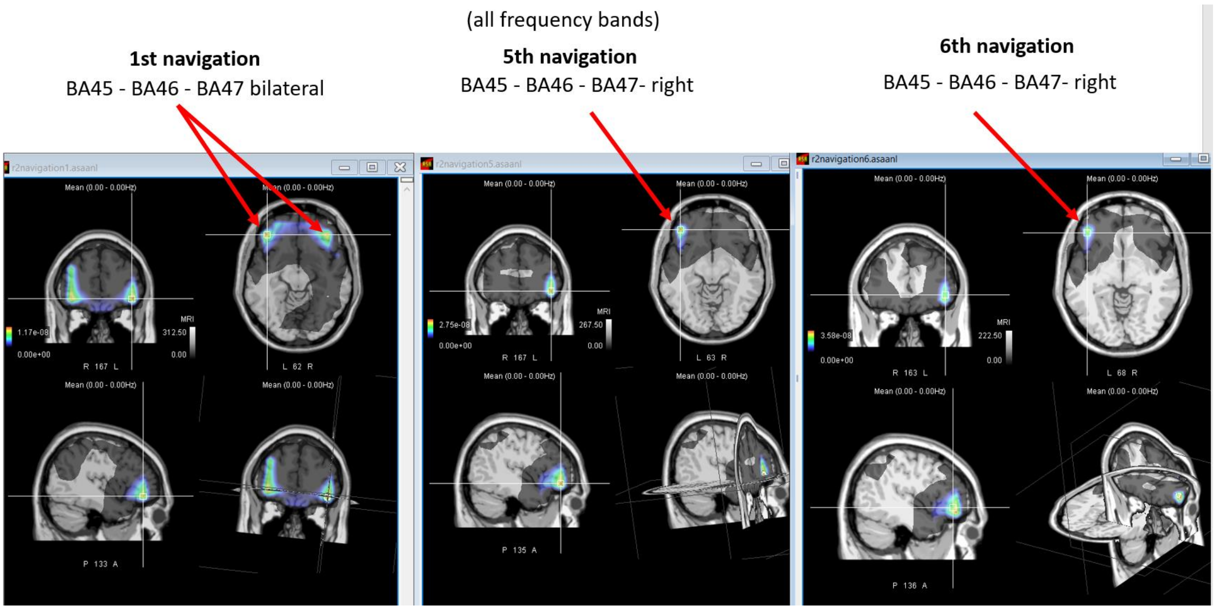

Figure 55. Brain generators estimated for one participant during the 1st, 5th, and 6th navigations (6th navigation corresponds to the blocked pathway).

IV.4.3. Visuo-spatial memory in vestibular and vertiginous patients using the WalCT in a clinical setting in Paris, France.

In the cabinet of Dr Bernard Cohen (Otorhinolaryngologist) in Paris, a project is being elaborated to explore visuo-spatial locomotor memory deficits in patients with vertigo or vestibular deficits. Several studies have shown that vestibular deficits induce errors in VSWM (Brandt et al., 2005) and vestibular projections to the hippocampus are well documented by experiments from the A. Berthoz research group demonstrated in rodents and humans (Vitte et al., 1996).

The project was granted the permission of an Ethical Committee and will end in the summer 2023. The protocol is a simplified version of the WalCT using the VC method. More than 70 patients and control subjects were tested up until August 2022. Regarding the data analysis, a software was developed in the frame of the thesis by a cooperation between Mohamed Zaoui, Alexander Castilla, Bernard Cohen, and Alain Berthoz. The data is being analyzed and a preliminary report will be proposed and an article drafted before the end of 2022.

IV.4.4. Artificial intelligence methods for quantification of data analysis, in Oujda; and e) Exploring Gregarious Positioning behavior, CF and IC using the VHLM in Hospital Salpêtrière, Paris, France.

In broad strokes, we formed groups or categories and outlined the varied behaviors of persons who completed the VC paradigm. The primary idea behind our technique was a data-driven strategy whose main goal was to extract relevant information from raw spatial data to categorize individuals without having any prior information about a subject's medical condition. First, we examined the spatial raw data kinematically, which enabled us to extract parameters such as the average speed along the whole trajectory and the average duration spent on a target (i.e., tile). These characteristics enabled us to separate three categories based only on speed (the slowest, average speed, and the fastest) (Annaki et al., 2021).

Nonetheless, during the analysis of the average time spent within a target, we noticed numerous irregularities that might have a substantial influence on the categorization. As a result, the groups included both control and pathological subjects (based on the expert opinion without having a specification on the individual condition of each subject).

There was a need to proceed onto more complex approaches like machine learning, particularly unsupervised learning. We first used K-Means in this part (Annaki, Rahmoune, Bourhaleb, Berrich, et al., 2022) (see Figure 56). We enhanced our approach to extract more homogeneous clusters by using numerous clusters higher than three (K > 3). However, we aimed to let the machine determine the number of categories, which is a limitation for K-Means because K is an important input, as well as how this technique handles outliers.

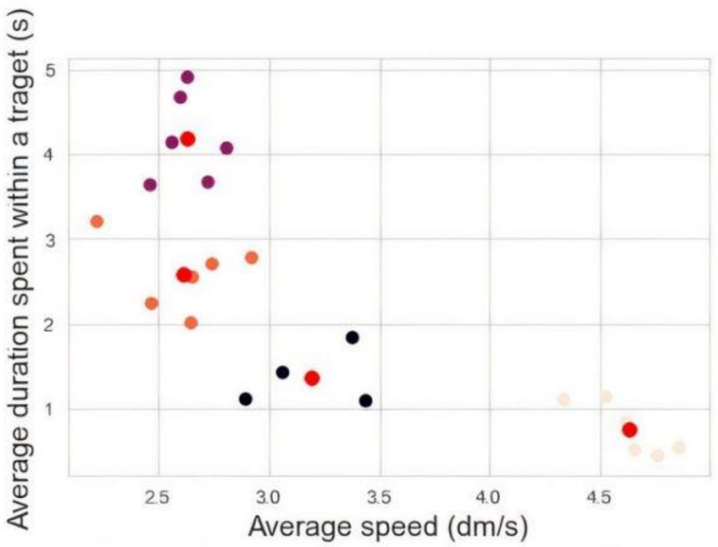

Figure 56. K-means clusters, indicating the difference between in the groups of participants.

As a result, we used DBSCAN (density-based spatial clustering of applications with noise), which requires a distance metric and the number of neighbors (Annaki, Rahmoune, Bourhaleb, Rahmoun, et al., 2022). DBSCAN is a density-based clustering algorithm that forms clusters of dense regions of data points while ignoring low-density areas (considering them as noise). Clusters can adopt any irregular shape, as opposed to K-Means, which requires clusters to be more or less spherical.

The HAC (Hierarchical Agglomerative Clustering) method yielded four clusters, confirming the K-Means results (Annaki, Rahmoune, Bourhaleb, Berrich, et al., 2022) (see Figure 57). In general, HAC and K-Means can create relatively comparable clusters, but the ability to visualize the route of each data point makes HAC more useful in studying similarities and differences between individual data points or clusters. Clustering attempts, on the other hand, have shown encouraging (but insufficient) results (according to experts).

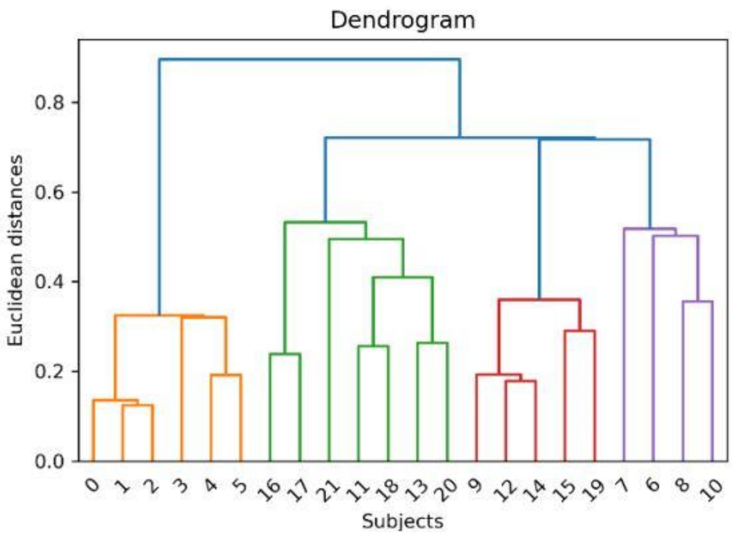

Figure 57. HAC dendrogram, indication the difference between different groups of participants.

As a result, we performed a more thorough study based on session analysis rather than aggregated parameters, which did not account for differences across sessions, necessitating the usage of deep learning applied to time series, especially in the feature extraction phase which may lead to more parameters, keeping in mind the limitation of explainability when it comes to deep neural network.

IV.5. Limitations and perspectives

Regarding the results obtained, some limitations need to be acknowledged. The main limitation of this thesis was the small sample sizes in the studies. However, we have considered increasing the number of the participant in future research. Regarding the perspectives for future studies, it is important to consider supplementary methods for exploration behavior and cognition such as the eye tracking. With the eye tracking we can measure the gaze during the exploration and navigation of visuospatial arrays such WalCT, VLHM, and Virtual city. This method will allow us to analyze how the participant encodes spatial information (VSWM) as well as plans forward action planning. Additionally, eye movement could be useful for recognition of cognitive impairment in patient with Alzheimer's disease, MCI and dementia (Liu et al., 2021).

Concerning EFs, this thesis focused only on the cognitive component of EFs such IC, WM, and CF. However, we believe that social-emotional components of the EFs (i.e., hot executive functioning) should be analyzed according to spatial processing and spatial adaptation. Furthermore, additional research should consider assessing the affective-related component of EF during spatial navigation and spatial processing. For instance, recording the levels of stress or anxiety by means of physiological measures before and during the experimentation could be helpful to better understand the performance of the participants.

We consider that the experimental protocols presented in this thesis contributes to a better understanding of the neurocognitive capacities during spatial navigation. However, further improvements and methods need to be considered for future research. For instance, considering using the VC technology to present a more realistic, detailed, and enriched environment. The augmented reality is a good option to include in future experimentation and rehabilitation protocols thanks to the combination of different sensory modalities such as visual, auditory, haptic and somatosensory information (Venkatesan et al., 2021). Thus, the augmented reality offers the possibility to present real-world environments crucial for the exploration of spatial cognition abilities during locomotion. Moreover, animal model for Alzheimer's disease suggested that enrichment environment reduces the progression of the symptoms such as memory deficits and prevents the beginning of the illness for up to at least 12 months (Berardi et al., 2007). In humans, enriched environment contributes to the decrease of the progression of age-related decline and helps in the rehabilitation of neurodevelopmental disorders (Leon & Woo, 2018).

Additionally, we propose the use of the VHLM protocol to analyze non pathological dimensions of personality. For instance, to study the possible correlation between different dimensions of the Gregarious Positioning (e.g., Submission and Dominance)(Lefrançois et al., 2013) and the navigational pattern during the performance in the VHLM. Moreover, we hypothesize that submission is characterized by a strict following of rules and learned behaviors and tends to conserve an egocentric point of view during navigation. Contrary to submission, dominance behavior is characterized by not respecting the instructions and is globally linked to a more general allocentric encoding and finding new solutions. In addition to these two dimensions, the assertive behavior in participants can be analyzed as a combination of both the ego and allocentric navigation strategies, presenting an optimal performance during the navigation. Before performing the navigation task, participants will be required to fill out a questionnaire which will be analyzed to determine in which dimension of the Gregarious Position they fit in. Once they completed the task, the results and the trajectories will be analyzed to see if there are correlations between them.

Conclusion

This thesis set out to study IC, CF, and VSWM involved in typical and atypical neurodevelopment. We mainly explored brain processes involved in the capacity to choose appropriate behavior during the resolution of visuo-spatial locomotor tasks using behavioral paradigms. We focused on three thematics a) memorization and generations of sequences of visuospatial targets, b) planning and adjusting trajectories when faced with unpredicted changes during the reaching of a goal, and c) inhibition and replanning of previously over perfected learned paths.

In the first study of memorization and generations of sequences of visuospatial targets, we found that age and sex have an impact on the VSWM, cognitive strategies, and MR during locomotion. We demonstrated that the WalCT protocol is a beneficial tool to assess EFs, online MR capacities, visuo-spatial memory as well as the switching of navigational strategies. Our results indicate that during navigation, factors such as age and sex made an impact on the VSWM, MR and cognitive strategies. Additionally, we proposed a new way to categorize the performance of the participants in spatial navigation. This novel categorization is named the score point attribution (SPA) which can be used as a complementary method and applied to the rehabilitation of spatial impairments.

In the second study, we found that there was an association of EFs and the VSWM performances in both the reaching space and the navigational space. In addition, we found that healthy OA presented less activation of the dorsolateral prefrontal cortex than YA during the encoding of VSWM. Thus, we observed that the activation to the prefrontal cortex is related to the performance in the WalCT.

