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Spatial memory profiles in Williams and Down Syndromes

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FACULTÉ DES SCIENCES SOCIALES ET POLITIQUES

INSTITUT DE PSYCHOLOGIE

Spatial memory profiles in Williams and Down Syndromes

THÈSE DE DOCTORAT

présentée à la

Faculté des sciences sociales et politiques
de l'Université de Lausanne

pour l'obtention du grade de

Docteure en Psychologie

par

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« Spatial memory profiles in Williams and Down syndromes »

Marie SANTIAGO DELEFOSSE
Doyenne

Lausanne, le 19 mars 2021

Abstract

Williams syndrome (WS) and Down syndrome (DS, Trisomy 21) are two neurodevelopmental disorders with genetic origins. Despite the fact that individuals with these two syndromes have similar mental ages, they exhibit heterogenous cognitive profiles with different strengths and weaknesses, in particular with respect to their spatial memory capacities. When individuals learn and remember locations in environments in which they must move around, they may use several types of spatial representations, including: (1) the place learning system, responsible for creating allocentric spatial representations or cognitive maps; and (2) the response learning system, responsible for creating fixed egocentric responses. Surprisingly, few previously published studies met the requisite standards in order to determine whether allocentric or egocentric spatial learning capacities were impaired or preserved in WS and DS. In this thesis, I conducted a series of experiments in which individuals with DS or WS were free to move around in the real world and employ either egocentric or allocentric spatial representations in order to learn and remember goal locations. My studies revealed a dissociation between the allocentric and egocentric spatial memory capacities in these two different syndromes. Whereas individuals with WS were severely impaired in two different allocentric memory tasks, they exhibited facilitated performance in an egocentric response learning task, as compared to typically developing children. In contrast, individuals with DS exhibited preserved allocentric spatial capacities as compared to individuals with WS, and also facilitated response learning capacities as compared to typically developing children. My studies emphasized that syndrome-specific spatial cognitive profiles should be taken into consideration when designing interventions aimed at improving spatial navigational abilities in individuals with intellectual disabilities that can lead to greater autonomy, self-confidence and social inclusion.

Résumé

Le syndrome de Williams (SW) et le syndrome de Down (SD, Trisomie 21) sont deux troubles neurodéveloppementaux ayant une origine génétique. Malgré le fait que les personnes avec ces deux syndromes ont des âges mentaux similaires, ils présentent des profils cognitifs hétérogènes avec des forces et des faiblesses, en particulier concernant leurs capacités de mémoire spatiale. Quand des individus apprennent et mémorisent des emplacements en se déplaçant dans un environnement, ils peuvent utiliser plusieurs types de représentations spatiales, incluant : 1) le système d’apprentissage de lieu, responsable de la création de représentations spatiales allocentrées ou cartes cognitives; 2) le système d’apprentissage de réponse, responsable de la création de réponses égocentrées fixes. Etonnamment, peu d’études publiées ont satisfait aux exigences requises pour déterminer si les capacités spatiales allocentrées ou égocentrées étaient préservées ou déficitaires chez les personnes avec SW et SD. Dans cette thèse, j’ai réalisé une série d’expériences dans lesquelles les participants pouvaient se déplacer librement et utiliser des représentations spatiales allocentrées ou égocentrées afin d'apprendre et de mémoriser l'emplacement de buts dans un environnement réel. Mes études ont révélé une dissociation entre les capacités de mémoire spatiale allocentrée et égocentrée chez les personnes avec SW et SD. Alors que les personnes avec SW sont sévèrement déficitaires dans deux tâches différentes testant la mémoire spatiale allocentrée, elles ont démontré une performance facilitée dans une tâche d'apprentissage de réponse égocentrée, par rapport à des enfants au développement typique. En revanche, les personnes avec SD ont montré des capacités de mémoire allocentrée préservées par rapport aux personnes avec SW, et des capacités d'apprentissage de réponse facilitées par rapport à des enfants au développement typique. Mes études soulignent que les profils de capacités cognitives spatiales propres à chaque syndrome doivent être pris en considération pour établir des interventions éducatives ayant pour but l’amélioration des capacités de navigation spatiale chez des individus présentant des handicaps intellectuels qui peuvent mener à une augmentation de l’autonomie, de la confiance en soi et de l’inclusion sociale.

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Summary

Williams syndrome (WS) and Down syndrome (DS, Trisomy 21) are two neurodevelopmental disorders with genetic origins. Despite the fact that individuals with these two syndromes have relatively similar mental ages, they are characterized by different cognitive profiles. For example, individuals with WS have severe visuospatial memory impairments, whereas these capacities are relatively preserved in DS. Researchers initially investigated spatial processing in WS and DS with small-scale visuospatial tasks that were administered using paper-and-pencil tasks, small apparati or more recently computers placed directly in front of the participant. However, results of small-scale visuospatial tasks cannot be used to infer the spatial memory capacities of individuals with WS and DS in large-scale environments. When individuals learn and remember locations in environments in which they must move around, they may use several types of spatial representations, which may differ from those used in small-scale paradigms. Indeed, animals including humans have the ability to use different strategies to identify locations in the environment, including two different spatial memory systems in order to identify locations in large-scale environments: (1) the place learning system, responsible for creating allocentric spatial representations or cognitive maps; and (2) the response learning system, responsible for creating fixed egocentric responses. In this context, several studies using large-scale environments attempted to evaluate the capacity of individuals with WS and DS to use egocentric and allocentric memory. However, few of these studies met the requirements to conclude whether allocentric or egocentric spatial learning capacities were impaired or preserved in WS and DS. Therefore, there was a need to examine the different spatial learning and memory capacities of individuals with WS and DS in laboratory conditions in which the cues available to the participants and the types of spatial representations necessary to solve a given task were strictly controlled. For my doctoral work, I conducted a series of experiments in which participants must move around in the real world in order to better characterize allocentric and egocentric learning and memory capacities of individuals with WS and DS.

The first aim of my doctoral work was to assess the capacity of individuals with WS, DS and typically developing children to create and use allocentric and egocentric spatial representations in a real-world, controlled laboratory environment. For this aim,

I tested the capacity of participants to remember one location among four potentially rewarded locations distributed in a 4 m x 4 m open-field arena. In the allocentric place learning condition, participants had to learn and remember the reward location in relation to distal objects in the environment. In the egocentric response learning condition, participants had to learn that they could find the reward by performing a fixed motor response. I found that 95% of typically developing children and 78% of participants with DS could solve the place learning task, thus showing basic allocentric capacities. In contrast, only 17% of participants with WS were capable of using a low-resolution allocentric spatial representation to learn and remember the location of one reward amongst four possible locations in the presence of visual information. For the egocentric task, 72% of participants with WS, 56% of participants with DS and only 16% of typically developing children could use a response learning strategy to learn and remember the location of one reward. These results provided answers to several questions raised by methodological issues inherent to previous studies. Moreover, my results lead to the elaboration of hypotheses regarding spatial learning strategies that may be used by individuals with WS and DS to successfully navigate in the real world, outside controlled laboratory conditions.

The second aim of my doctoral work was to characterize the capacity of individuals with WS, DS and typically developing children to use path integration to build egocentric and allocentric spatial representations. First, blindfolded participants were tested on their ability to return to a starting point after being led on straight and two-legged paths. Performance on this egocentric homing task informed us about the capacity of participants to walk straight and return to their starting point when blindfolded. Second, I evaluated the capacity of individuals with WS and DS to build an allocentric spatial representation without vision, in order to navigate between four objects placed in a large room. After an initial learning phase, participants were asked to walk directly to specific objects using novel paths (shortcuts), a hallmark of the capacity to create a cognitive map of the environment. In the homing task, I found that 96% of typically developing children, 84% of individuals with DS and 44% of individuals with WS could return to the starting point of the outbound journey consistently. In the cognitive mapping task, 64% of typically developing children and 74% of individuals with DS were able to take shortcuts and use never-traveled trajectories. In contrast, only one of eighteen individuals with WS demonstrated the ability to build a cognitive map, without vision, using vestibular and proprioceptive information. My findings rule out the possibility that the spatial impairments of individuals with WS arise from the integration of a corrupted signal from the dorsal visual stream. Instead, these results indicate that allocentric spatial memory capacities are impaired in the vast majority of individuals with WS, irrespective of the type of available sensory information.

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1. GENERAL INTRODUCTION

1.1. Why investigate spatial memory ?

Where did I park my car today? Where did I put my keys when I went back home yesterday? Where is the cinema in my home town? How can I get back to my hotel? Spatial memory is part of our everyday life and we depend on it for many daily life activities. One important reason for studying spatial memory is because some types of spatial memory, such as allocentric and egocentric memory, can be considered as a type of declarative or explicit memory. Declarative memory can be defined as the conscious recollection of facts and events, such as the memory for words, scenes, faces or stories (Squire, 1987; Squire & Zola-Morgan, 1991) and is comprised of semantic memory and episodic memory. Semantic memory refers to the capacity to recollect facts and general knowledge about the world (e.g., the capital of Switzerland), whereas episodic memory is the capacity to store and remember autobiographical events (e.g., last holidays in Switzerland) (Squire & Zola-Morgan, 1998; Tulving, 2002). Allocentric spatial memory, the memory for locations coded in relation to the surrounding environment, is a fundamental component of episodic memory, the ‘‘where’’ component of the defining ‘‘what, where and when’’ of episodic memories (Nyberg et al., 1996; Tulving, 2002). To better understand the functioning of episodic memory, researchers can study each component individually since it seems logical that if the “where” component of episodic memory is impaired in a certain population, episodic memory might not function very well. Consequently, studying allocentric memory can also provide insights on declarative memory functions in specific populations such as in individuals with neurodevelopment disorders.