In the second thematic, we identified the presence or absence of minor and major navigational disorders in spastic bilateral CP by means of behavioral signatures such as anticipatory control in locomotor navigation. These behavioral signatures allowed us to classify the performances into three groups characterized by the navigational behavior of each participant. The findings suggest that some participants with CP need rehabilitation in navigation capacities and indicate that there is a distinction between navigation and gait control. Moreover, this navigational protocol based on the modeling of a goal-oriented locomotion task allowed us to present a double motor control task to detect this distinction. Therefore, it is important to take into consideration the implications of this distinction for developing new methods of rehabilitation that specifically address not only gait, but more importantly navigation.

In the last thematic, first we designed and tested a new experimental protocol named the virtual house locomotor maze - VHLM to assess behavioral inhibition and CF during navigation. We examined behavioral parameters such as tangential velocity, latencies, head and chest rotation. We identified several distinguishable strategies used by the participants during the replanning of a new trajectory for reaching a target. Moreover, based on this protocol, we developed a new study to assess inhibition and mental flexibility during locomotion using the negative prime paradigm which is currently being drafted.

In conclusion, these combined findings indicate that the assessment of spatial cognition has contributed to the understanding of neurocognitive processing during the development. We are confident that these research protocols and our findings may provide new tools for the diagnostic and remediation for children with neurodevelopmental disorders, and the study of aging processes in elderly persons and their pathologies.

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Annexes 1

Procedure de calibration

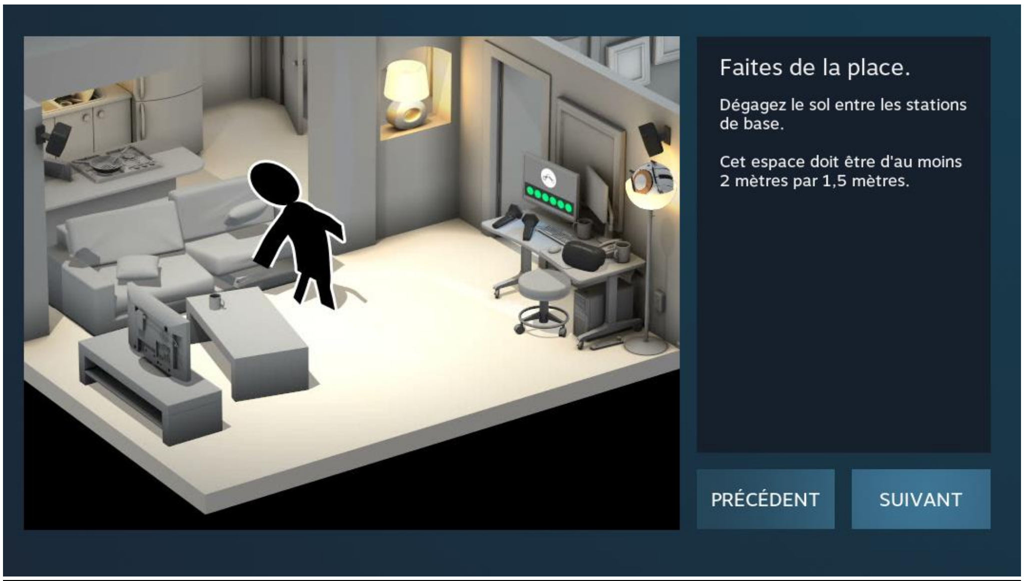
Launch **Steam VR** software

Step 1: Launch the SteamVR software: and click on the triangle

1.1 Click on > Launch the room setup wizard.

1.2 Select: “On the scale of a room,”

1.3 Click on **Next**



1.4. Place the controllers and the HTC headset in the center of the projection and then click on NEXT.

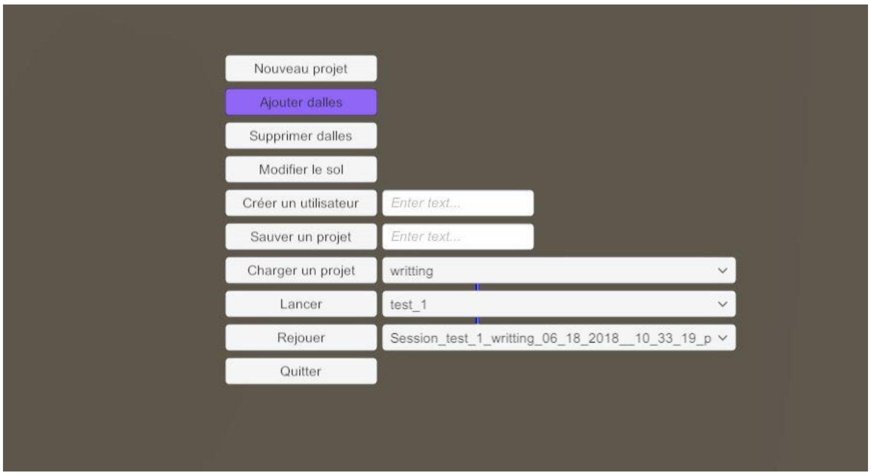
1.5 Point to the screen with the controller and click NEXT.

1.5.1 Create navigation space.

Etape 2 – Calibration procedure

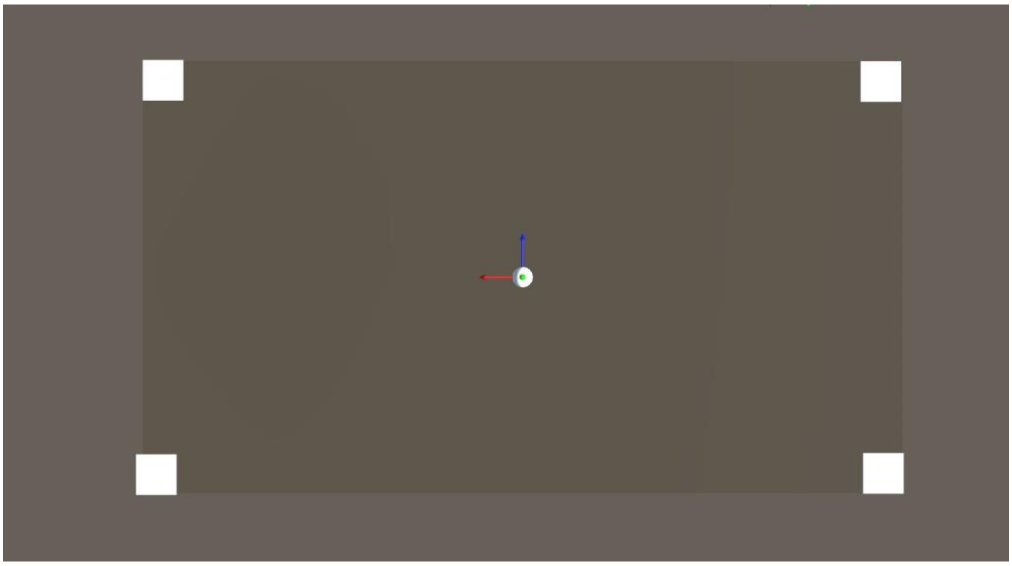
2.1 Lauch ***Rigid Body Viewer***

2.1.1 Click on Nouveau Projet to create a new project.



2.1.2 Click on "Ajourter dalles". Use the controller to generate the slabs.

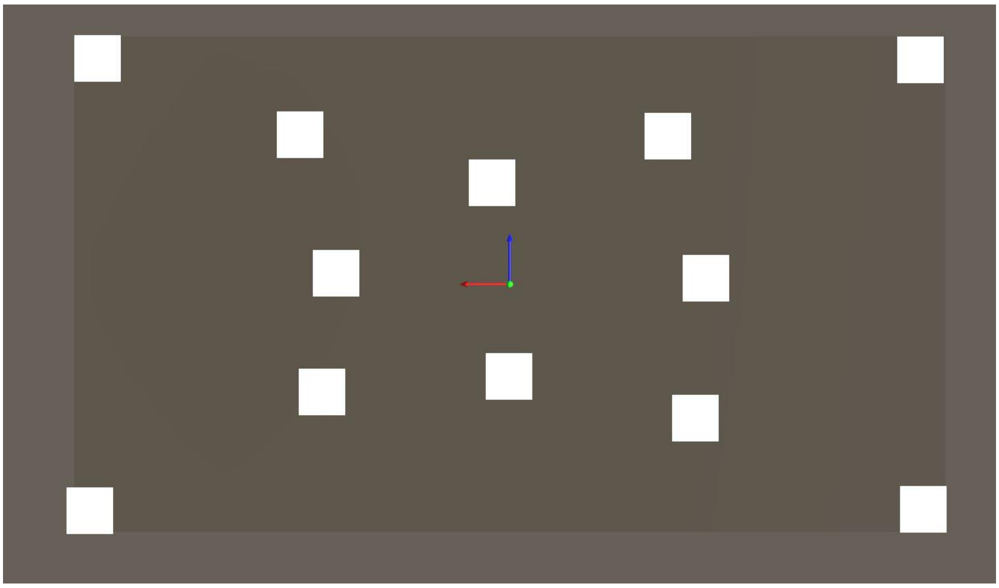
2.1.3 Create the 4 reference corners using the controller by pressing the trigger. Start for the corner to the left of the starting point.



2.1.3 Install the controllers on the participant (the helmet and the belt)

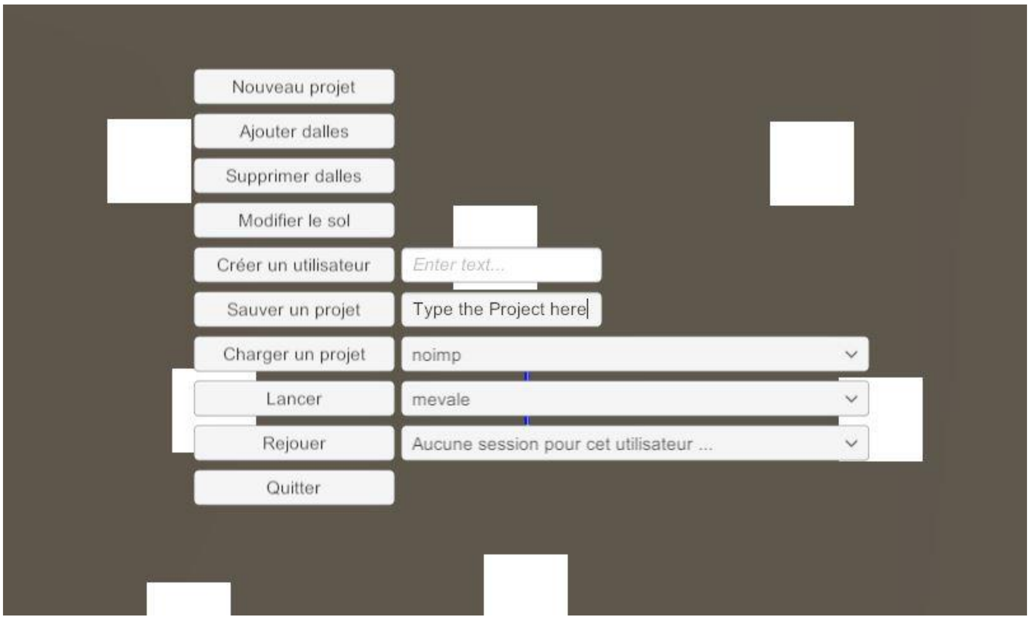
2.1.4. Place the participant on each tile using the controller (pressing the trigger) to create the tiles in the virtual space following the marked order.

2.1.5 Count the number of tiles created on the screen to check if there are extra tiles.



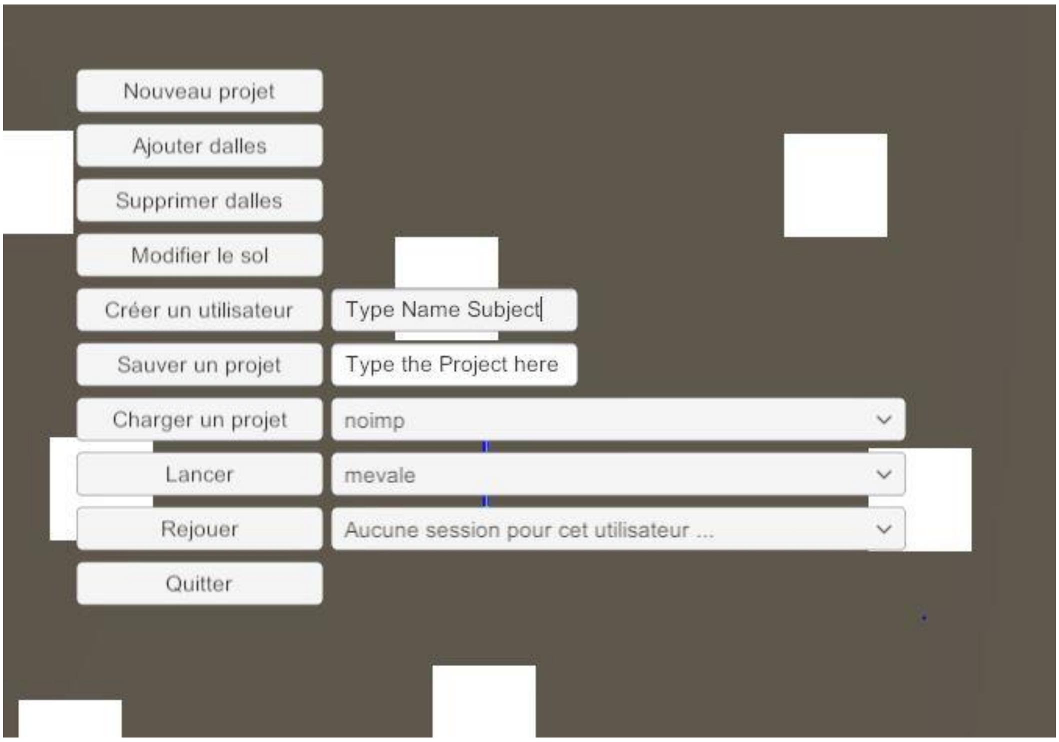
>>> Use the escape key. to return to the main menu

3. Write the name of the project (name of the participant or the date) then click on **SAUVER UN PROJET**



3.1. Click on the arrow (⇩) in front of the **CHARGER UN PROJET** box and select the project you created by clicking on **CHARGER UN PROJET.**

3.2. Record the participant's first name next to the box **CREER UN UTILISATEUR**



.

3.3. To record the trajectory:

> Click on START and to stop on STOP.

> Click on REPLAY to see the trajectory.

Annexes 2

frontiers in Psychiatry

BRIEF RESEARCH REPORT
published: 12 August 2021
doi: 10.3389/fpsyt.2021.708434

Check for updates

The Virtual City Paradigm^{TM} for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study

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OPEN ACCESS

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Specialty section:
This article was submitted to Child and Adolescent Psychiatry, a section of the journal Frontiers in Psychiatry

Received: 11 May 2021
Accepted: 19 July 2021
Published: 12 August 2021

Citation:
Del Lucchese B, Belmonti V, Brovedani P, Caponi MC, Castilla A, Masi G, Tacchi A, Zaoui M, Cioni G and Berthoz A (2021) The Virtual City Paradigm^{TM} for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study. Front. Psychiatry 12:708434. doi: 10.3389/fpsyt.2021.708434

Navigation is a complex process, requiring target localization, route planning or retrieval, and physical displacement. Executive functions (EFs) such as working memory, inhibition and planning are fundamental for succeeding in this complex activity and are often impaired in Attention Deficit and Hyperactivity Disorder (ADHD). Our aim was to analyze the feasibility of a new ecological navigation task, the Virtual City paradigm^{TM} (VC^{TM}) to test visuo-spatial memory and EFs in children with ADHD. Visuo-spatial short and working memory, inhibition and planning skills were tested with standardized tasks. The VC^{TM}, a new paradigm developed by our group, used the Virtual Carpet^{TM} technology, consisting of a virtual town with houses, streets and crossroads projected on the ground. It includes a motion capture system, tracking body movement in 3D in real time. In one condition, children were required to walk through the city and reach a sequence of houses. In the other, before walking, they had to plan the shortest path to reach the houses, inhibiting the prepotent response to start walking. The results show a good feasibility of the paradigm (feasibility checklist and ad hoc questionnaire), being ecological and motivating. VC^{TM} measures of span positively correlated with visuo-spatial short and working memory measures, suggesting that VC^{TM} heavily relies on efficient spatial memory. Individual subject analyses suggested that children with ADHD may approach this task differently from typically developing children. Larger samples of ADHD and healthy children may further explore the specific role of EFs and memory, potentially opening new avenues for intervention.

Keywords: visuo-spatial memory, executive functions, navigation, ADHD, children, neurodevelopmental disorders

INTRODUCTION

Spatial navigation is certainly one of the most complex neural functions in humans and one that is absolutely vital to everyday life. Retrieving locations and paths, planning routes to distant destinations, ascertaining one's location in space, drawing and reading maps, are all daily navigational tasks. A lack of navigation skills may impair one's ability to find things, reach targets, avoid obstacles, and return home. It may lead to complete dependence on others, or even to death, if experienced in a dangerous environment. In spite of a large amount of studies on navigation deficits in patients with neurological deficits (1–5), the availability of validated diagnostic tools for navigation disorders is still extremely limited. In addition, there are no studies assessing navigation in patients with neurodevelopmental disorders, as Attention Deficit and Hyperactivity Disorder (ADHD).

Traditionally, spatial navigation has been assessed by means of paper mazes, in manual space and not requiring locomotion. Only recently, novel tests for the assessment of navigation have been created and validated in adults and children (6, 7). The Magic Carpet is such a test and has been validated both in typically developing children and in children with cerebral palsy (8). It is derived from the Walking Corsi Test (9–11) and assesses locomotor navigation via the same procedure of the Corsi Block-Tapping Test for short-term visual-spatial memory, but translated from manual into locomotor space. By analyzing the errors made on the Magic Carpet (6, 8, 12) it has been possible to gain insight into the cognitive strategies used by different groups at different ages and to formulate hypotheses on the development of human navigation. However, the Magic Carpet did not allow measuring the kinematics of the trajectory, nor also the head direction as an index of gaze direction, as was done previously in the study of Belmonti (8) in typically developing children and children with Cerebral Palsy, capturing body motion during task execution.

The Virtual City paradigm (VC™) has therefore been developed in collaboration with the group in Paris of A. Berthoz [see (13)]. It is implemented using the Virtual Carpet™ experimental design (7, 14, 15), with the aim of assessing real locomotor navigation in a controlled laboratory space and under specific experimental conditions, allowing for grading of task difficulty and analysis of different neuropsychological functions. The nature of processes necessary for successfully completing such locomotor navigation tasks, such as egocentric and allocentric strategies, have been analyzed in the literature, both in adults (16–18) and in children (6, 8, 19, 20).

This new and ecological way of testing neuropsychological functions and cognitive strategies, in a motivating context, suitable for children with neurodevelopmental disorders, can be potentially highly informative for understanding executive functions (EFs) and memory in children with ADHD, for whom such functions are specifically challenging.

ADHD is a neurodevelopmental disorder with persistent inattention and/or hyperactivity/impulsivity, present in at least two life contexts, associated with significant social and academic impairment and with onset before 12 years of age (21). According to the Diagnostic and Statistical Manual of Mental Disorders – Fifth edition (DSM-5, 2013) (21), there are three ADHD presentations: predominantly inattentive, predominantly hyperactive/impulsive and combined. ADHD is one of the most prevalent childhood disorders with a worldwide prevalence of around 7%, with problems persisting into adulthood (22).

ADHD has a high heterogeneity at the clinical, genetic and neurocognitive levels (23). Children and adolescents with ADHD have been shown to consistently display differences in brain structure and function with respect to typically developing peers. Review of neuroimaging data indicate alterations prevalently in fronto-striatal, fronto-parieto-temporal, fronto-cerebellar and fronto-limbic networks, according to different neuropsychological and clinical phenotypes [for a review of neuroimaging studies see (24–26)]. At the cognitive level, ADHD is associated with a wide range of neuropsychological deficits, the most frequently reported being deficits in inhibition, memory, temporal discounting, decision making and timing, indicating that these constitute key cognitive domains, with EFs being heavily studied (27, 28). There are indications however that children and adolescents with ADHD may fall in distinct neuropsychological subgroups, displaying some but not all of the key cognitive deficits (29).

Among deficits in several cognitive areas, working memory, that is the function of actively holding in mind and manipulating information relevant to a goal, has received much attention (30, 31), also for tailoring rehabilitation (32). Visual-spatial short memory has been found to be more impaired than verbal short-term memory, and memory difficulties have been reported both at the level of storage and of active control/updating components in central executive tasks (33). Indeed, visual-spatial working memory may be thus a leading candidate endophenotype for ADHD.

Response inhibition is fundamental when alternative courses of thoughts or actions (planned or already initiated) have to be inhibited to allow the emergence of goal-directed behavior, and its deficit is associated with impulsive behaviors, a core DSM-5 diagnostic feature of ADHD. Reward-delay impulsivity has been explored with a meta-analytic method to examine differences in children and adolescents with and without ADHD (34), showing that youths with ADHD exhibited moderately increased impulsive decision-making compared to controls.

Deficits in planning abilities are also frequently reported in ADHD. A meta-analysis examined performance and latency measures in five tower planning task variants in 41 studies including ADHD, to calculate between-group effect sizes, and found moderate-magnitude planning deficits (35). Children with ADHD responded more quickly on planning tasks when compared to normal peers.

It has been also proposed that cognitive impairments in ADHD may result from both central controlled processes and more automatic information processes (36), with reciprocal functional interactions between subcortical regions and higher-order brain networks (37). The automatic processes, underpinned by dynamic subcortical circuits (including superior

TABLE 1 | Demographic and clinical data of the ADHD sample.

n.	Age (yrs;mo)	Sex	Adhd presentation	Specific learning disability	Intelligence (WISC-IV indices)			
					VCI	PRI	WMI	PSI
1	7;11	M	Combined		104	98	82	68
2	7;3	F	Combined		116	93	82	56
3	9;6	M	Combined		120	106	121	123
4	8;0	M	Combined		100	91	61	53
5	8;2	M	Combined		104*	96**	NA	NA
6	9;5	M	Combined		120	93	97	94
7	7;10	M	Combined		90	80	79	82
8	8;11	M	Combined	Yes	108	100	94	94
9	9;8	F	Combined	Yes	98	89	79	94
10	13;8	M	Combined	Yes	122	108	112	74
11	12;10	M	Combined	Yes	96	102	82	94
12	8;5	M	Combined		100	91	70	85
13	8;0	F	Combined		112	126	94	79
14	10;7	M	Combined		114	124	103	118
15	9;3	M	Combined		132	113	94	88
16	8;9	F	Combined	Yes	114	100	91	71
17	10;7	M	Combined		106	124	94	79
18	12;8	M	Inattentive	Yes	112	119	103	123
19	13;1	M	Inattentive		108	104	94	88
20	12;3	M	Inattentive		120	122	103	79
21	8;8	F	Inattentive	Yes	128	91	85	82
22	10;3	M	Inattentive	Yes	108	91	82	109

*VCI Verbal Comprehension Index; PRI Perceptual Reasoning Index; WMI Working Memory Index; PSI Processing Speed Index; *Verbal Intelligence quotient and **Performance Intelligence quotient at WPPSI-III at 6;8 years; NA not applicable.*

culliculus, pulvinar, and basal ganglia), may play a pivotal role in pathological distractibility of ADHD, representing "biological shortcuts," which may bypass more complex systems, such as those involved in strategic planning (37, 38). Following this model, deficits in executive functions may be due, at least partly, to deficits in this automatic processing, leading to higher cognitive loads and limited resources available for EFs (39). Structural differences in subcortical structures in individuals with ADHD compared with those without this diagnosis may support this model.

Based on these considerations, the VC™ paradigm was intended as a new and more ecological tool for assessing cognitive processes which are challenging for children with ADHD, as focused attention, memory, planning and inhibition, especially when they have to be recruited together as is the case in real-life situations.

The aim of this brief research report was to analyze, in a group of school-aged children diagnosed with ADHD, the feasibility of a navigation approach transferred to the VC™ paradigm and its capacity to explore and measure the cognitive strategies used by these children during a visuo-spatial memory task. The feasibility study was thus specifically intended for this clinical population with significant impairments in these areas of cognitive functioning, which were also tested with classical neuropsychological tasks.

METHODS

Subjects

The feasibility study included a clinical group of drug-naïve children with a diagnosis of ADHD, recruited in our third-level hospital of Child and Adolescent Neurology and Psychiatry. All participants underwent a multi-dimensional assessment, and diagnoses were made according to the DSM 5 (21), based on clinical history and a structured interview, Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version (K-SADS-PL) (40). The inclusion criteria were: (1) Diagnosis of ADHD; (2) Drug naïvité for stimulant treatment and any other pharmacotherapy; (3) Absence of intellectual disability; (4) Absence of comorbid conditions, except for Specific Learning Disabilities-SLD- (DSM 5); (5) Verbal intelligence of 85 or above (Wechsler Scales) (41, 42) to ensure full comprehension of the verbal instructions of the VC™ paradigm; (6) Absence of any visual (non-corrected) or gait problems.

Twenty-two patients aged 7–13 years were recruited (mean 9;8 years; sd 1;9 years; males $n = 17$; 77%), all eligible to be included in the study. ADHD presentation was 77% combined ($n = 17$) and 23% inattentive ($n = 5$), 36% displaying comorbid SLD ($n = 8$). Mean verbal intelligence was 110.5 (sd 10.6). Demographic and clinical data for the entire sample of 22 participants is presented in **Table 1**.