Another reason for studying spatial memory is because behavioral results showing a preservation or an impairment in allocentric memory in a group of patients can be used to infer the function of underlying brain structures. Indeed, like episodic memory, allocentric spatial memory is dependent on the integrity and function of the hippocampus in adult individuals (Banta Lavenex et al., 2006; Morris et al., 1982; O'Keefe & Nadel, 1978; Olton et al., 1978). Moreover, experiments carried out in rodents and primates have identified the brain structures supporting allocentric spatial memory processes (Banta Lavenex et al., 2006; Morris, 1984; Packard & White, 1991). Therefore, it is important that humans are tested with paradigms that emulate as closely as possible those used in animals, in order to assess human spatial memory processes and infer the functional integrity of underlying brain structures. For this aim, fundamental features of the tasks used in this thesis work were designed to replicate the features of original tasks developed for use in rodents and primates (Banta Lavenex et al., 2006; Packard & McGaugh, 1996).

Investigations of spatial memory are ideal since they can assess a range of populations that have no access to language or have language impairments, such as in some neurodevelopmental disorders. Indeed, the capacity to consciously learn and remember facts and events, such as the memory for words, scenes, faces or stories, can be assessed in typically developed adults by asking what they recall about a certain event or episode. However, it is not necessarily possible to ask very young children and individuals with intellectual disabilities what they remember about the past. Thus, to study declarative memory, researchers may ask participants whether they remember "where" something was located, which does not require any verbal report.

Finally, deficits in spatial memory can have a strong impact on daily life, and individuals with intellectual disabilities frequently depend on family members or caregivers for their displacements (e.g. going to and from work, grocery shopping, and social gatherings). Consequently, individuals with intellectual disabilities are often excluded from social life and suffer from a lack of individual autonomy. Therefore, characterizing the spatial memory profile of individuals with intellectual disabilities can not only help identify which memory processes are impaired, but more importantly can help to identify preserved spatial memory capacities. Focusing on individuals' strengths can encourage their independence and provide critical navigational skills, giving them control of their own displacements, developing their self-efficacy and raising their self-esteem.

1.2. Williams and Down syndromes

Williams syndrome (WS) is a genetic syndrome caused by a deletion of approximately 28 genes on the long arm of chromosome 7 (Beuren, 1972; Ewart et al., 1993; Fanconi et al., 1952; Korenberg et al., 1997; Williams et al., 1961). Prevalence of the syndrome is estimated at 1 in 23,500 live births (Yau et al., 2004), although a Norwegian study reported a prevalence of 1 in 7,500 (Stromme et al., 2002). The physical phenotype of WS includes a facial dimorphism typically described as an “elfinlike”, cardiovascular dysfunctions, endocrine perturbation such as hypercalcemia and impaired glucose tolerance, gastrointestinal and orthopedic problems (Morris & Lenhoff, 2006). The genetic deletion also affects the brain and results in neurological problems including coordination difficulties, hyperreflexia, strabismus and nystagmus (Chapman et al., 1996), as well as cognitive impairments (Mervis et al., 2000). Their unusual personality is also striking and individuals with WS are described as highly sociable, overfriendly, and empathic (Doyle et al., 2004; Jones et al., 2000). Individuals with WS exhibit mild to severe intellectual disability, with intellectual quotients ranging from 40 to 70 and a typical mental age from 5.6 to 8 years of age (Vicari et al., 2005, 2006; Vicari et al., 2007).

Down syndrome (DS) is a genetic syndrome resulting from the presence of a partial or complete triplication (trisomy) of chromosome 21. DS is the most common genetic cause of intellectual disability with an incidence of 1 in 625-1,000 live births (Bittles et al., 2007; de Graaf et al., 2017; Down, 1866; Lejeune et al., 1959). The physical phenotype of DS includes facial dimorphism, physical problems including congenital heart disease, musculoskeletal anomalies, and brain anomalies resulting in cognitive impairments (Chapman & Hesketh, 2000; Desai, 1997; Lott, 2012). People with DS show mild to severe intellectual disability, with intellectual quotients ranging from 25 to 70 and a mental age from 5 to 9 years of age (Carretti et al., 2013; Vicari et al., 2005, 2006).

Historically, people with neurodevelopmental disorders were often described as having global learning disabilities (Beuren, 1972; Burn, 1986; Connolly et al., 1980; Kataria et al., 1984; Langdon & Down, 1995; Williams et al., 1961). Nevertheless, since the early nineties researchers have shown that different genetic syndromes are heterogeneous in nature and characterized by different profiles of cognitive impairments (Atkinson et al., 1997; Bellugi et al., 1990; Bellugi et al., 1999; Bellugi et al., 1994; Udwin et al., 1987). Thus, although individuals with WS and DS have similar mental ages, they exhibit specific cognitive profiles that have been revealed by a number of studies specifically comparing and contrasting the deficits that accompany these two syndromes (Jarrold et al., 1999; Porter & Coltheart, 2006; Vicari, 2001; Vicari et al., 2005; Wang & Bellugi, 1993). Indeed, it has been shown that some capacities considered to be relatively well-preserved or a strength for individuals with one syndrome are often more impacted and considered to be a weakness for individuals with the other syndrome. For example, individuals with WS show good narrative abilities (Vicari et al., 2004) and facility in using sentences with complex syntax, above what would be predicted by their intellectual quotient scores (Bellugi et al., 2000). They also perform similar to typically developing children and better than individuals with DS in tests evaluating word comprehension and verbal fluency in which subjects are asked to name as many animals as they can in 60 seconds (Bellugi et al., 2000; Bellugi et al., 1994; Volterra et al., 1996). The relatively preserved verbal capacities of individuals with WS contrast with their impaired spatial abilities. Individuals with WS are impaired compared to mental age-matched typically developing children in visuospatial tasks, such as the Benton Line Orientation Test or in visuo-constructive tasks in which subjects are required to copy series of figure such as lines, triangles and combination of forms, or to rearrange blocks that have various color patterns to match a model pattern (Bellugi et al., 1990; Bellugi et al., 1994). Interestingly, individuals with DS show an opposite cognitive profile. They usually perform according to their mental age in visuospatial tasks, such as in drawing and copying geometric shapes, but have impaired linguistic capacities compared to mental age-matched typically developing children and individuals with WS (Bellugi et al., 1990; Chapman, 1997; Jarrold et al., 2008; Laws, 2002; Ricketts, 2011; Wang & Bellugi, 1993). In addition, studies comparing short-term memory of individuals with WS and DS in verbal and spatial memory tasks (Jarrold et al., 1999; Wang & Bellugi, 1993) have shown that WS participants outperform individuals with DS in verbal working memory tasks (e.g., digit span), whereas the opposite pattern is observed for spatial working memory tasks (e.g., Corsi task). As such, the cognitive profiles of WS and DS have been described by some as being the mirror images of each other (Pezzini et al., 1999).

Another difference between the cognitive abilities of DS and WS is that global processing and local processing of spatial information are differentially impaired in WS and DS (Bellugi et al., 1999; Bihrle et al., 1989; Porter & Coltheart, 2006; Rondan et al., 2008). For example, as illustrated in Figure 1A, a house drawn by individuals with WS typically exhibits poor global organization and disconnected details (e.g., windows and doors outside the house), whereas a house drawn by individuals with DS tends to be more correct globally, but with inaccuracies in what are considered local internal details (e.g., more windows and doors than on the model) (Bellugi et al., 1999; Bihrle et al., 1989). When assembling cubes in a block construction task (Fig. 1B), whereas individuals with WS exhibit an incorrect global organization but select the correct internal details, DS subjects place the internal details in wrong positions while succeeding in reproducing the overall global configuration. Finally, the global vs. local processing differences between individuals with WS and DS are best demonstrated by the drawing of the letter “D” which is composed of many small “Y” letters (Navon, 2003). Whereas individuals with WS “see” the “Ys” but “ignore” the “D”, a classic example of a local processing bias, individuals with DS “see” the “D” but “ignore” the “Ys”, a classic example of a global processing bias (Fig. 1C). Based on these results, it was suggested that there is an abnormal bias toward global processing in DS and, in contrast, an abnormal bias toward local processing in WS (Bellugi et al., 1999; Bihrle et al., 1989; Porter & Coltheart, 2006). It is worth noting that D'souza et al. (2016) present contradictory evidence suggesting that individuals with WS and DS do not systematically show global or local processing deficits, respectively. For example, individuals with WS might preferentially process local information when drawing or in visuo-constructive tasks, but not in tasks administrated on computer screens such as in the informatized version of the Navon task (Navon, 2003).