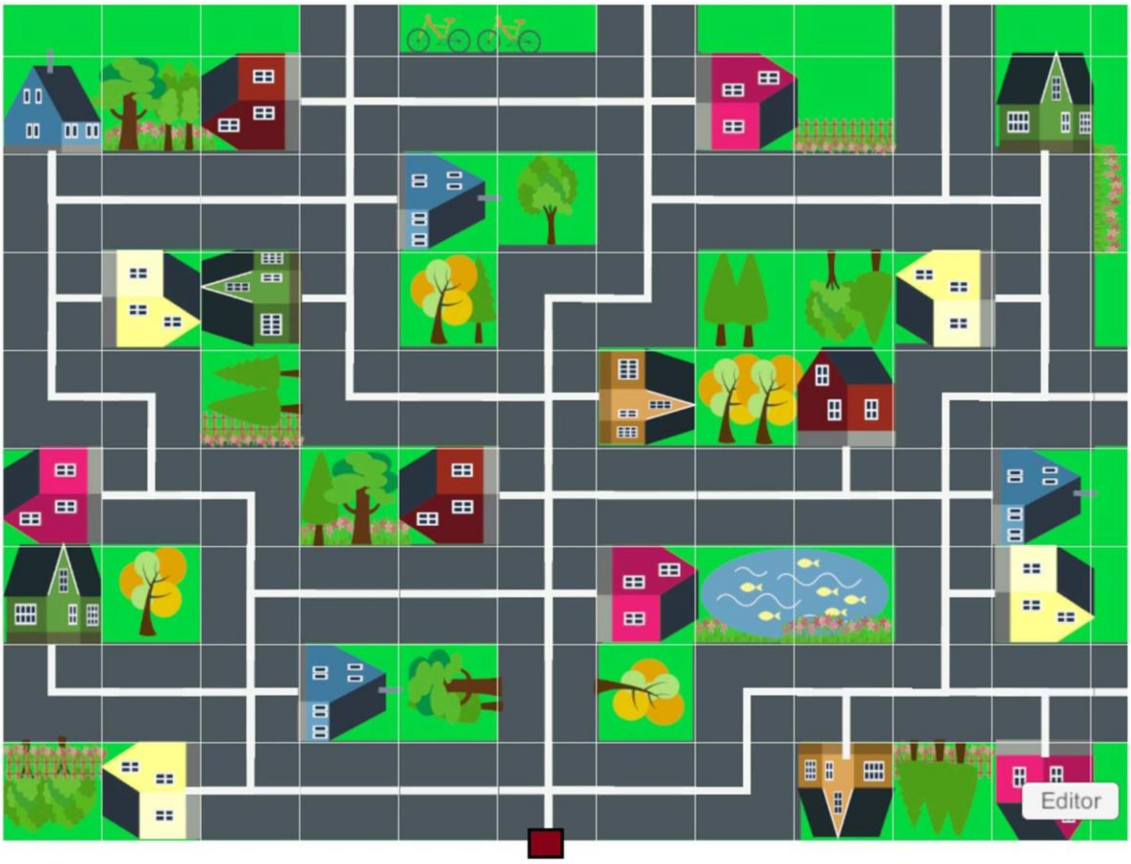

FIGURE 1 | VC™ projection on the ground. The red square indicates the starting position.

This study complied with the Declaration of Helsinki and was approved by the Regional Pediatric Ethical Committee (n.175/2019). Parents and children signed a written consent form (for children, in a child friendly format).

Procedures and Measures

The experimental design was divided into two assessments administered to each child: the VC™ paradigm and neuropsychological tasks, both testing visuo-spatial memory and EFs. The VC™ paradigm and neuropsychological tests were carried out at different times of the same day or on two different days (no longer than a week apart), in order to reduce the fatigue effect as much as possible. Order of assessments was randomized with half of the participants starting with the VC™ paradigm and the other with the neuropsychological evaluation, in the majority of cases. Duration of the entire VC™ paradigm ranged from 40 to 50 min in a single session although for some children, due to variability in collaboration, duration could be longer. Subsequently, the psychologists (BDL and MCC) who administered the task, filled out a feasibility VC™ questionnaire created ad hoc. The duration of the neuropsychological assessment was 1 h on average in one single session but varied again as a function of degree of collaboration.

The experimental set up and the procedures were the following:

The Virtual City Paradigm™

The VC™ is a projected virtual town on the floor, consisting of 20 houses, street lanes and crossings (**Figure 1**), created on Unity 5.5.1© platform. Two projectors were installed and connected to a computer so as to project the town on an off-white carpet (2.6 m × 3.2 m) in a dark laboratory space. The child had to move around the virtual town to reach the houses which flickered (the targets). Houses flickered either in a sequence, or all together. For tracking the trajectory of the child, the motion capture system (HTC® Vive and Steam© software), included two handheld three-dimensional space (3D) motion sensors applied one on the head (fixed on a bike helmet worn by the child) and one on the trunk (fixed on a belt worn by the child) (see (13)) and two infrared cameras allowing tracking of body movement in 3D in real time (see videos in the **Supplementary Material**).

The VC™ paradigm included three different conditions in which the number of houses to be reached (span level), the sequence order, flicker duration, and the instructions varied.

1 City Pointing: While keeping the starting position, the child was asked to point (with a laser pointer) each house as it flickered (for 2.5 s). The sequence of flickering houses was randomized and the houses' order was set so that no contiguous houses flickered in a sequence. This procedure allowed assessing efficacy of visual search abilities in a large space and visuo-spatial span. If the child correctly pointed to at least 80% of the houses, the other conditions were administered.
2 City Following: A given number of houses was made to flicker in sequence. The child was asked to remain in the starting position and observe each house as it flickered (for 2.5 s). Then the child was asked to walk on the streets to reach each house in the same order he/she had seen them flickering. The sequences were randomized and the houses' order set with a mathematical algorithm to ensure both easy sequences (the houses are near to each other and not too many rotations are needed to reach the next one) and some difficult ones (i.e., more distant houses and more rotations). There was a maximum of five span levels (from the starting level of two houses for all subjects up to a level of six houses). Criterion for success on any given level was three out of five trials correct and in case of failure, five additional trials for the same level were presented before proceeding with the third condition. Similarly to the Corsi Block Tapping test, a span measure was obtained, but for this paradigm it was the longest sequence reached by the subject (even if the three out of five criterion was not met).
3 City Planning: The child was asked to observe the houses that were flickering simultaneously while keeping the starting position, and then to walk on the streets to reach the houses he/she had seen flickering. The specific instruction was to plan the shortest path. There was a maximum of three span levels (from a span of two to a span of four) each with 10 trials, with the starting span level being the span level reached in the second condition. Flickering duration for each span level was respectively 7.4, 11.3, and 13.1 s.

The cognitive strategies needed to complete the VC™ tasks could be the following: a first encoding phase in which the subject mentally encoded the spatial distribution of the houses and eventually the temporal sequence of their presentation. This encoding may be perturbed in ADHD due to a deficit in selective attention and/or spatial memory. For this reason, a control condition was added (City Pointing), to ensure that children do indeed pay attention to all houses in the town as they flicker; a second recall phase in which before starting the task, the subject had to mentally rehearse the encoded representation of the flickering houses' spatial distribution and to generate the trajectory. Both phases imply spatial short- and long-term memory and inhibition, intended, the latter, as the capacity to inhibit the prepotent response to start walking in the town before having generated a trajectory or the shortest path as in the City Planning condition; finally, when the subject navigated the town, he/she needed to update the mental trajectory of the houses he/she had generated. That is, he/she had to represent the position of the houses relative to his actual position in the town and no longer the one relative to the starting position in which he/she had originally encoded them. This phase could tax the updating component of spatial memory (working memory).

In addition to the span measure, the VC™ paradigm provides kinematics data on the movement trajectory of each subject. In particular, the HTC© Vive system and Steam© software allows both to generate the target positions (i.e., the houses) in the virtual environment (calibration procedure) and to record the trajectories of each child during navigation. The calibration procedure was performed by the psychologist (BDL) who positioned herself over each target house following a standard order, enabling to configure the global navigational array and to set the houses' positions in a cartesian coordinate system by triggering the 3D motion sensor.

To record the trajectory of the children, the system detected the locomotion during the experimental sessions and computed, for specific time frames (in ms), head and trunk sensor positions on X, Y, and Z axes, and rotation angles with respect to the X, Y, Z axes direction. These data were treated using Matlab 2021 to yield parameters such as trunk and head position and rotation in the horizontal plane, trunk and head velocity, acceleration, and stops during the trajectory. Further details on automatic kinematic data analysis are reported in (13).

Neuropsychological Assessment

Visuo-spatial short-term memory/working memory tasks in the reaching space included the Corsi Block Tapping task forward and backward (43) and a computerized block tapping task, the Spatial Span Task (CANTAB®) (44). The span measure was the longest sequence correctly retrieved. The Digit span WISC-IV subtests-forward and backward- served as a control verbal measure of spatial memory. Parents and children filled out a pilot questionnaire on everyday visuo-spatial and navigation abilities (Santa Barbara Sense of Direction Scale-Parent and Child Version: p-CBSOD and c-CBSOD) adapted by Murias et al. (45) (see **Supplementary Material 1**).

The Stop Signal Task (CANTAB®) (44) was administered as a measure of response inhibition. It is a go-no-go task adapting the time interval between the go stimulus and the stop stimulus to the performance of the subject providing as the outcome measure, the estimate of time during which an individual can successfully inhibit the response 50% of the time. The Tower of London (46) was administered as a measure of planning expressed in terms of total decision time, execution time and number of rule violations. As an ecological measure of EFs, parents filled out the Behavior Rating Inventory of Executive Function - Second Edition (BRIEF-2) (47) on their children's abilities for inhibition, working memory, monitoring and self-monitoring, shift, planning and emotional regulation.

Feasibility Assessment

The feasibility of the VC™ paradigm was investigated with two measures, an *ad-hoc* questionnaire on acceptability and usability filled out by the two experimenters (BDL and MCC) and a feasibility checklist. The questionnaire (see **Supplementary Material 2**), conforming to the standard definitions of usability (48–50) and acceptability (51, 52) [for a review study see (53)], consisted of 14 questions ranked on a 5-point Likert scale (1 most negative, 5 most positive). The feasibility checklist with criteria for success, based on a literature review (see **Supplementary Material 2**, **Table 1**), consisted of nine outcome measures grouped in four areas specific for the VC™ (accessibility, training motivation, technical smoothness, and training compliance) and 5 for the entire study design and procedures (participation willingness, participation rates, loss to follow-up, assessment timescale and assessment procedures).

RESULTS

Feasibility Analyses

Feasibility questionnaire data and checklist measures were available for 21/22 subjects. Feasibility questionnaire results for usability and acceptability revealed a prevalence of positive responses, indicating a satisfactory feasibility of the VC™ paradigm. For usability (6 questions), there were 74/126 responses graded as 5 and 29/126 as 4. For acceptability (8 questions), there 73/168 graded as 5 and 44/168 as 4.

Feasibility criteria were met for all measures both for the VC™ (accessibility 91%; compliance 91%; technical smoothness 32%; motivation 14%) and for the entire study design and procedures (participation willingness 95%; participation rates 4%; missing data: VC™ and neuropsychological assessment 13%; time scale 91%; procedure 91%).

VC™ Span Level and Neuropsychological Measures

The VC™ span level and neuropsychological measures were available for 18 out of 22 subjects due to 1 drop-out because parents refused to continue the study, 1 to technical sensors problems, and 2 for failure to complete the entire VC™ in a single session. Missing data (either Tower of London or WISC-IV digit span) concerned three subjects.

Group data will be presented first and then data from two 10 year-old children with ADHD deemed exemplary. A typically developing 10 year-old child served as a comparison subject.

Statistical analyses were computed with RStudio version 2020 for Windows (www. R-project.org). Preliminary Spearman correlation analyses were computed between the VC™ span and neuropsychological measures. The span level of the City Following condition, intended as the longest sequence reached (but not passed), was compared with the raw data of the different neuropsychological measures (Corsi Span, CANTAB© Spatial Span, CANTAB© Stop Signal, Tower of London, BRIEF-2) and with the standard WISC-IV Digit Span scores.

As expected, there was significant correlation between the VC™ span level and both the Corsi forward (r = 0.67, p = 0.002) and backward spans (r = 0.60, p = 0.008). In addition, there was a significant positive correlation between the VC™ span and the backward digit span (r = 0.57, p = 0.01). Age correlated significantly with the VC™ span level (r = 0.70, p = < 0.001). A significant negative correlation was found between c-SBSOD and VC™ span level (r = −0.70, p = 0.001). No other significant correlation was observed with other neuropsychological test measures (Tower of London and CANTAB© span and inhibition) and questionnaire measures (BRIEF-2, p-SBSOD).

Individual VC™ Trajectories and Neuropsychological Data

Based on trajectories analyses, a qualitative description of the behavior during VC™ performance is presented for two children with ADHD (subject 22, Inattentive and subject 17 Combined, **Table 1**), and the comparison subject. **Figure 2** compares the trajectories of the same sequence (span level 3, trial 3) in the City Following condition, where the child is asked to reach three houses flickering in an easy sequence.

In **Figure 2A**, the child with Combined ADHD performed the trial correctly by reaching the 3 target houses in the right order. However, he reached the first and second target houses, then stopped, not remembering the exact position of the third target house. He therefore returned to the starting position, looked around (as indicated by the red arrows), then he presumably remembered the position of the third target house and headed toward it. In **Figure 2B**, the child with Inattentive ADHD failed the task. The child started from the initial position and correctly reached the first and second houses. He then reached a wrong house, then stopped, looked around, understood that he had failed and thus proceeded to reaching another (incorrect) house. From **Figure 2B**, this child's head movements, shown by red arrows, indicate a high distractibility of the subject, given his frequent deviation from the trajectory and they do not predict the following movement directions. **Figure 2C** shows that the comparison child reached the target houses in the right order with a linear locomotion trajectory. The head movements did not deviate from the path when linear, while they were anticipatory when body rotations were necessary, predicting the following movement directions. Neuropsychological assessment data of the two children with ADHD and the comparison subject revealed some important qualitative differences. They concern not only visuo-spatial memory abilities (Corsi span forward and backward), but also EFs, a core deficit of ADHD children. Specifically, with regards to the parent report questionnaire BRIEF-2, the cognitive regulation abilities (Cognitive Regulation Index) were much poorer in the children with ADHD than in the control, with T scores in the clinical/borderline range. Tower of London performance indicated significant difficulties only in the Inattentive presentation. Such skills could be crucial for carrying out the task, and include planning, working memory and self-monitoring. CANTAB© and SBSOD (child and parent report) data were not available for the comparison subject and thus are not presented.