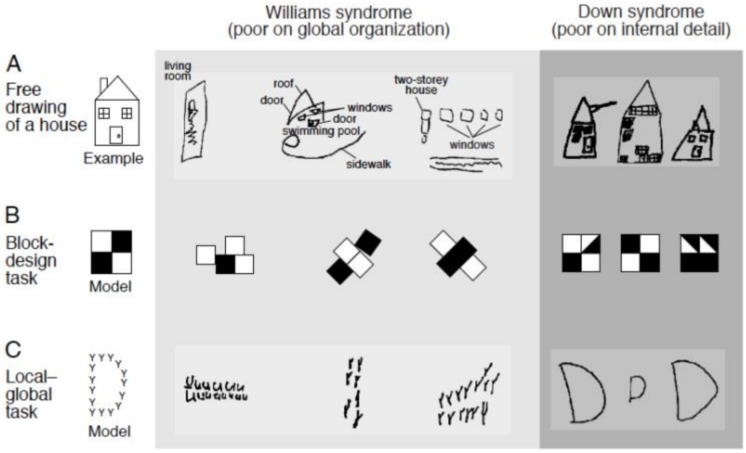

Figure 1. Productions of individuals with WS and individuals with DS (Bellugi et al., 1999)

Individuals with WS and DS also exhibit differential impairments in their capacity to encode and retrieve spatial characteristics of visual stimuli (visuospatial memory) and their capacity to encode and retrieve physical characteristics of visual stimuli such as objects or faces (visual-object memory). Persons with DS exhibit better performance in visuospatial tests, whereas individuals with WS exhibit better performance in visual-object tasks (Atkinson et al., 2003; Atkinson et al., 1997; Bellugi et al., 1999). For example, Vicari et al. (2005) investigated the capacity of individuals with DS and WS to learn visuospatial and visual-object stimuli. In the visuospatial learning task, subjects had to remember the location, on a piece of paper, of a series of images, with one image per page (Fig. 2A). In the visual-object learning task, subjects had to remember images of common objects, such as trees or flowers (Fig. 2B). Individuals with WS exhibited greater difficulty in the visuospatial task. They made more mistakes in recalling where they saw the objects compared to mental age-matched typically developing children, and their performance did not improve from the first to the third trial, demonstrating that they did not learn the position of the stimuli. In contrast, in the visual-object task they were able to recall which specific objects were seen, and their performance was similar to that of typically developing children. Participants with DS exhibited an opposite pattern of performance. In the visuospatial task, individuals with DS were able to recall where objects had been presented as well as mental age-matched typically developing children, whereas they were impaired in the visual-object task compared to both typically developing children and individuals with WS. They made more mistakes at recalling which items had been presented and their performance did not improve over repeated trials. Figure 2C further illustrates the fact that participants with WS and DS did not have the same capacity to learn different types of stimuli over repeated trials, as shown by the differential increase in the number of items recalled between the first and the third trial. Individuals with WS had a higher learning rate in the visual-object learning task compared to participants with DS, whereas the opposite pattern was observed for the visuospatial learning task (Vicari et al., 2005).

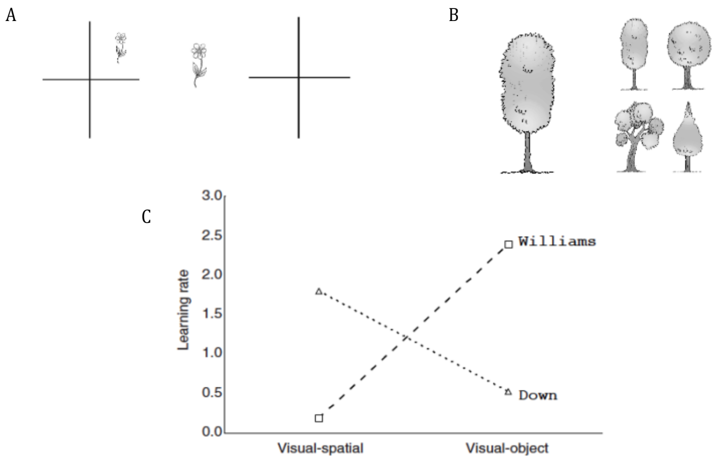

Figure 2. Illustrations of the visual-object and visuospatial tasks and results of Vicari et al. (2005). A. Visuospatial task: participants studied individually 15 objects that were placed in one of four quadrants for 5 seconds (left). Immediately after the study phase, the target stimuli were presented individually and the participants were asked to indicate the position previously occupied by each stimulus on an empty page subdivided into four quadrants (right). B. Visual-object task: participants studied individually 15 objects (e.g., a tree, a knife) for 5 seconds (left). Immediately after the study phase, four similar objects were presented and participants had to designate which specific objects were presented previously (right). C. Learning rates represent the difference in performance between the third and the first trial of individuals with WS and DS in the two memory tasks.

To conclude, most researchers agree that spatial processing is impaired in WS. But, for the most part, these assessments of spatial capacities have employed small-scale visuospatial tasks that were administered using paper-and-pencil (e.g., line dissection task; (Schenkenberg et al., 1980)), small apparati (e.g., the Corsi block tapping task; (Corsi, 1972)) or more recently on computers (Vicari et al., 2003) placed on a desktop in front of the individual. However, the capacity to encode and retrieve spatial characteristics of visual stimuli (i.e., visuospatial memory) assessed with small-scale tasks is just one component in the broader domain of spatial memory. Indeed, being able to remember locations in a large-scale environment, in which participants must move around, is fundamentally different from being able to recall where, on a piece of paper, an item was previously seen, or being able to reproduce a sequence tapped during a Corsi block test (Banta Lavenex & Lavenex, 2009). Moreover, performance on small-scale spatial tasks does not necessarily correlate with or predict performance on large-scale spatial tasks (Farran et al., 2010; Hegarty et al., 2006; Quaiser-Pohl et al., 2004). Finally, when individuals learn and remember locations in large-scale environments in which participants must move around, they may use several types of memory representations which may differ from those used in small-scale environments. Therefore, although classical visuospatial tasks are indeed spatial in the sense that participants must localize targets, they cannot be used to infer the spatial memory capacities of individuals with WS and DS in large-scale environments.

1.3. Different types of spatial memory

To remember the locations of objects in the environment, individuals can rely on two principal spatial memory representations (Banta Lavenex & Lavenex, 2009; O'Keefe & Nadel, 1978; Tolman, 1948). Participants can remember these locations in relation to their own point of view, such as “the item is on my right”, in a viewpoint-dependent manner. This type of spatial representation is called egocentric (Fig. 3). In contrast, participants can also remember these locations in relation to other objects or locations in the environment, in a viewpoint independent manner. This type of spatial representation is called allocentric (Banta Lavenex et al., 2006; Konkel & Cohen, 2009; O'Keefe & Nadel, 1978) (Fig. 3). Thus, for example, a speaker’s lectern is both in front of the audience and between the projection screen and the door, and it maintains these same relations independently of where an observer is standing in the lecture hall. Moreover, studies investigating brain lesions provide further evidence that egocentric and allocentric spatial representations are distinct processes. Indeed, allocentric memory is dependent on the integrity and function of the hippocampus in adult rodents and primates, including humans (Banta Lavenex et al., 2006; Morris et al., 1982; O'Keefe & Nadel, 1978; Olton et al., 1978), whereas egocentric memory is subserved by parahippocampal, striatal and parietal brain structures (Burgess et al., 2002; Morris et al., 1990; Weniger et al., 2009; Weniger et al., 2010).

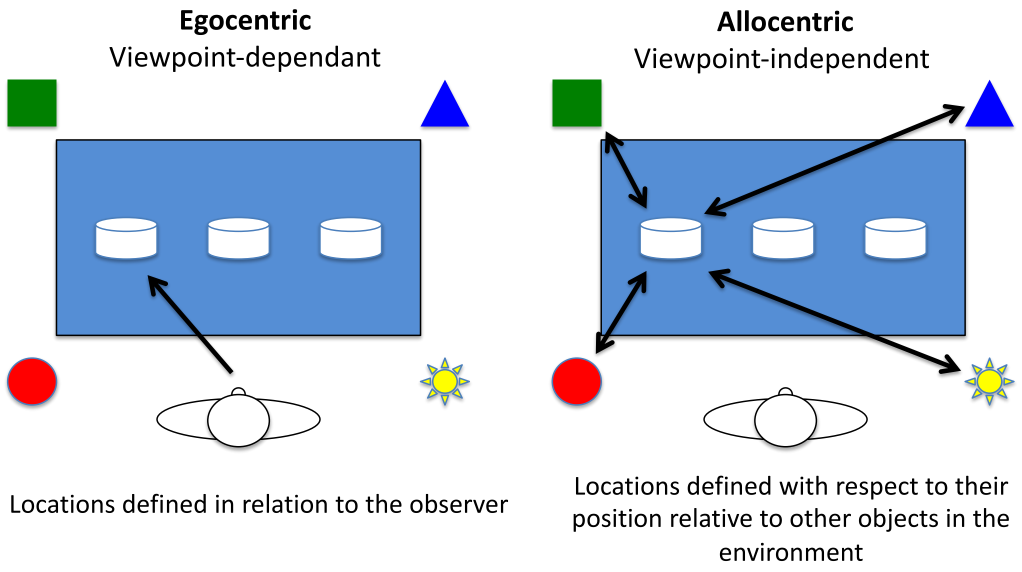

Figure 3. Spatial representations that may be used to remember the location of a target amongst an array of similar objects.