Correlations Between Virtual City™ Span and Neuropsychological Measures

Significant associations were found between VC™ span - Following condition- and verbal and visuo-spatial memory abilities. A larger correlation was found between the VC ™ span and the Corsi Block Tapping test. No associations were found between the VC™ span (Following condition) and EF measures differently than expected from the literature (6, 8). The VC™ span was the sole measure to be analyzed, while other available parameters such as head deviation from the trunk, latency and kinematic parameters may offer new insights into the role of EFs. Furthermore, the EF measures chosen may not have been sensitive enough. The negative correlation between the Child SBSOD questionnaire and the VC™ span was unexpected. Better perception for one's spatial orientation abilities was associated with lower VC™ span. This could be due to difficulty in fully understanding the questions, as well as to a reduced awareness of one's own deficits.

Performance Differences in ADHD Subjects Compared With the Control Child

The trajectory analyses of ADHD and control subjects reveal some qualitative differences in spatial navigation behavior which may be associated with the deficits displayed by children with ADHD.

Although the child with combined ADHD performed the sequence correctly, the locomotor pathway was non-linear. In fact, this child went back to the starting point possibly to rehearse the trajectory previously encoded. This suggests that he recruited an egocentric storing strategy less functional than an allocentric one. This return-to-start behavior has been described in adults (54) in a "virtual starmaze" task and accounted for as "a mixed strategy." During navigation, sensory stimuli can be encoded in spatial reference frames centered on the sensory organs (egocentric) or in an allocentric reference frame, with allocentric spatial encoding strategy introducing a substantial computational simplification, acquired later in childhood and probably subsumed by EFs (7). Since executive dysfunction is one of the core deficits of ADHD, these children may have difficulties in activating an allocentric strategy to store the targets. The child with inattentive ADHD showed the worst performance, being highly distractible, failing the sequence, following a linear path (he did not return to the starting point), with head and trunk not moving in the same directions.

Given the novelty of this complex navigation paradigm, tapping processes beyond executive functions, it is premature to interpret the preliminary results in terms of specific models or hypotheses on attentional/executive dysfunctions in ADHD. Further analyses on the planning trajectories and on the pattern of responses of typically developing children could provide insights on the role of automatic processes which could be preponderant in approaching this task in ADHD but also in younger children.

Infact, no age-matched control group was recruited for this study. However, as already highlighted, this is a feasibility study aimed at analyzing usability and acceptability of a new way of testing cognition in navigation in a clinical population with significant impairments in cognitive functions tapped in the VC™ paradigm. A study on typically developing children will be conducted, matched to a larger group of children with ADHD for analyzing if there are specific patterns of behavior which characterize this clinical population, as suggested by the preliminary trajectories' analyses. To better understand the cognitive processes involved in the VC™ task, further investigations will be necessary, taking into account parameters other than span such as decision time, head deviation from trajectory, to name the most relevant that have been studied in other navigational tasks. These indicators could clarify the role and nature of EFs that did not clearly emerge in this feasibility study, but are certainly involved in such a challenging navigational task. Further neuropsychological assessments could be advantageous as to allow disentangling specific cognitive processes which may be pivotal for understanding how children approach this ecological yet complex task.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Regional Pediatric Ethical Committee (n.175/2019), Tuscany region, Italy. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

BDL: methodology, investigation, resources, data curation, writing—original draft, and writing—review and editing. VB: conceptualization, methodology, formal analysis, and writing—review and editing. PB: methodology, formal analysis, supervision, writing original draft, and writing—review and editing. MCC: formal analysis, investigation, resources, and writing—review and editing. AC: methodology, software, validation, data curation, and writing—review and editing. GM: methodology, supervision, resources, and writing—review and editing. AT: methodology, resources, and writing—review and editing. MZ: resources, data curation, visualization, and formal analyses. GC: conceptualization, supervision, writing, review and editing, and funding acquisition project administration. AB: methodology, conceptualization, formal analysis, supervision, writing, and review and editing. All authors contributed to the article and approved the submitted version.

FUNDING

The research was funded by the Italian Ministry of Health (RC 2018-19) and public funds 5 per 1,000.

ACKNOWLEDGMENTS

We wish to thank Prof. Chiara Pecini, University of Florence, Italy and Dr. Maria Chiara Di Lieto, IRCCS Stella Maris, Psychologists, for their contribution in the initial phase of planning the Virtual City and the ADHD team of IRCCS Fondazione Stella Maris for collaboration. For the feasibility measures, we are greateful for the supervision of Prof. Giuseppina Sgandurra and Dr. Elena Beani of IRCCS Fondazione Stella Maris. For the evaluation of everyday navigation skills, we wish to thank Prof. Giuseppe Iaria and Dr. Kara Murias, University of Calgary, Canada, for giving us permission to use the spatial orientation questionnaire adapted for children (c-SBSOD and p-SBSOD). BDL was supported by the Tuscan Program of Neuroscience.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.708434/full#supplementary-material

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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RÉSUMÉ DE LA THÈSE

Contexte

En prenant en compte les études en images cérébrales et les différences de performances cognitives observées lors de la comparaison de tâches homologues telles que le Blocking Corsi Test (CBT) et le Walking Corsi Test (WalCT) dans l'espace proche et dans l'espace locomoteur (Belmonti et al., 2015; Nemmi et al., 2013; Perrochon et al., 2018; Piccardi et al., 2008, 2010, 2011), ces résultats fournissent des preuves convaincantes de la discrimination entre les circuits neuronaux et le traitement cognitif pour l'espace proche et l'espace de navigation, aussi bien dans la mémoire visuospatiale que l'apprentissage spatial. Les études de la cognition spatiale représentent un domaine en plein essor dans les neurosciences cognitives, et l'évaluation des capacités cognitives reste limitée par rapport à l'évaluation neurocognitive classique. Ainsi, pour comprendre la complexité du traitement cognitif spatial, comment il se développe au cours de notre vie et de notre développement, et comment il est affecté dans les troubles neurodéveloppementaux, l'étude des capacités de navigation spatiale est d'une grande importance pour contribuer à établir un diagnostic et proposer un programme de réadaptation.

L'objectif de cette thèse était d'étudier le control inhibiteur (IC), la flexibilité cognitive (FC) et la mémoire de travail visuospatiale (VSWM) impliqués dans le développement neurologique typique et atypique en s'appuyant sur des protocoles de navigation spatiale fondés sur le Virtual Carpet Paradigm (VC) ainsi qu'une tâche locomotrice orientée vers un objectif (GOLT). Nous avons regroupé cinq études, subdivisées en trois thématiques portant sur a) la mémorisation et les générations de séquences de cibles visuospatiales, b) la planification et l'ajustement des trajectoires face à des changements imprévus lors de l'atteinte d'un objectif, et c) l'inhibition et la replanification de trajectoires apprises précédemment trop perfectionnées.

Méthodologie

Le paradigme du tapis virtuel

Le paradigme VC a été créé par Alain Berthoz et Mohamed Zaoui au Collège de France (2015) pour étudier le comportement et les fonctions cognitives dans l'espace proche (péripersonnel) et dans l'espace locomoteur (espace de navigation). Le VC est un système technologique polyvalent qui nous permet de présenter des stimuli visuels et auditifs (par exemple, des vidéos et des images) ainsi que d'enregistrer des trajectoires locomotrices avec une plus grande précision grâce aux capteurs.

Dans cette thèse, nous présentons cinq études lors lesquelles nous avons utilisé deux méthodologies distinctes de locomotion orientée vers un objectif : le paradigme du tapis virtuel (VC) et la tâche de navigation spatiale. Les quatre études utilisant le tapis virtuel sont :

e) A new paradigm for the study of cognitive flexibility in children and Adolescents: The "Virtual House Locomotor Maze" (VHLM) (Castilla et al., 2021),

f) Age and sex impact on visuospatial working memory (VSWM), mental rotation, and cognitive strategies during navigation (Castilla, Berthoz, Urukalo, et al., 2022),

g) Age-related decline in visuo-spatial working memory is reflected by dorsolateral prefrontal activation and cognitive capabilities (Kronovsek et al., 2020).

h) The Virtual City Paradigm™ for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study. (Del Lucchese et al., 2021),

La cinquième étude menée a être basé sur la tâche de navigation spatiale :

Anticipatory orienting strategies and trajectory formation (Castilla, Berthoz, Cioni, et al., 2022).

Montage expérimental

En ce qui concerne le paradigme VC, nous avons utilisé deux ordinateurs portables, un vidéoprojecteur(s) et un système HTC Vive (système de réalité virtuelle) pour l'expérimentation (HTC® Vive, Taïwan), un logiciel pour enregistrer les trajectoires locomotrices et un logiciel MATLAB pour les analyses de données et la visualisation des données. (Castilla et al., 2022) (Figure 1).

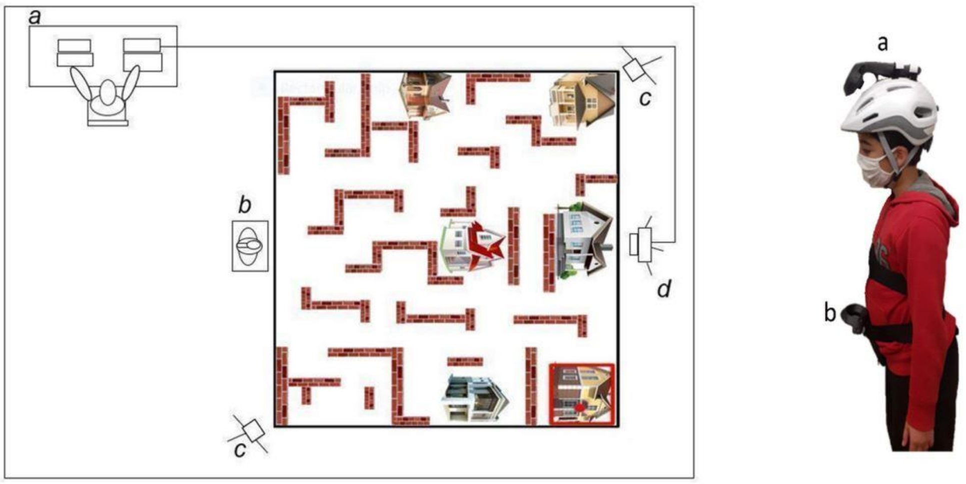


Figure 1. (A) La représentation de la configuration expérimentale : (a) l'emplacement du poste de contrôle où l'expérimentateur exécute l'expérience, (b) le point de départ, (c) deux caméras

HTC Vive, (d) le vidéoprojecteur. (B) les capteurs de mouvement sensoriels 3D. (a) un capteur de mouvement 3D portable est adapté à un casque de vélo et est porté sur la tête du participant et (b) le deuxième capteur de mouvement 3D portable est fixé à la ceinture portée à la taille du participant.

Un ordinateur était relié au vidéoprojecteur pour projeter l'espace de navigation au sol (3 m x 2,4 m) et les stimuli, 9 dalles de 30 x 30 cm. Cette projection a servi de modèle pour configurer les coordonnées de l'environnement virtuel et présenter les séquences au participant. Un deuxième ordinateur était connecté au système HTC Vive (c'est-à-dire deux caméras infrarouges, deux capteurs de mouvement 3D portatifs et un casque de réalité virtuelle). Les deux caméras étaient placées en diagonale à 5 mètres (16,4042 pieds) de l'une de l'autre afin de couvrir tout l'espace de navigation. Les deux capteurs de mouvement 3D portatifs étaient utilisés comme des capteurs de trajectoire qui enregistraient les positions X, Y, Z toutes les 11 millisecondes (90,90 Hertz) (Niehorster et al., 2017). Ces capteurs de mouvement 3D étaient fixés sur un appui-tête (casque de vélo) qui était porté sur la tête du participant et un autre capteur de mouvement 3D était ajouté à une ceinture qui était portée à la taille. Nous avons pu mesurer et calculer (a) la position du participant dans l'espace de navigation (coordonnées X, Y); (b) la direction tête/taille sur le plan horizontal (rotations) dans la composante horizontale (c'est-à-dire le plan de lacet).

Nous avons utilisé le Basic Trajectory Software version 1 (BTS) pour le paramétrage de l'espace de navigation et de l'enregistrement des données. Le BTS utilisait les disques du système HTC Vive ; (a) pour générer les cibles virtuelles (par exemple, les dalles virtuelles) dans l'environnement virtuel, connu sous le nom de procédure de calibration, et (b) pour enregistrer les trajectoires du participant. La procédure de calibration nous a permis (a) de mesurer l'espace de navigation des enregistrements et (b) de définir les positions de la cible dans un système de coordonnées cartésiennes (voir annexes 1 pour une description complète de la procédure de calibrage). En utilisant les coordonnées des dalles, nous avons créé un algorithme pour établir un périmètre autour du centre de chaque dalle de 30x30 cm. Cette configuration nous a permis d'identifier les dalles et de déterminer si les participants ont atteint ou non une cible de la séquence.