Small-scale spatial tasks are thus generally less well-suited to assess allocentric spatial memory. Indeed, in a small-scale apparatus in which individuals remain static, participants may encode the location of the target in an egocentric, viewpoint-dependent spatial representation as well as in an allocentric viewpoint-independent spatial representation. Over short delays, visuospatial tasks administered directly in front of stationary participants likely implicate egocentric processes preferentially (Banta Lavenex & Lavenex, 2009; Eichenbaum et al., 1990). In contrast, when individuals move around and change position in the environment, they cannot recall the location of the target using the same egocentric point of view. In consequence highly controlled large-scale spatial tasks, in which egocentric strategies are precluded by having participants solve the task from multiple locations, are best suited to assess allocentric spatial memory capacities and can serve as a specific assay for hippocampus-dependent memory function.

In experiments assessing large-scale spatial memory capacities, researchers can ask participants to search, find and remember the location of items (e.g. toys, pieces of food) in indoor rooms; to find and remember specific location(s) in outdoor cities; to find and remember their way in mazes, buildings or cities; to collect several rewards in mazes or arranged in different geometric configurations in open spaces, etc. (Farran et al., 2010; Morris, 1984; Nardini et al., 2008; Ribordy Lambert et al., 2013; Smith et al., 2009). Depending on the experimental paradigm and procedure, individuals can use egocentric or allocentric spatial strategies to solve these tasks. For example, as illustrated in Figure 4, a route to a destination can be encoded as a sequence of egocentric turns (e.g., “I go straight, then right, then left”) (Bohbot et al., 2004; Farran et al., 2015; Packard et al., 1989; Packard & McGaugh, 1996; Yin & Knowlton, 2006).

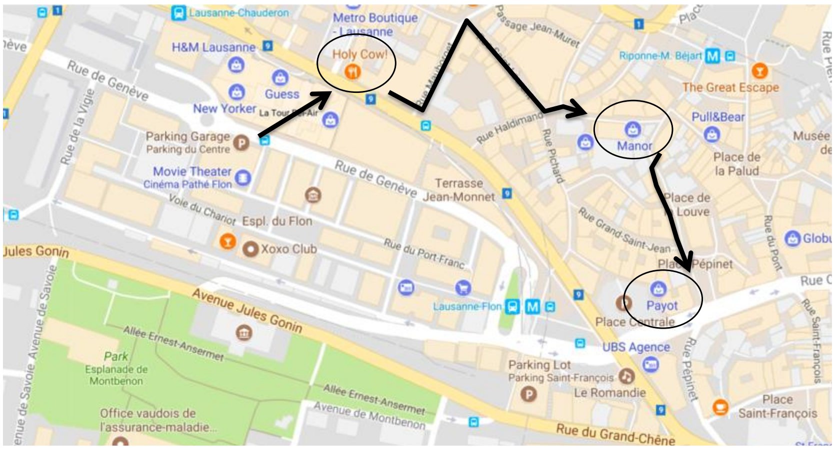

Figure 4. To remember a route in the city of Lausanne, individuals can use egocentric representations. Thus, to remember the itinerary that goes from the parking du Centre to the Payot bookstore, passing by the Holly Cow restaurant and Manor, individuals can remember a sequence of left and right turns.

In laboratory conditions, the cross maze is often used to assess the preference of rodents to use either egocentric or allocentric strategies to learn and remember the location of a reward (Packard, 1999; Tolman et al., 1946; Yin & Knowlton, 2006) (Fig. 5). During a first learning phase, animals are placed in the same starting position and trained several times to find a piece of food always placed at the same location, and in this case corresponds to the animal making a right turn at the center of the maze (Fig. 5A). After animals have experienced 16 trials in this condition, they are placed in the opposite arm (Fig. 5B). Interestingly, under these specific conditions most animals respond by turning right to find the reward (“Response”), just as they have done during the training phase (Packard & McGaugh, 1996). Thus, animals rely on a motor response i.e., they use a turning response at the choice-point without regard to the spatial location of the goal (Bohbot et al., 2004; Packard et al., 1989; Packard & McGaugh, 1996; Yin & Knowlton, 2006). In these conditions, response learning can be defined as a type of egocentric responding (Packard et al., 1989; Packard & McGaugh, 1996).

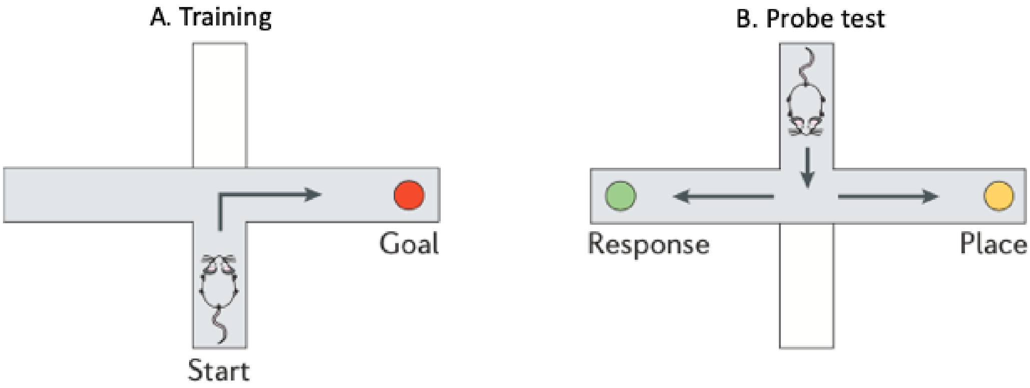

Figure 5. Cross maze paradigm (Yin & Knowlton, 2006). A. Training phase: The animal is placed in the same starting position. The animal is trained several times to find a piece of food placed at the same goal location. B. Probe trial: The rat is placed at the opposite starting arm of the maze and has to find the reward. If the animal turns right, it demonstrates an egocentric response learning strategy to remember to location of the reward. If the animal turns left, it demonstrates an allocentric place learning strategy to remember the location of the reward.

Another way to find a location in a large-scale environment is to define the location in relation to other locations in the environment, in an allocentric spatial representation, a.k.a. a cognitive map (Banta Lavenex et al., 2014; O'Keefe & Nadel, 1978; Tolman, 1948) (Fig. 6). The strategy allows the navigator to arrive at the desired destination using a novel, never-before experienced path (Foo et al., 2005; Landau et al., 1984; Morrongiello et al., 1995; Tolman, 1948).

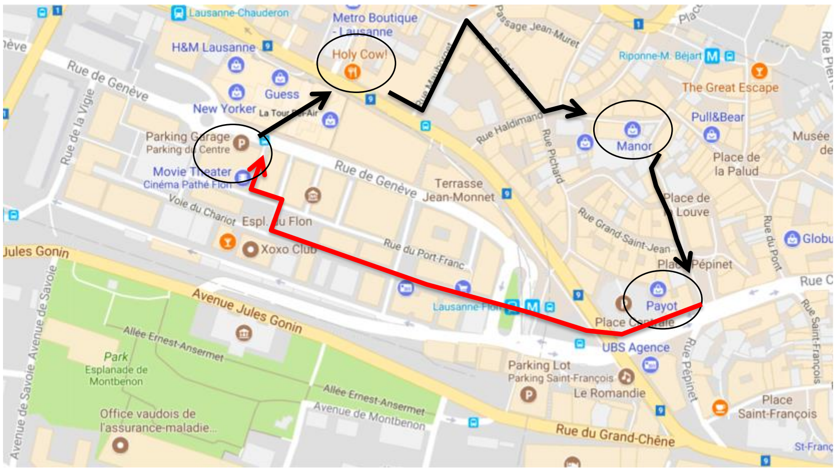

Figure 6. An individual can use an allocentric representation to remember a specific location in the city of Lausanne. Thus, the individual may find the Payot bookstore following the itinerary marked in black on the map from the Parking du Centre, passing by the Holly Cow restaurant and Manor. To go back to his/her car at the parking du Centre, he/she does not need to take the same route in reverse order. Instead, he/she can take a shortcut directly from Payot to the parking garage even though he/she has never taken this path before.

As mentioned above, the cross-maze apparatus can also be used to assess allocentric memory in rodents (Fig. 5). Indeed, when animals are given only a very few trials from one arm before being placed in the opposite arm, most animals will look for the food in the absolute spatial location (Fig. 5B; "Place"). This allocentric strategy is also defined as a place learning strategy (Packard & McGaugh, 1996; Poldrack & Packard, 2003).

Finally, it is worth mentioning another strategy, a non-spatial strategy, that can be used to remember a location in large-scale environments known as a beacon or visual cue guidance strategy. Although visual cues are critical to creating an allocentric representation of the environment in most instances, it is important to distinguish between (1) distal visual cues that are used in a relational manner to construct an allocentric representation of the environment including the location of the individual and the goal location relative to other objects in the environment, and (2) local and distal visual cues that can be used in a simple associative manner to define a goal location henceforth referred to as a beacon or visual guidance strategy. For example, if a goal location can be visually associated with a single object, such as ‘‘the location closest to the desk’’ or ‘‘when viewed from the doorway, it is the location visually aligned with the window’’, then memory for the spatial location itself is no longer necessary in order to localize the target.

To conclude, different spatial representations may be used to learn and remember locations in large-scale environments. Animals, including humans, rely primarily on two different spatial memory systems in order to identify locations in large scale-environments in which they must move around: (1) the place learning system, responsible for creating allocentric spatial representations or cognitive maps and (2) the response learning system, responsible for creating fixed egocentric motor sequences (Bohbot et al., 2004; Iaria et al., 2003; Packard & McGaugh, 1996; Poldrack & Packard, 2003). In that context, several studies using virtual and real-word environments attempted to evaluate the capacity of individuals with WS and DS to use these two different spatial memory systems to learn and remember the location of objects in their environment. Assessing these memory systems are important in order to understand the reasons why individuals with neurodevelopment disorders may have difficulties in navigating in the real world and attaining autonomy. Therefore, the elaboration of clear hypotheses regarding learning strategies that can be used to help individuals with intellectual disabilities orient and navigate successfully, and may help to reduce their dependence on caregivers, as well as improve their self-confidence and social inclusion.

1.4. Large-scale spatial capacities in WS and DS

1.4.1. Virtual reality studies

In order to more closely approximate navigation in the real world, experiments conducted in virtual environments using 3D technology have increased in popularity (King et al., 2002). Such experiments aim to imitate real-world tasks such as the Morris water maze, the radial arm maze or labyrinth tasks that are often used with animals but are not very practical for use with humans (Astur et al., 1998; Astur et al., 2004). Numerous studies have thus investigated the large-scale spatial capacities of individuals with WS or DS in virtual reality environments.

Williams syndrome. Broadbent et al. (2014) tested the capacity of participants with WS and typically developing children with similar mental ages to learn an itinerary in a virtual maze surrounded by landmarks (Fig. 7). Individuals with WS were able to learn a specific route in the maze comprising 4 directional changes although they needed more trials to learn the routes than typically developing children. The authors also reported that individuals with WS used a so-called “mixed strategy” to orient in the maze. At the beginning of the learned route they relied on an egocentric strategy, and then later followed visual landmarks to find the exit using a cue guidance strategy. In contrast, typically developing participants primarily used an egocentric strategy to find the exit of the maze. This suggests that the capacity of individuals with WS to orient in virtual reality is atypical. In a second condition, when participants were forced to use an allocentric strategy to find the exit of the maze, 20% of participants with WS chose the correct exit. Their performance was comparable to that of 5-6 year old typically developing participants (Broadbent et al., 2014).

In another study, Farran et al. (2015) tested the ability of individuals with WS and typically developing children to learn two routes in a virtual city containing several landmarks along the paths (Fig. 7). They found that 65% of individuals with WS could learn at least one of two different routes. However, when participants were asked to take a shortcut in the environment to test their allocentric capacities, whereas 59% of typically developing children were able to find the shortest route between two locations in the environment, only about 35% of participants with WS could (Farran et al., 2015).

Other studies provided further evidence that individuals with WS are able to learn an egocentric sequence of left and right turns and to learn landmarks along the paths, even though they sometimes need more trials compared to typically developing children (Broadbent et al., 2015; Farran et al., 2012; Farran et al., 2016; Purser et al., 2015). Overall, these results suggest that individuals with WS are capable of using egocentric strategies to navigate in virtual large-scale environments even though their performance is not always comparable to that of individuals with similar mental ages. In contrast, individuals with WS were reported to be impaired when using allocentric spatial strategies. However, it should be noted that in both studies assessing allocentric memory (Broadbent et al., 2014; Farran et al., 2015), an important percentage of typically developing children of the same mental age were not able to successfully use allocentric strategies. For example, in the study by Farran et al. (2015), typically developing children also had serious difficulties solving the virtual reality task, since only 59% children could take the shortcut. These results question the validity of these paradigms to evaluate allocentric capacities in individuals with these mental ages, including individuals with neurodevelopmental disorders.

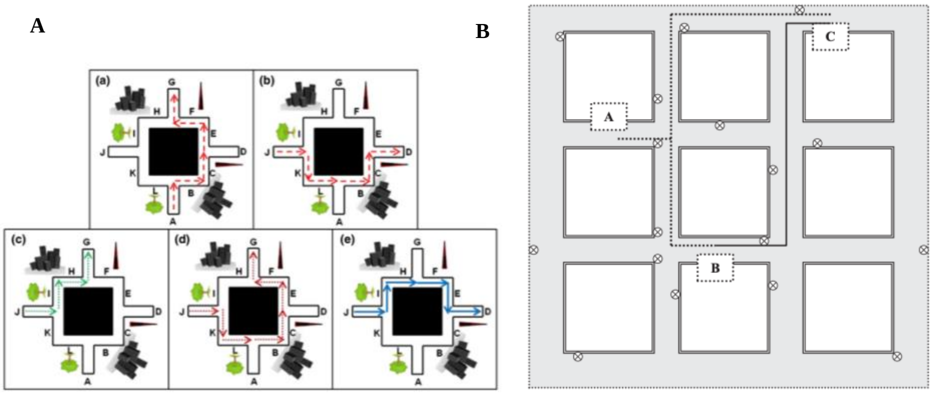

Figure 7. A. Schematic layout of cross-maze used in Broadbent et al. (2014): (a) learning phase, (b) route taken following an egocentric strategy, (c) route taken following an allocentric strategy (d) route taken following a "mixed" strategy, (e) route taken following a "mirrored egocentric" strategy. B. Schematic of the maze used in Courbois et al. (2013). Participants were asked to take a shortcut between the two end points B and C.

Down syndrome. Three studies attempted to assess allocentric spatial capacities of individuals with DS using virtual reality environments. Pennington et al. (2003) investigated the performance of adolescents with DS on a virtual version of the Morris water maze. In this task, subjects had to learn the position of a target in a virtual room containing distal visual cues such as a door and picture frames. Each participant completed four visible-target practice trials, after which the target became invisible and the participants were instructed to move around the arena until the target was found. Individuals with DS performed less well than typically developing children: they spent less time searching in the correct quadrant of the room than the typically developing children. Indeed, typically developing children spent 30% of their time searching in the correct quadrant that normally contained the target and individuals with DS spent 17% of their time searching in the correct quadrant. However, in a second series of experiments, Edgin et al. (2010) did not find differences between individuals with DS and typically developing children; both groups did not show any preference for the correct quadrant that normally contained the target. Actually, they both spent about 25% of their time searching in the quadrant, a percentage that would be expected by chance. These results suggest that both groups may have failed to create an allocentric representation to solve the task. Moreover, the lack of consistent results between Edgin et al. (2010) and Pennington et al. (2003) raises questions about the usefulness or reliability of this task to characterize the spatial cognitive profile of individuals with DS. In another study, Courbois et al. (2013) investigated the route-learning capacity of individuals with DS and typically developing children in a virtual town containing three target buildings and a number of visual landmarks (Fig. 7B). Seven out of 10 participants with DS were able to learn an itinerary suggesting that they could use egocentric strategies, although individuals with DS learned fewer landmarks located along the routes and made more wrong choices compared to mental age-matched typically developing children. However, only 2 out of 7 participants with DS and 5 out of 9 typically developing children were able to take a previously untraveled shortcut between two locations in the same environment. Using a similar paradigm and procedure, Farran et al. (2015) found that only 10% of participants with DS could successfully find a shortcut in the virtual environment. The inability to take shortcuts was interpreted by the authors as an inability to create allocentric representations in DS (Courbois et al., 2013; Farran et al., 2015). In sum, as for individuals with WS, individuals with DS are able to learn a sequence of left and right turns to find a location in a virtual environment, thus suggesting preserved egocentric memory. In contrast, their allocentric memory was reported to be severely impaired. However, because in the studies by Farran et al. (2015) and Courbois et al. (2013) participants were given ten trials of unguided exploration to find the shortcut, it is not clear whether the individuals who succeeded had built an allocentric representation of the environment during initial learning or whether they had learned the new path over several unguided test trials.