PROTOCOLES EXPERIMENTAUX

Le protocole de Virtual house locomotor maze (VHLM)

Le VHLM^{TM} est composé de 6 maisons placées dans un labyrinthe simplifié délimité par des murs créés à l'aide du logiciel Microsoft PowerPoint 2016 (Figure 2). Chaque maison peut être identifiée comme une cible pour le participant par un point vert apparaissant sur la maison et l'entourant d'un carré de lumière verte. Au même temps que le bip de démarrage est lancé, la maison cible est éclairée par un carré de lumière verte pour augmenter la concentration attentionnelle des participants sur la maison cible. La projection au sol délimitait l'environnement de l'espace de navigation (3,5 x 2,5 m). Ce labyrinthe évalue le traitement de la mémoire spatiale des images d'un labyrinthe simplifié avec des maisons projetées au sol. Cela nécessite que le participant génère des représentations mentales de l'espace de navigation, les mémorise et puisse les rappeler. Lorsque le participant doit naviguer dans le labyrinthe virtuel en se redirigeant vers le point de départ, le processus peut même engager des processus de rotation mentale (Carbone et al., 2020; Meilinger et al., 2011).

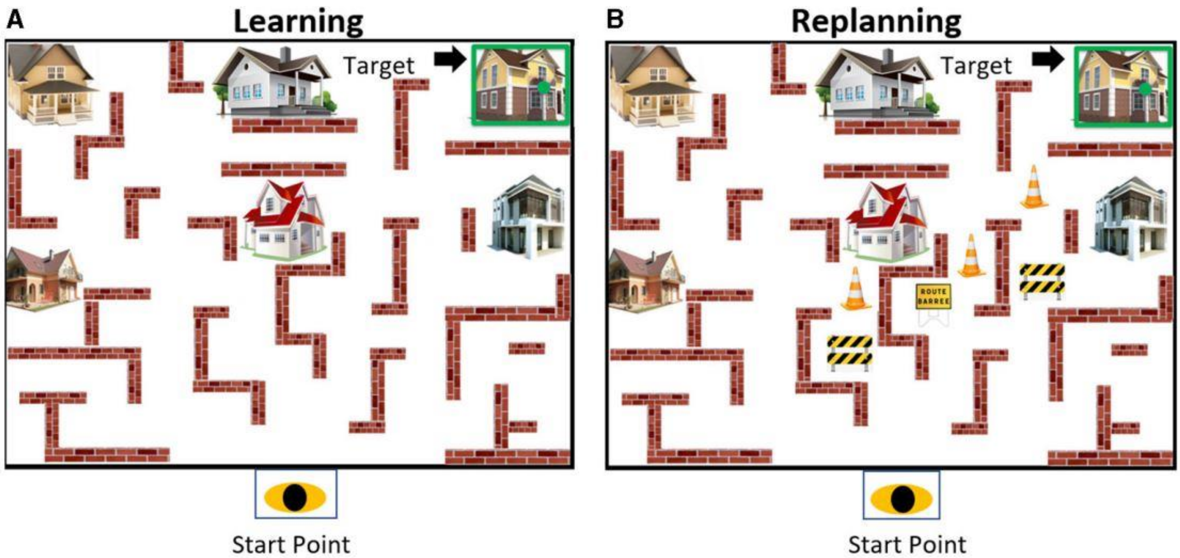


Figure 2. La disposition du labyrinthe virtuel. (A) L'image de gauche montre une maison cible encadrée en vert. La même maison a été montrée 5 fois pour induire une trajectoire de surapprentissage. (B) L'image de droite montre une maison cible encadrée en vert et les obstacles bloquant l'accès à la maison par les chemins les plus courts. Cela a induit la nécessité de replanifier la trajectoire surappris (Castilla et al., 2021a).

Procédure

Dans le VHLM, les participants sont demandés de se diriger le plus vite possible pour atteindre une maison cible après la présentation des stimuli (en vert et le signal acoustique) et revenir au point de départ. De plus, les participants sont demandés à éviter de traverser les murs, les obstacles et les autres maisons tout au long du parcours. Les participants sont aussi informés qu'il est possible qu'un chemin soit bloqué, et qu'ils peuvent sélectionner d'autres chemins alternatifs pour atteindre la maison cible.

Le test Virtual Walking Corsi (VWalCT)

Le VWalCT est une adaptation du WalCT au VC (Castilla, Berthoz, Urukalo, et al., 2022 ; Kronovsek et al., 2020). Dans le VWalCT, 9 dalles de 30 x 30 cm (c'est-à-dire les stimuli) ont été projetées sur le sol (3 m x 2,4 m) (Figure 3). Au cours de l'expérimentation, chaque dalle a été allumée pendant une seconde avec un intervalle interstimulus d'une seconde. Le nombre de dalle a augmenté d'une dalle par séquence (c'est-à-dire, une séquence de 2 essais de 2 dalles, à une séquence de 2 essais de 9 dalles)

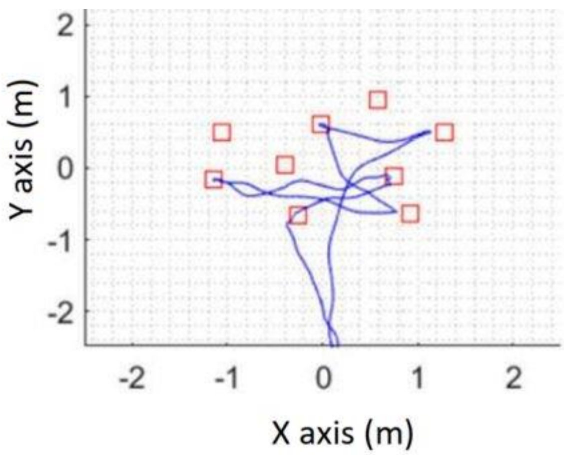


Figure 3. L'espace de navigation et la trajectoire locomotrice pour une séquence de six dalles : les carrés rouges représentent les positions des dalles dans l'espace de navigation. La ligne bleue représente une trajectoire locomotrice (2D) générée par un participant lors de la réponse (phase de rappel) (d'après Castilla et al., (2022)).

Procédure

Dans chaque essai, une séquence de dalles était présentée automatiquement aux participants. La tâche des participants était de reproduire la même séquence en marchant sur chaque dalle pour quelques secondes. Les trajectoires des participants sont enregistrées au moyen des capteurs.

Le protocole de la ville virtuelle

Le protocole Virtual City a été développé par Alain Berthoz en collaboration avec l'équipe de recherche de Giovanni Cioni à l'hôpital Stella Maris de Pise, en Italie. Il a été mis en œuvre dans le projet de thèse de Benedetta Del Lucchese de l'Université de Florence, en Italie. La Ville Virtuelle est une ville simplifiée constituée de 20 maisons de couleurs différentes, de voies, de rues et de carrefours projetés au sol pour la navigation locomotrice (Figure 4). Il a été créé sur la base du paradigme VC en utilisant la plate-forme Unity 5.5.1©. Le protocole a été utilisé dans une étude récente intitulée "The Virtual City Paradigm TM for Testing Visuo-Spatial Memory, Executive Functions and Cognitive Strategies in Children With ADHD: A Feasibility Study" (Del Lucchese et al., 2021).

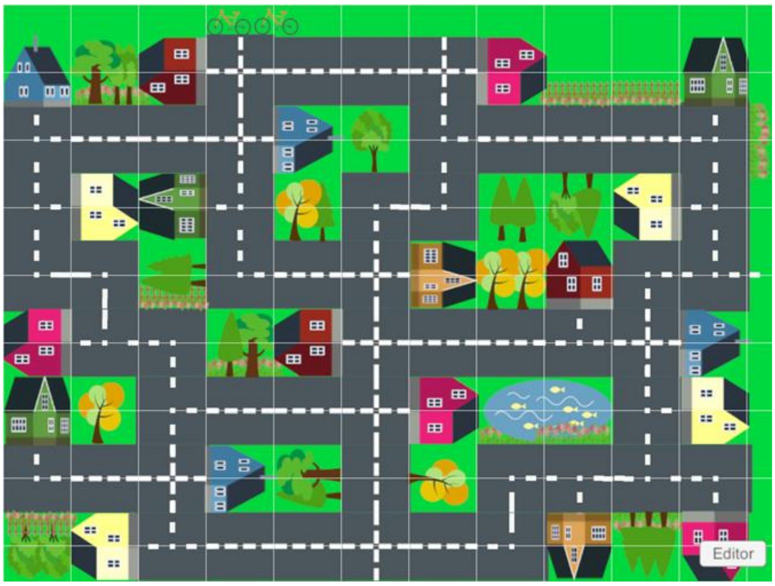


Figure 4. Représentation de la projection du protocole The Virtual City au sol, composée de 20 maisons (Del Lucchese et al., 2021).

Procédure

Les participants étaient demandés à observer attentivement la VC et à atteindre les maisons qui clignotent (stimuli) sur l'espace de navigation locomotrice. Les stimuli ont été présentés séquentiellement (une maison après l'autre, chaque maison a clignoté pendant 2500 ms) ou simultanément (c'est-à-dire que plusieurs maisons sont éclairées en même temps). Trois conditions différentes ont été conçues pour le protocole de ville virtuelle : a) le pointage de la ville – City Pointing (condition de contrôle), b) le suivi de la ville - City following et c) la planification de la ville - City planning.

a) Dans le City Pointing, le participant est invité à se tenir sur la position de départ, puis une séquence aléatoire de maisons est présentée au participant. La tâche du participant était d'indiquer les maisons qui clignotaient à l'aide d'un pointeur laser. Cette condition contrôle était introduite pour évaluer les capacités d'exploration visuospatiale des participants. Le participant était exclu de l'étude s'il obtenait un score inférieur à 80 % du nombre total de séquences présentées.

b) Dans la City following, le participant est placé sur la position de départ et une séquence aléatoire de maisons était présentée. Ensuite, le participant était invité à reproduire la même séquence dans le même ordre de présentation.

c) Dans City planning, le participant était placé sur la position de départ puis une présentation simultanée des maisons était affichée. Il était demandé au participant d'atteindre chaque maison présentée en utilisant le chemin le plus court.

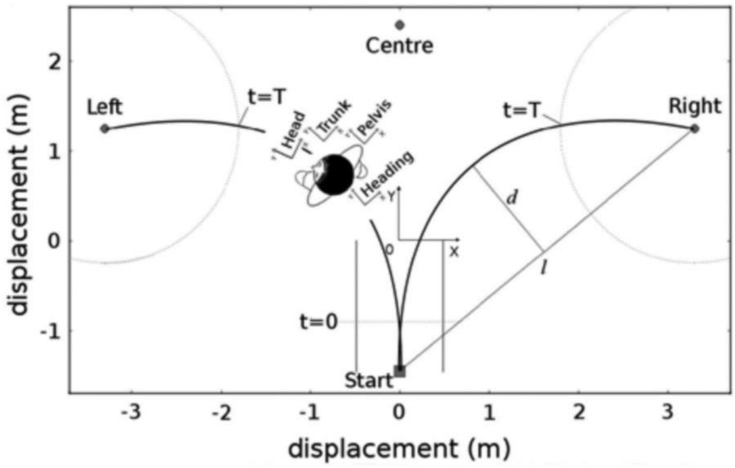
La tâche d'atteinte locomotrice

La tâche d'atteinte locomotrice a été utilisée pour explorer les capacités de navigation et les fonctions exécutives chez des sujets développementaux typiques et des patients atteints de troubles du développement (par exemple, la paralysie cérébrale) dans l'espace locomoteur proche (Belmonti et al., 2013, 2016). La tâche d'atteinte locomotrice est une tâche axée sur l'objectif locomoteur conçue pour évaluer le développement des fonctions comportementales et cognitives chez les sujets cliniques et typiques. Ce protocole nous a permis d'enregistrer les mouvements cinématiques lors des trajectoires locomotrices.

Montage expérimental

Le montage expérimental était composé d'un point de départ (Start), un couloir visuel et trois cibles (central, left et right) (Figure 5). Chaque cible était représentée par une lampe ronde en plastique munie d'un haut-parleur (30 cm de diamètre) posé sur une table. Un signal de démarrage lumineux ou visuel était présenté un par un simultanément d'un signal de démarrage acoustique (bip) donné par un automate programmable. De plus, ce contrôleur programmable a donné les résultats au système de capture de mouvement. La cible centrale était placée sur une petite table (50 l × 730 w × 70 h cm) en face de la position de départ des participants (Start) à une distance de 3,8 m. Les cibles gauche et droite étaient positionnées à une distance de 4,20 m (soit 3,3 m de chaque côté et 2,6 m devant Start). Les deux cibles (Gauche et Droite) étaient posées sur deux table plus grandes (250 l × 7,120 w × 90 h cm) positionné latéralement du Start, en face de l'un l'autre.