Another limitation common to all virtual reality studies is that participants remain static in front of a computer screen while they perform the spatial tasks with a joystick. Therefore, although spatial experiments conducted in virtual reality have been designed to approximate real-world tasks more closely than standard tabletop neuropsychological tests (Astur et al., 2002; Hamilton et al., 2003; Massetti et al., 2018; Standen & Brown, 2005), their ethological validity has been questioned (Banta Lavenex & Lavenex, 2009; Taube et al., 2013). A first consideration is that, when navigating in the real world, individuals have access to nearly a 180° visual field, whereas computer screens are normally 41 cm wide and placed directly in front of the subject at a distance of about 61 cm, yielding a field of view of approximately 37° (Tan et al., 2006). Second, when memorizing objects and locations in large-scale environments in which individuals must move around, they have access to vestibular and proprioceptive information that is not available when navigating in a virtual environment. Importantly, the construction of spatial representations, including especially allocentric representations, is associated with the movement of an individual through its environment and requires input from all of the sensory modalities, not only vision (Etienne & Jeffery, 2004). Accordingly, removing vestibular and proprioceptive information decreases spatial memory performance in humans (Ruddle & Lessels, 2006). Similarly, the response properties of hippocampal place cells (neurons in the hippocampal formation that encode spatial locations in an allocentric frame of reference) are less specific when vestibular and proprioceptive information is removed and only visual information is available (Matsumura et al., 1999; Ravassard et al., 2013). Finally, in virtual reality studies, different inputs derived from different sensory modalities are inconsistent with each other. For example, in the case of a person sitting in front of a computer screen, vestibular, proprioceptive and tactile information are all coherently coding the absence of movement, whereas visual information is used to make the person believe that s/he is actively moving while exploring the virtual environment, provoking a mismatch between different modalities. To conclude, whereas findings that demonstrate allocentric spatial competence of individuals with WS and DS in virtual environments may be convincing, impaired performance in virtual environments cannot be considered as unequivocal evidence for the impairment of real-world allocentric spatial capacities in individuals with neurodevelopmental disorders.

1.4.2. Real-world studies

A number of studies have used a variety of real-world paradigms designed to assess the spatial capacities of individuals with WS or DS. These experiments tested the ability of participants with WS or DS to learn large outdoor routes, to find rewards in radial arm mazes, to use search strategies efficiently, to use geometric cues to reorient in a rectangular room, or to locate an object hidden in an array disconnected from the external environment.

Real-world spatial capacities in WS

A number of studies investigated the spatial capacities of individuals with WS in real-world environments over the past 15 years. In a first study, Nardini et al. (2008) designed a task in which participants saw an object hidden under one cup in an array of cups surrounded by toys placed on a movable 82 cm x 82 cm board (Fig. 8). After seeing the object hidden and before searching for it, the participant's view of the array was obstructed, and the participant and/or the array were manipulated so that either: (1) there was no change in their original position; (2) the participant walked to another point of view so that the difference in viewing angle of the array between the two positions was 135°; (3) both the participant and the array were rotated by 135° relative to the room; or (4) the array alone was rotated by 135°. In condition 1, participants could use three types of representations to encode and recall the reward location: they could use the distal landmarks surrounding the array to localize the reward (allocentric strategy), they could use a body-centered frame of reference to localize the reward (egocentric strategy), or they could use the proximal landmarks on the array to localize the reward location (cue learning strategy). In condition 2, participants could use either an allocentric strategy or a cue learning strategy to localize the reward location, but not an egocentric strategy. In condition 3, participants could use an egocentric strategy or a cue learning strategy to localize the reward location, but not an allocentric strategy. And, in condition 4, participants could use a cue learning strategy to localize the reward location. Individuals with WS were severely impaired compared to mental age-matched typically developing children in every condition. However, individuals with WS exhibited better performance in the two conditions where they moved and the array remained static (condition 1 and 2) in comparison to the two conditions in which the array moved (condition 3 and 4). For this reason, the authors stated that WS participants could use both egocentric and allocentric spatial representations, but that they were not capable of using the landmarks on the array to define the reward location, since their performance was severely impaired in the condition where the array moved (condition 4). However, an alternative interpretation is that individuals with WS are actually capable of using a cue guidance strategy, but only when the orientation of the array remains coherent with self-motion information generated when walking, which would allow them to update their position relative to the array, as was the case in conditions 1 and 2 in which individuals with WS had the best performance. In contrast, in conditions 3 and 4, self-motion information is incoherent with the position of the array. For example, in condition 4 the array alone was rotated by 135° but the participant did not move. Thus, after the array was rotated, the participant's visual perception of the items in the array (i.e., items have moved) is not coherent with the proprioceptive and vestibular signals they are receiving (i.e., "I have not moved"). It is therefore possible that participants with WS were unable to mentally represent the rotation of the board and which would lead them to respond incorrectly. Indeed, young adults with WS have been shown to be impaired on mental rotation tasks as compared to typically developing children (Hirai et al., 2013). Thus, this experiment does not provide conclusive evidence that individuals with WS were not capable of using the array frame of reference to solve the task, nor can it be used to conclude that individuals with WS used an allocentric frame of reference instead.

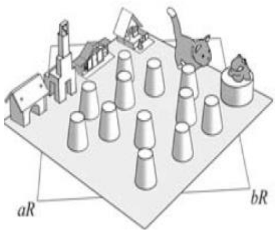

Figure 8. The rotating platform used in Nardini et al. (2008) to measure the ability of children and adults with WS to remember locations using different spatial strategies.

Mandolesi et al. (2009) used a radial arm maze in which several rewards were hidden (Fig. 9). In a free-choice condition in which all arms were accessible, participants had to visit each arm once to collect the rewards. Individuals with WS took longer to complete the task compared to typically developing children with similar mental ages, and they did not collect all of the rewards, whereas by the second of three sessions typically developing children did. These results indicate spatial exploration difficulties in individuals with WS. In a forced-choice condition, four arms of the eight arms were closed in the initial exploration phase. In the second recall phase, participants had to avoid arms that were open during the initial exploration phase and visit only arms that were closed during the initial exploration phase. Individuals with WS entered more often into arms that had been previously visited both in the recall and the initial exploration phase than typically developing children, suggesting spatial memory deficits in WS. However, it is difficult to conclude from this experiment exactly which learning strategy or strategies are required to solve the task. Indeed, the surrounding visual environment was not controlled, and thus some arms could be associated with unique visual landmarks outside the maze, such as the tree illustrated in Figure 9. As such, it is possible that typically developing children relied on a cue guidance strategy to locate the rewards, but that individual with WS could not. More importantly, however, the task has a substantial working memory component, and impaired working memory performance is also characteristic of WS (Jarrold et al., 1999). Therefore, the performance observed in the radial arm maze may potentially reflect spatial memory deficits or working memory deficits, but this experiment does not provide conclusive evidence that allocentric spatial memory is either impaired or preserved in WS.

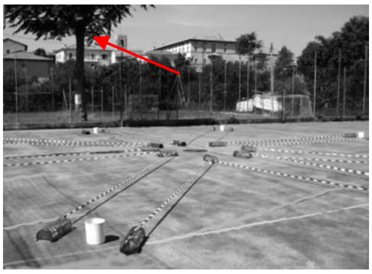

Figure 9. The radial arm maze of Mandolesi et al. (2009). Note the big tree located at the end of one arm of the maze, an example of the unique guidance cues that participants could associate with the different arms in order to guide search behavior.

Foti et al. (2015) tested the capacity of individuals with WS and typically developing children to locate a reward in a relatively small 8-arm radial arm maze (3 m in diameter) surrounded by proximal and distant cues/landmarks (Fig. 10). In a first phase in which four arms were closed, thus produce a cross maze, participants were required to always start from the same arm in order to find a reward located in the same position. Similar to typically developing children, individuals with WS were able to locate one reward hidden in this cross maze. In a second phase, consisting of only one trial, the intra-maze cues were switched (Fig. 10) and participants were again asked to find the reward, starting from the same arm. 80% of individuals with WS turned right, thus producing the same egocentric motor response to find the reward, whereas only 31.25% of typically developing children turned right to find the reward. These findings suggest that typically developing children and individuals with WS used different strategies to orient in this large-scale environment. Compared to typically developing children, individuals with WS tended to rely more on a response learning strategy to orient in space. Nevertheless, this study did not provide information about the processing of allocentric cues in WS.

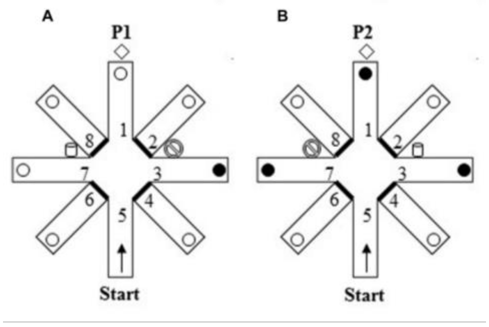

Figure 10. The radial arm maze of Foti et al. (2015). A. In the first phase (P1), two big plastic containers, one blue and one white, were placed between arms 2 and 3, and between arms 7 and 8. A brown coat rack placed at the distal end of arm 1. The bucket at the end of arm three contained a concealed reward (dark circle). Arms 2, 4, 6, and 8 were closed. B. In a second phase (P2), the intra-maze cues of arms 3 and 7 were switched, and the buckets at the ends of arms 1, 3 and 7 contained concealed rewards. The participants started always from arm 5.

When individuals are disoriented, the geometric properties of their immediate environment such as the lengths of surfaces, and the angles of their intersections can be used to orient (Hermer & Spelke, 1996). Lakusta et al. (2010) tested the capacity of individuals with WS and mental age-matched typically developing children to use those geometric cues to reorient in a 1.8 m X 1.2 m rectangular room with four black walls (Fig. 11). Participants were brought into the room and watched a reward being hidden in a container located at one of the four corners. Then, participants were blindfolded and led to the center of the room, where they were turned around in circles by the examiner to produce disorientation. After the mask was removed participants were instructed to find the reward. If participants use the geometry of the room to find the reward, they should search the geometrically appropriate corners (corners C and R in Fig. 11) more often than the geometrically inappropriate corners (corners N and F). Only five individuals with WS searched the geometrically appropriate corners (C and R) more often than the geometrically inappropriate corners (N and F), six individuals with WS showed the opposite pattern, and eight participants with WS searched the two corner types the same numbers of times showing no preference for any corner type. In contrast normally developed adults searched at the geometric corners (C and R) on 97% of the trials. Three-year-old children were also tested: Eight typically developing children searched the geometrically appropriate corners (C and R) more often than the geometrically inappropriate corners (N and F), and only two typically developing children showed the opposite pattern, and four children searched the two corner types the same numbers of times showing no preference for any corner. Overall, these results suggested impaired geometric reorientation in WS (Lakusta et al., 2010). Ferrara and Landau (2015) also tested participants with WS and typically developing children with the same paradigm and procedure. However, the authors introduced a string of tiny lights around the upper edge of the entire array, rendering the interior of the chamber more brightly lit, instead of the single light in the center of each of the four walls used in Lakusta et al. 2010. Moreover, they also used small cylindrical containers to hide the reward instead of the floor-length panels that were used in the first experiment and which might have concealed the 90-degree intersections of the room's walls in Lakusta et al. (2010). Ferrara and Landau (2015) found that 14 out of 16 WS participants performed similar to the typically developing participants suggesting that they were able to use the geometry of the room to find the reward, in contrast to what was reported in Lakusta et al. (2010). However, it has been proposed that geometric disorientation tasks may be solved by view matching (Cheng, 2008; Ferrara and Landau, 2015). View matching, or snapshot is a type of visual guidance strategy where a goal location is defined in relation to either a coincident visual cue or a distal, visually aligned, cue. It differs from visual guidance or cue guidance in the fact that the goal is recognized from essentially only one viewpoint. For example, when approaching a goal location an individual employing a view matching must move around the goal until the live scene ‘‘matches’’ the stored visual representation. In conclusion of these results (Ferrara & Landau, 2015), individuals with WS might be able to use the geometry of the room to find a location or to use a view matching strategy. Nevertheless, this study did not provide information about the processing of allocentric cues in WS.

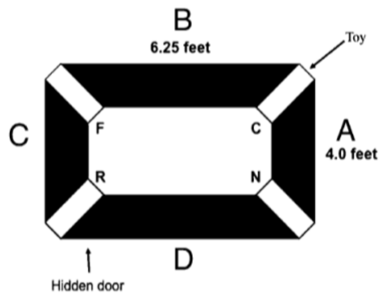

Figure 11. Testing room used by Lakusta et al. (2010) to test geometric reorientation. A, B, C, and D denote each of the four walls. C, R, N, and F illustrate the four corners in which the toy could be searched.

Finally, in Farran et al. (2010), individuals with WS and control participants were guided along two unfamiliar 1-km routes with 20 junctions. At each junction, participants had to learn whether to turn left, turn right or walk straight ahead. For one of the routes, participants were given verbal aids that included directional information and information about features along the route. Participants were then asked to retrace the routes from the beginning to the end. Whereas, typically developing children had almost a perfect performance with an average of 18 out of 20 correct turns, participants with WS executed on average 12 out of 20 correct turns. However, when individuals with WS were given verbal labels and a second learning experience, their performance improved and reached that of typically developing children. This suggests that with proper training using egocentric right and left turns, individuals with WS are capable of learning a route. In order to test whether participants had encoded spatial relationships between the landmarks in the environment, and thus had formed an allocentric spatial representation, participants were asked to point to the landmarks along the route that were not visible from their current position. Although on average individuals with WS pointed toward the correct direction, typically developing children were more accurate than participants with WS. Their mean errors were under 36°, whereas the mean errors of participants with WS was consistently above 65°. However, from the data reported by Farran et al. (2010), it is not possible to determine whether the WS group inaccuracies in pointing were due to a failure to use an allocentric representation or whether the allocentric representation that individual created were less accurate that typically developing children. Indeed, an error in pointing could reveal that participants did not understand the correct relationship between the locations in the environment and thus failed to construct an allocentric representation. In contrast, it could mean that they have a correct allocentric representation of the environment in which the relationships between the elements in the environment are represented correctly, but that the pointing error reflects a spatial representation that is less accurate in term of distance and direction.

A number of other real-world studies have mainly assessed egocentric spatial memory. For example, Smith et al. (2009) used a search task in which participants started each trial from the same location and had to find a target hidden amongst 49 possible locations in a room without any distinguishing visual landmarks (Fig. 12A). Similar to the results of Mandolesi et al. (2009), individuals with WS did not exhibit an efficient large-scale search: they took longer to search the arrays and made more erroneous revisits. These results were largely confirmed by Foti et al. (2011) in another search task (Fig. 12B), in which individuals with WS exhibited inefficient exploration when asked to retrieve 9 rewards hidden under 9 buckets arranged in different configurations. Compared to typically developing children, individuals with WS took more time to collect the 9 rewards, performed fewer error-free trials and revisited more often buckets that had already been visited or forgot to visit certain buckets.

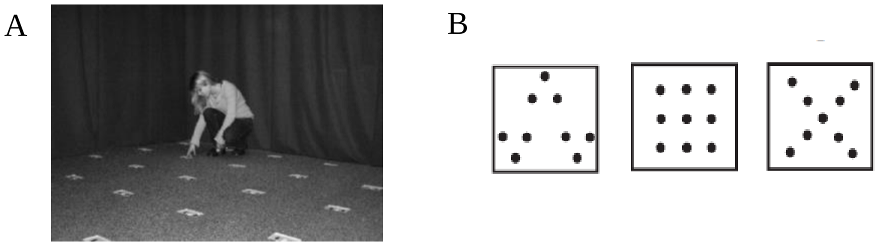

Figure 12. The search tasks of (A) Smith et al. (2009) and (B) Foti et al. (2011).

Real-world spatial capacities in DS

Two studies investigated the spatial memory capacities of individuals with DS in a real-world setting. Mangan (1992) tested 16-28-month-old children with DS and age-matched typically developing children with an apparatus that consisted of a circular platform with 11 holes, surrounded by many distal objects, which could serve as visual landmarks (Fig. 13). Participants were tested in 3 conditions designed to study egocentric response learning, cue learning, and place learning/allocentric capacities. In the egocentric response learning condition children with DS and typically developing children were required to always turn in the same direction on the platform to find the reward. Children with DS needed more trials than typically developing children to learn how to find the reward. But, after reaching a criterion of two successful trials and following a 1-min delay, all the participants were able to successfully locate the reward. These results suggest that children with DS are capable of egocentric response learning from 16 months of age. In the cue learning or visual guidance condition, the reward was always covered by a colored lid. After watching the reward being hidden in one of the holes, the child was placed in a randomly selected position on the apparatus. To find the reward, participants could identify the red lid and go directly to it to collect the reward. As for the response learning task, although children with DS needed more trials than typically developing children to learn the task, they were able to find the reward following a 1-min delay between when the object was hidden and when the child was allowed to search. Finally, for the allocentric condition, after watching the reward being hidden, children started from a different pseudo-randomly chosen location on the outside edge of the platform for every trial. As for the response and cue learning tasks, children with DS required more trials than typically developing children to learn the place-learning task. Moreover, following a 1-min delay children with DS did not focus their search at the goal location, but instead searched locations surrounding their start location on the outside edge of the platform, suggesting severe allocentric memory impairments. However, the performance of typically developing children was far from perfect and the children under 2 years of age performed below chance level, whereas children older than 2 years of age were capable of finding the reward. These results are thus consistent with those of other studies showing that the ability to form an allocentric spatial representation emerges at 2 years of age (Newcombe et al., 1998; Ribordy Lambert et al., 2013; Ribordy Lambert et al., 2015; Ribordy Lambert et al., 2016). Obviously, however, since typically developing children under two years of age do not demonstrate allocentric spatial capacities, one cannot reasonably expect individuals with DS of the same age to demonstrate these capacities. Thus, the results of Mangan (1992) cannot be used to determine whether allocentric capacities of individuals with DS are preserved or impaired in real-world environments.

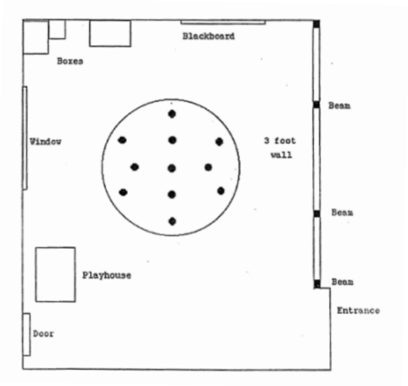

Figure 13. Experimental paradigm of Mangan (1992).