Figure 5. La représentation de la disposition spatiale sur le plan de lacet (plan horizontal)



(Belmonti et al., 2013). Start indique la position de départ. Gauche, Centre et Droite désignent les trois cibles lumineuses. Les deux lignes grises verticales en gras représentent le couloir limitant la direction de marche initiale.

Procédure

Les participants sont demandés de rester immobiles sur la dalle de départ en attendant un signal acoustique et la présentation d'une cible lumineuse. Après la présentation des stimuli (signal acoustique et une cible lumineuse), les participants devaient se diriger pour atteindre la cible lumineuse, la toucher et ensuite revenir au départ.

RÉSULTATS EXPÉRIMENTAUX : ÉTUDES PUBLIÉES

Dans cette partie, nous allons présenter les articles scientifiques déjà publiés et celles soumis aux revues scientifiques spécialisées et révisés, ainsi que les articles en cours de préparation. Ces articles sont regroupés selon les trois thématiques abordés pendant la thèse : a) l'exploration développementale des capacités cognitives spatiales et de l'activité cérébrale chez l'adulte à l'aide du WalCT, b) la replanification à la suite d'un changement de cible pendant la locomotion, et c) le contrôle inhibiteur et flexibilité cognitive dans la tâche locomotrice visuo-spatiale.

Dans la première thématique, notre recherche a examiné l'exploration des capacités cognitive spatiale et l'activité cérébrale chez les jeunes adultes (YA) et les personnes âgées

(OA) en utilisant le WalCT. Les résultats de la recherche nous a permit de publier deux articles scientifiques :

Le premier article est intitulé « Age and sex impact on visuo-spatial working memory (VSWM), mental rotation (MR), and cognitive strategies during navigation » publié dans la revue du Neuroscience Research Journal (Castilla et al., 2022). L'article vise à étudier les capacités cognitives spatiales telles que la VSWM, la MR et les stratégies cognitives pendant le vieillissement typique en utilisant un GOLT. Dans cette étude, nous avons vérifié les hypothèses suivantes ;

- Le groupe des YA aurait une meilleure performance que les OA dans le WalCT.
- Les capacités de MR concernant les cartes cognitives spatiales sont intimement liées aux performances de VSWM dans l'espace de navigation.
- Les participants ayant les performances les plus élevés du VSWM auront une préférence à utiliser les stratégies *place sparing* contrairement aux participants ayant des performances plus modérées qui utiliseront plus les stratégies de *path sparing*
- Le groupe de OA présentera plus d'erreurs aléatoires que les YA quand ils manqueront d'utiliser les stratégies cognitives spatiales. (Perrochon et al., 2014).
- Les différences liées au sexe dans le VSWM sont seulement observées dans le groupe des YA lors de la tâche locomotrice. (Lambrey and Berthoz, 2007).
- Les groupes des YA-F et OA-F seront plus susceptibles à utiliser des stratégies egocentriques pendant la phase de rappel. (Colombo et al., 2017; Lambrey and Berthoz, 2007).

Cet article étudie la mémoire de travail visuo-spatiale (VSWM), la rotation mentale et les stratégies cognitives au cours du vieillissement typique à l'aide d'une tâche de locomotion orientée vers un objectif. Cinquante participants en bonne santé ont été recrutés et regroupés en personnes âgées (OA) et jeunes adultes (YA). Les participants ont effectué le test Virtual Walking Corsi (WalCT) en utilisant le paradigme Virtual Carpet ™ et le test de rotation mentale (MRT).

Nous avons enregistré des informations cinématiques lors de la navigation (c'est-à-dire les trajectoires et les orientations de la locomotion). Les analyses se sont concentrées sur : a) la comparaison des performances de VSWM entre deux méthodes différentes (c'est-à-dire, Classic et Score Point Attribution - SPA) afin d'analyser quelle méthode produisait plus d'informations quantitatives, b) l'étude de deux différents types de capacités de rotations mentales (c.-à-d. MRT et rotations mentales en ligne de navigation) et c) les stratégies cognitives spatiales appliquées pendant la locomotion, basées sur l'analyse des erreurs. Nos données suggèrent que le SPA et la rotation mentale de navigation en ligne étaient modulés par le sexe (les jeunes hommes ont une performance plus élevée que les jeunes femmes) et l'âge (les YA ont obtenu des scores plus élevés que OA). Nous avons observé une utilisation préférentielle des stratégies cognitives liées au genre dans le groupe des YA qui n'était pas observée dans le groupe des OA. Les jeunes femmes s'appuyaient davantage sur des stratégies égocentriques tandis que les jeunes hommes s'appuyaient davantage sur des stratégies allocentriques. Les différences observées dans les stratégies cognitives dans le groupe des YA ont disparu dans le groupe des adultes âgés indiquant plus d'erreurs aléatoires par séquence. Les résultats ont mis en évidence les effets de l'âge et du sexe sur la VSWM, les stratégies cognitives et la rotation mentale pendant la navigation.

Les travaux actuels ont indiqué que le VWalCT est un outil idéal pour évaluer la mémoire visuo-spatiale, les stratégies de navigation et les capacités de rotation mentale en ligne dans l'espace locomoteur et l'espace proche. Pris ensemble, ces résultats indiquent que l'âge et le sexe ont un impact significatif sur la VSWM, les stratégies cognitives et la rotation mentale pendant la navigation. Nous suggérons que l'utilisation de cette SPA peut être mise en œuvre comme : a) évaluation cognitive complémentaire et b) être utilisée dans la réhabilitation des déficiences spatiales.

Dans la deuxième étude intitulée « Age-related decline in visuo-spatial working memory is reflected by dorsolateral prefrontal activation and cognitive capabilities investigate » (Kronovsek et al., 2020), nous avons étudié l'effet de l'âge sur l'oxygénation cérébrale dans les tâches VSWM en fonction de l'espace (proche ou navigation) et déterminé si les fonctions exécutives (EF) et l'oxygénation cérébrale étaient impliquées dans les performances VSWM, que ce soit dans l'espace proche ou l'espace de navigation.

Les performances de la mémoire de travail visuo-spatiale (VSWM) diminuent au cours du vieillissement et sont affecté par l'espace dans lequel la tâche est effectuée (proche ou navigation). L'oxygénation cérébrale et les capacités cognitives pourraient expliquer ce déclin. Nous avons évalué les effets de l'âge sur l'oxygénation cérébrale des cortex préfrontal dorsolatéral (dlPFC) dans les tâches VSWM dans l'espace proche et de navigation. Nous avons également évalué les corrélats cognitifs de la performance VSWM dans chaque espace. Méthode : 31 jeunes adultes (YA) et 24 adultes âgés en bonne santé (OA) ont effectué une batterie de tests neuropsychologiques et le test électronique Corsi Block-tapping dans l'espace proche (e-CBT) et dans l'espace de navigation en utilisant le "tapis virtuel" (VWCT). Nous avons demandé aux sujets de mémoriser, se rappeler et reproduire des séquences de dalles, augmentant progressivement le nombre de dalles de 2 à 9 dalles. Leur score d'étendue reflétait les performances de VSWM. L'oxygénation dlPFC (oxyhémoglobine : ΔO_2Hb et désoxyhémoglobine : ΔHHb) a été mesurée en utilisant l'imagerie spectroscopique proche infrarouge (fNIRS) lors de l'encodage de la voie séquentielle dans les deux tâches.

YA avait des scores d'étendue plus élevés que OA dans les deux espaces. Nous avons observé une diminution significativement plus importante de ΔHHb dans YA comparé au OA lors de l'encodage dans VWCT. L'arthrose présentait également une charge cérébrale significativement plus faible d'oxygénation dans VWCT par rapport à e-CBT. Une diminution de ΔHHb était également associée à une meilleure performance en VWCT. Enfin, nous avons étudié l'association de la rotation mentale et des fonctions exécutives avec la performance VSWM dans les deux tâches.

Les performances du VSWM et l'oxygénation cérébrale lors de l'encodage sont donc impactées par l'âge. L'espace dans laquelle la tâche a été effectuée s'est avérée être associée à différentes fonctions cognitives et a révélé des différences dans l'oxygénation cérébrale. Cette étude pilote a démontré que les OA typique semble avoir moins d'activation de leur dlPFC en comparaison des YA lors des performances des tâches VSWM, en particulier dans l'espace de navigation. De plus, nous avons distingué l'association de certains fonctions cognitives, telles que la rotation mentale et EF avec performance VSWM dans l'espace proche et l'espace de navigation.

En conclusion, nous avons enregistré l'activité neurophysiologique grâce à la spectroscopie fonctionnelle dans le proche infrarouge (fNIRS). L'activation préfrontale dorsolatérale et les capacités cognitives a confirmé un déclin de la VSWM lié à l'âge ainsi que le VSWM et l'oxygénation cérébrale lors de l'encodage. L'oxygénation et les performances cérébrales étaient modulées par le type d'espace (espace proche, espace lointain) et liées aux fonctions cognitives.

Dans la deuxième thématique, nous avons publié un article intitulé « Goal-oriented locomotion in children with spastic diplegia: Anticipatory orienting strategies and trajectory formation » (Castilla et al.,(2022)), apparue dans la revue Developmental Neurorehabilitation. L'objectif était d'étudier la navigation spatiale pendant la performance d'une tache locomotrice pour atteindre une cible chez les enfants diagnostiqués de CP, les enfants typiques et les adultes. Trois principales questions de recherche étaient posées :

1) Peut-on détecter des troubles de l'orientation anticipatoire et/ou de la formation de trajectoire chez les sujets atteints de CP diplégie spastique ?

2) Les compétences de navigation sont-elles nettement altérées dans la CP diplégie spastique, indépendamment des troubles de la marche ?

3) Contrairement à la locomotion autonome, la locomotion accompagnée aide-t-elle les sujets atteints de CP diplégie spastique à faire face à leurs troubles de la perception et de l'équilibre, leur permettant de générer de meilleures trajectoires ?

Nous avons cherché à examiner les signatures comportementales du contrôle anticipatif de navigation locomotrice chez les sujets att eints de CP bilatérale spastique. Il est important de rappeler que les troubles visuo-spatiaux sont fréquents dans la CP. Cependant, ils ne sont mesurés qu'au moyen d'une évaluation dans l'espace proche et non pas explorer dans l’espace de navigation. Même si les signatures comportementales du contrôle anticipatif dans la navigation locomotrice sont bien décrites chez les adultes et pendant le développement typique, elles n'ont jamais été étudiées dans la CP. De plus, ce qui ne semble pas apparent, c'est de savoir si les patients atteints de CP diplégie spastique ne souffrent que de troubles de la marche, ou s'ils présentent également des troubles du contrôle anticipatif de la navigation locomotrice. Pour répondre à cette question, une étude transversale descriptive a été menée portant sur 13 patients diplégies spastiques âgés de 5 à 23 ans. Les données de contrôle ont été obtenues à partir d'une étude précédente sur le développement typique. Les sujets ont effectué un GOLT pour atteindre des cibles lumineuses. Les trajectoires du corps entier et l'orientation des segments du corps ont été extraites de 15 marqueurs réfléchissants.

Nous avons analysé les paramètres comprenant : la variabilité de la trajectoire intra-sujet, l'écart maximal de la tête par rapport à la trajectoire et l'anticipation moyenne de la tête sur la trajectoire. Nous avons comparé ces paramètres cinématiques entre les sujets CP et les témoins du même âge, et entre chaque sujet et les témoins appariés selon l'âge. Les résultats ont suggéré des déficiences majeures en ce qui concerne l'orientation de la tête et les trajectoires dans une sous-population d'enfants atteints de PC. Sur la base de l'analyse, nous avons identifié trois sous-groupes de patients : a) les participants qui présentaient des troubles majeurs de la navigation caractérisées par une grande variabilité de trajectoire et des profils d'orientation de la tête anormaux, b) les participants qui présentaient des anomalies mineures de la navigation générant des trajectoires cohérentes, et c) les participants qui ne différaient des contrôles dans aucun paramètre de navigation, malgré leur démarche locomotrice. La locomotion orientée vers un objectif (Goal oriented locomotion) est considérée comme une double tâche intrinsèque en intégrant la navigation et le control de la démarche locomotrice. Les profiles de démarche locomotrices anomale ne constituent pas et ne peuvent être distingue des désordres navigationnels dans la diplégie spastique. Cette classification a d’importantes implications pour proposer la rééducation et devrait donc inclure la navigation, pas seulement la démarche.

Exploration du contrôle inhibiteur et de la flexibilité cognitive par le biais d'une tâche locomotrice visuo-spatiale.

Concernant la troisième thématique, nous avons publié un article intitulé « A New Paradigm for the Study of Cognitive Flexibility in Children and Adolescents » (Castilla et al., (2021)) parue dans Frontiers in psychiatry. Une deuxième étude est en cours de rédaction qui est intitulé provisoirement « Contrôle inhibiteur et flexibilité cognitive pour la replanification dans une tâche de mémoire visuo-spatiale. Une étude chez des enfants typiques et des enfants atteints de troubles neurodéveloppementaux » (Castilla et al.,).

Dans la première étude, l'objectif était d'étudier le développement du IC et la CF chez des sujets typiques et atypiques, de l'enfant à l'adulte, à l'aide d'un nouveau protocole de navigation. Nous avons conçu et testé un protocole expérimental nommé « Virtual house locomotor maze (VHLM) » en utilisant la technologie du paradigme du VC. Nous avons analysé des paramètres comportementaux tels que la vitesse tangentielle, les latences, l'orientation tête-poitrine avant et pendant la locomotion. Nous avons également testé les capacités d'inhibition et de CF lors de la planification et de la replanification des trajectoires locomotrices. Nous avons pu identifier des indices comportementaux d'impulsivité et différentes stratégies lors de la performance.

Additionnement, le but de cette étude était de tester le protocole VHLM pour étudier le contrôle inhibiteur ainsi que CF à l'aide d'une tâche visuo-spatial locomotrice. Le VHLM est un labyrinthe simple comprenant six maisons utilisant la technologie du VC. Des enfants au développement typique (TD) ont participé dans cette étude. Les participants devaient atteindre une maison cible le plus rapidement possible respectant les consignes expérimentales. Nous avons examiné leur capacité de planification et de replanification des trajectoires pendant la sélection du chemin le plus court pour atteindre la maison cible. Nous avons également mis en place un indice spatio-temporel basé sur les mesures des comportements cinématiques (c'est-à-dire les trajectoires, la vitesse tangentielle et la direction de la tête).

Le surapprentissage de la trajectoire a été testée en répétant d'abord un chemin choisi par le sujet pour atteindre une maison cible. Après avoir surappris ce chemin, il est bloqué par l'expérimentateur, obligeant le participant d'inhiber la trajectoire surapprise et de planifier une nouvelle trajectoire pour atteindre la même maison cible. Nous avons mesuré la latence du départ après la présentation de chaque maison et la direction initiale de la trajectoire. Les résultats suggèrent que les sujets utilisaient plusieurs stratégies pour la replanification et que nos mesures pourraient servir d'indice d'impulsivité.

Titre : Contrôle inhibiteur et flexibilité cognitive pour la replanification dans une tâche de mémoire visuo-spatiale. Une étude chez des enfants typiques et des enfants atteints de troubles neurodéveloppementaux (Article en préparation)

Concernant la rédaction du nouvel article, nous avons adapté une tâche d'amorçage négatif au VLHM pour évaluer IC et CF dans un GOLT. Au total, 109 participants ont participé à l'étude, y compris des sujets typiques, des sujets ayant des troubles déficitaires de l'attention et hyperactifs, des sujets ayant des troubles du spectre autistique et des sujets ayant des troubles développementaux de la coordination.

L'identification et la sélection des informations pertinentes est un élément clé pour s'adapter à un environnement en évolution rapide. Cette sélection d'informations implique la suppression des informations non pertinentes ou pertinentes. Il est important de rappeler que l'IC est responsable du filtrage des informations appropriées. Nous avons proposé de montrer expérimentalement le processus de l'IC en utilisant le paradigme d'amorçage négatif qui est couramment utilisé en neuropsychologie et en neurosciences cognitives pour tester la suppression d'informations non pertinentes (Borst et al., 2013; Neill et al., 1995; Tipper, 1985).

Nous avons combiné le protocole d'amorçage négatif avec une tâche de navigation en utilisant un nouveau labyrinthe simplifié appelé le VHLM (Castilla et al., 2021a). Une adaptation du protocole d'amorçage négatif a été créée pour évaluer le processus d'inhibition lors de la replanification de la trajectoire chez les enfants, les adolescents et les adultes. Le design expérimental est une tâche comportementale basée sur un paradigme non corrélationnel afin d'étudier le contrôle cognitif lors de la reconfiguration d'une trajectoire alternative.

L'idée principale du paradigme d'amorçage négatif part du principe que le traitement cognitif du même stimulus ayant été précédemment inhibé ou ignoré, sera perturbé. Cette perturbation cognitive entraine des réponses moins précises ou sollicite plus de temps pour traiter les mêmes informations (Borst et al., 2013; Houdé & Guichart, 2001; Tipper, 2001). Le paradigme classique de l'amorçage négatif consiste en l'association entre l'amorçage du stimulus *prime* et *probe*. Le premier stimulus présenté est le *prime* suivi de la présentation du *probe*. Pendant la condition de test-*probe*, le *prime* est un distracteur (par exemple, un stimulus à inhiber) suivi par la présentation de la cible *probe*. Dans le contrôle-*probe*, le *prime* ne partage aucune relation avec le stimulus présenté. L'amorçage négatif est mesuré pour comparer les différences entre les test-*probe* et les contrôle-*probe*. Ainsi, la présentation d'un *prime* (stimulus qui est ignoré ou inhibé) influence la performance lorsque cette information préalable est requise dans la *probe* (Tipper, 1985). Un exemple de l'effet d'amorçage négatif peut être observé lors de la réalisation du test de Stroop classique. Dans le test de Stroop, la tâche consiste à lire la couleur de l'encre et à éviter de lire le nom de la couleur (par exemple, le mot « vert », et le texte de couleur est rouge). L'effet d'amorçage négatif est observé lorsque le nom du mot précédemment inhibé devait être généré en tant que réponse, provoquant un temps de réaction plus lent (par exemple, bleu, le texte de couleur est vert)(Dalrymple-Alford & Budayr, 1966).

Il est important de prendre en considération les résultats mentionnés précédemment et de se rappeler de l'évaluation conventionnelle utilisée en neuropsychologie et en neurosciences cognitives pour davantage explorer le contrôle de l'inhibition qui se limite à l'espace péripersonnel. L'objectif de cet article était d'évaluer le développement de l'IC dans un espace de locomotion en utilisant un paradigme d'amorçage négatif.

À notre connaissance, il s'agit du premier article de recherche expérimentale qui étudie IC dans un espace proche en utilisant une tâche de locomotion orientée vers un objectif (GOLT). Nous avons émis l'hypothèse que nous observerions un effet d'amorçage négatif comparé à la performance dans le VHLM, plus précisément. L'IC sera observé en comparant les performances de la test-*probe* (T3) où la trajectoire devait être inhibée et de la contrôle-*probe* (T6) où un nouveau labyrinthe était présenté et n'ayant aucun lien au labyrinthe d'origine (Voir figure 6). Ainsi, nous avons suggéré que les latences pour le départ seront moins significatives pour T6 comparées à T3 où le surapprentissage était inhibé. De plus, le mouvement de la tête avant le départ sera moins important en T6 qu'en T3.

Nous avons prédit que l'inhibition de la trajectoire en bloquant la trajectoire se traduirait par une latence accrue et une exploration accrue (tête-poitrine-lacet). En effet, nous avions anticipé que la différence tête-poitrine impliquait plus de mouvement en termes d'exploration et de reconfiguration. Les capacités d'inhibition sont étroitement liées au développement cognitif et nous nous attendions donc à ce que le processus d'inhibition cognitive soit modulé en fonction des différents types de groupes d'âge et de pathologies. De plus, nous nous attendions à observer des indices comportementaux concernant les différentes trajectoires développementales du CI et de la CF.

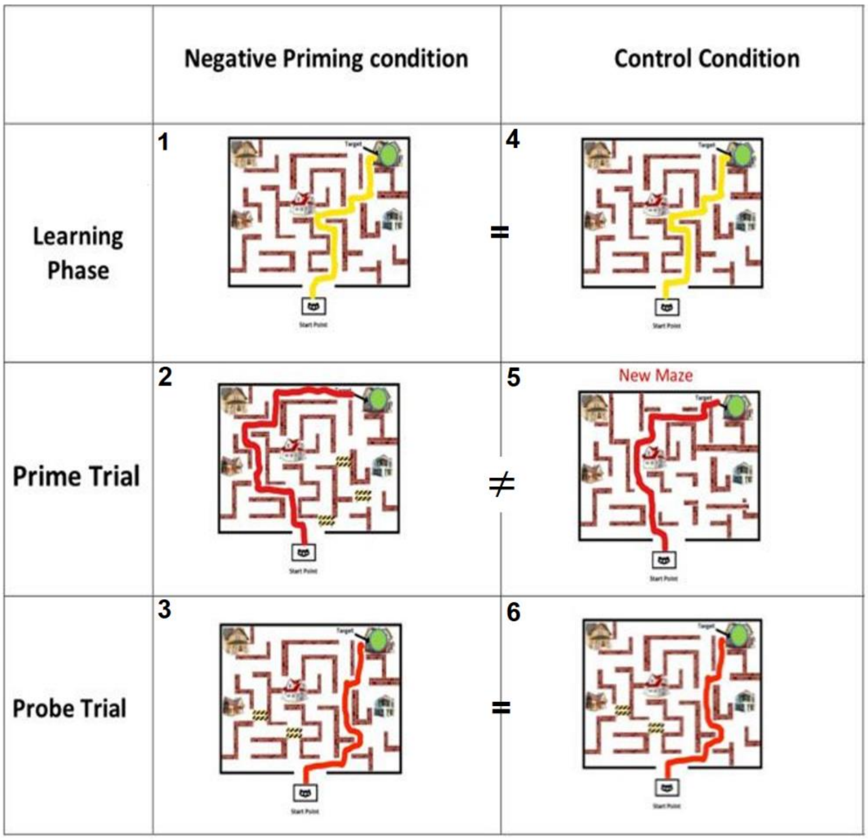


Figure 6. Représentation du plan expérimental. Les lignes jaunes et rouges représentent les trajectoires possibles effectuées par le participant pendant la condition expérimentale et de contrôle. Les numéros correspondent à l'ordre de l'expérimentation.

Discussion

Cette thèse visait à étudier IC, CF et VSWM impliqués dans le développement neurologique typique et atypique. Nous avons principalement exploré les processus cérébraux impliqués dans la capacité à choisir un comportement approprié lors de la résolution de tâches locomotrices visuo-spatiales à l'aide de paradigmes comportementaux. Nous nous sommes concentrés sur trois thématiques a) la mémorisation et les générations de séquences de cibles visuospatiales, b) la planification et l'ajustement des trajectoires face à des changements imprévus lors de l'atteinte d'un objectif, et c) l'inhibition et la replanification de trajectoires apprises précédemment trop perfectionnées.

Dans la première étude sur la mémorisation et les générations de séquences de cibles visuospatiales, nous avons constaté que l'âge et le sexe ont un impact sur le VSWM, les stratégies cognitives et la MR lors de la locomotion. Nous avons démontré que le protocole WalCT est un outil bénéfique pour évaluer les EF, les capacités d'IRM en ligne, la mémoire visuo-spatiale ainsi que la commutation des stratégies de navigation. Nos résultats indiquent que pendant la navigation, des facteurs tels que l'âge et le sexe ont eu un impact sur le VSWM, le MR et les stratégies cognitives. De plus, nous avons proposé une nouvelle façon de catégoriser les performances des participants en navigation spatiale. Cette nouvelle catégorisation porte le nom de SPA qui peut être utilisée comme une méthode complémentaire et être appliquée à la rééducation des déficiences spatiales.

Dans la deuxième étude, nous avons constaté qu'il existait une association entre les EF et les performances du VSWM à la fois dans l'espace proche et dans l'espace de navigation. De plus, nous avons constaté que OA typique présentait moins d'activation dans le cortex préfrontal dorsolatéral que YA lors de l'encodage de VSWM. Ainsi, nous avons constaté que l'activation du cortex préfrontal est liée à la performance dans le WalCT.

Dans la deuxième thématique, nous avons identifié la présence ou l'absence de troubles mineurs et majeurs de la navigation dans la CP bilatérale spastique au moyen de signatures comportementales telles que le contrôle anticipatif dans la navigation locomotrice. Ces signatures comportementales nous ont permis de regrouper les performances en trois groupes caractérisés par le comportement de navigation de chaque participant. Les résultats suggèrent que certains participants atteints de CP ont besoin d'une rééducation des capacités de navigation et indiquent qu'il existe une distinction entre la navigation et le contrôle de la marche. De plus, ce protocole de navigation basé sur la modélisation d’une GOLT nous a permis de présenter une double tâche de contrôle moteur pour détecter cette distinction. Par conséquent, il est important de prendre en considération les implications de cette distinction pour développer de nouvelles méthodes de rééducation qui traitent spécifiquement non seulement de la marche, mais surtout de la navigation.

Dans la dernière thématique, nous avons d'abord conçu et testé un nouveau protocole expérimental nommé le VHLM pour évaluer l'inhibition comportementale et le CF pendant la navigation. Nous avons examiné des paramètres comportementaux tels que la vitesse tangentielle, les latences, la rotation de la tête et de la poitrine. Nous avons identifié plusieurs stratégies distinctes utilisées par les participants lors de la replanification d'une nouvelle trajectoire pour atteindre une cible. De plus, sur la base de ce protocole, nous avons développé une nouvelle étude pour évaluer l'inhibition et la flexibilité mentale lors de la locomotion en utilisant le paradigme de l'amorçage négatif qui est actuellement en cours de rédaction.

En conclusion, l’ensemble de ces résultats indiquent que l'évaluation de la cognition spatiale a contribué à la compréhension du traitement neurocognitif au cours du développement. Nous sommes convaincus que ces protocoles de recherche et nos résultats peuvent fournir de nouveaux outils pour complémenter le diagnostic et aider avec la remédiation des enfants atteints de troubles neurodéveloppementaux, ainsi qu'étudier les processus de vieillissement chez les personnes âgées et leurs pathologies.

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