In that context, our research group studied adult individuals with DS in a real-world spatial memory task that required participants to use an allocentric spatial representation (Banta Lavenex et al., 2015). Participants had to learn and remember 3 reward locations among 12 potentially rewarded locations within a 4 m × 4 m testing arena (Fig. 14). Individuals with DS made fewer correct choices before erring, visited more locations to find the three rewards, and performed fewer errorless trials than mental age-matched typically developing children, suggesting impairments in allocentric memory in DS syndrome. However, task performance varied among individuals with DS and 50% of the individuals with DS performed above chance level. Interestingly, these individuals were able to choose preferentially the rewarded location located on the outer array (Fig. 14C), which could be identified using a low-resolution topological representation of the environment (Poucet & Benhamou, 1997). Only two individuals with DS (out of 20) were able to reliably identify the other two rewarded locations located on the middle and inner arrays, which required the ability to build a high-resolution spatial representation of the environment. These results thus suggest that low-resolution place learning, which relies only on gross topological relationships, may be relatively preserved in individuals with DS as compared to typically developing children, whereas high-resolution place learning, which relies on the encoding of precise angles and distances between objects and locations, may be impaired as compared to typically developing children. However, because participants had to remember three locations among 12 possible locations, performance may have also been impacted by the number of locations to be remembered (i.e., memory load). Consequently, it remains to be determined whether, as a group, individuals with DS are able to perform place learning for a single location, using a low-resolution topological representation of the environment.

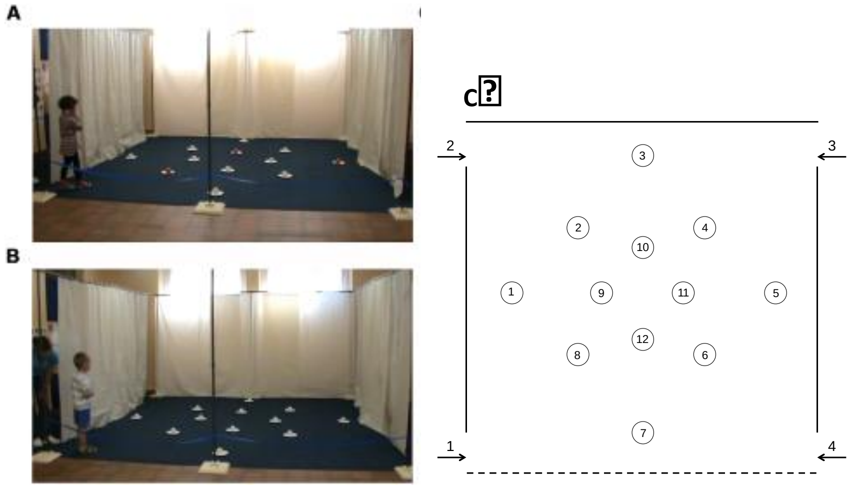

Figure 14. Experimental setup used in Banta Lavenex et al. (2015). A. Picture of a child participant in the arena in the control condition in which three red cups indicate the locations of the rewards (locations 5, 8 and 10). B. Picture of a child participant in the arena in the allocentric spatial condition (all cups are white). C. Schematic representation of the experimental arena illustrating the 12 potentially rewarded locations and their actual positions in the arena. The three rewarded locations were: location 5 on the outer array, location 8 on the middle array, and location 10 on the inner array.

1.4.3. Summary of large-scale studies: Where do we stand?

Allocentric capacities: Although the above-described studies have been instrumental in defining spatial impairments that accompany WS, to date none of these real-world studies has met all of the requirements necessary to unequivocally conclude that participants with WS are either able or unable to build and/or use an allocentric spatial memory representation. For example, real-world large-scale studies in participants with WS have either favored (Foti et al., 2011; Smith et al., 2009) or did not preclude (Farran et al., 2010; Foti et al., 2015; Nardini et al., 2008) the use of egocentric or cue guidance strategies when the participants performed the tasks. Plus, in essentially all previous studies, performance could be significantly influenced by impairments in other cognitive processes required to solve the task (e.g., working memory, higher order linguistic competence, mental rotation or visualization), which may confound the estimation of spatial memory impairments in individuals with WS. Therefore, there is a need to examine allocentric spatial memory of participants with WS in controlled laboratory conditions in which the cues available to the subjects and the frame of reference in which space must be encoded are strictly controlled. For DS, Banta Lavenex et al. (2015) proposed that high-resolution allocentric memory is impaired while low-resolution allocentric spatial memory is preserved, but this hypothesis has yet to be confirmed.

Egocentric response learning: Real-world and virtual reality studies using route-learning paradigms have reported that egocentric spatial capacities seem relatively preserved in WS and DS. However, a careful evaluation of the paradigms previously used indicates that route-learning could be solved with a number of complementary strategies. Indeed, to find a location, individuals can rely on a sequence of egocentric responses, but they may also rely on visual landmarks present along the route to be learned. Thus, a first question that must be addressed is whether participants with WS and DS can memorize a location relying solely on an egocentric response strategy, in a paradigm that precludes the use of both visual cue guidance and allocentric strategies. Moreover, in previous route-learning tasks, participants had to remember sequences of several left and right turns, again raising the possibility that working memory impairments may confound estimations of spatial ability. Therefore, a second question that must be addressed is whether individuals with WS and DS can perform the most basic form of response learning, for which subjects have to learn to find a location by performing a simple fixed motor response.

In sum, there is a need to assess the ability of individuals with WS and DS to succeed at the most basic forms of spatial learning, subserved by two distinct and dissociable memory systems: 1) the place learning system, responsible for creating allocentric spatial representations or cognitive maps (2) the response learning system, responsible for egocentric spatial representations of fixed motor sequences.

1.5. Building spatial representations without vision

All the studies discussed above tested spatial capacities in environments in which participants had access to visual cues. In the virtual reality paradigms cited previously, participants had access to visual information simulating movement, while self-generated vestibular and proprioceptive information were inconsistent since the participants were actually static. In contrast, in paradigms in which participants were freely moving, information from different sensory modalities, including visual, vestibular and proprioceptive information was available and usually consistent (except for in the study by Nardini et al. (2008)). Interestingly, even when visual input is absent, vestibular and proprioceptive information can be used to form egocentric and allocentric spatial representations (Etienne & Jeffery, 2004; Etienne et al., 1996; Taube, 2007). What is not known, however, is whether individuals with DS or WS are able to rely exclusively on self-generated movement information, i.e., in absence of visual information, in order to create a cognitive map.

Path integration (a.k.a. dead reckoning) is the ability to use self-motion information generated by one's own body movement (i.e., idiothetic cues) to keep track of one's position in space (Etienne et al., 1996; Mittelstaedt, 1999), and is generally described as a mechanism that predominates when visual information is minimized or absent. For example, path integration is used in certain environments (e.g., at sea or in the desert) or when navigation takes place in the dark. When using path integration angular displacements (rotations) are estimated primarily based on vestibular information from the semi-circular canals, and linear displacements (translations) are estimated primarily based on proprioceptive information coming from the muscles, tendons and joints, but also from vestibular information from the otoliths (Etienne & Jeffery, 2004; Etienne et al., 1996; Taube, 2007). As an individual moves along a path in its environment, information about rotations and translations must be integrated continuously in order to calculate its position as he/she moves away from the starting point.

Historically, a vast majority of experiments investigated path integration mechanisms with egocentric "homing tasks" in which subjects must return to a starting point after a sinuous trajectory in the absence of external landmarks, such as visual, tactile or olfactory cues (Fujita et al., 1993; Klatzky et al., 1990; Loomis et al., 1993; Mittelstaedt & Mittelstaedt, 1980). For example, in triangle completion tasks, participants are guided along a trajectory with two legs connected by an angle of a particular size, and then asked to return to the starting point using the most direct route. In this case, the memory representation that is created is the location of a fixed reference point in relation to one's body, and thus includes the direction and distance to this reference point (Loomis et al., 2001; Loomis et al., 1993). Humans, and a wide variety of species, such as ants, dogs and hamsters showed the ability to directly (using the most direct path) go back to a starting point after being led through a path including multiple turns (Loomis et al., 1993; Mittelstaedt & Mittelstaedt, 1980; Muller & Wehner, 1988; Seguinot et al., 1998; Seguinot et al., 1993).

Although path integration does enable an individual to return to a starting point, it should not be equated to “homing”. Path integration also plays a fundamental role in the formation of allocentric spatial representations of the environment which include the relative positions of objects and locations within the environment, as well as in coding the individual’s position with respect to those environmental landmarks (Etienne & Jeffery, 2004; Jayakumar et al., 2019; McNaughton et al., 2006; Savelli & Knierim, 2019). Indeed, the same information about direction and distance traveled by an individual between different objects' locations contributes to the definition of the position of those objects in relation to each other, within a representation of the environment that is independent of the observer's position (Jayakumar et al., 2019; McNaughton et al., 2006). Behavioral evidence has shown that blindfolded and blind subjects are able to point toward invisible locations or take shortcuts in large-scale environments (Foo et al., 2005; Passini & Proulx, 1988). The ability to take shortcuts in a previously explored environment remains hallmark evidence that individuals build a cognitive map of their environment. For example, Foo et al. (2005) tested freely-moving adult participants in a 12 m X 12 m virtual sand desert (Fig. 15). Subject were trained to return home from two targets situated 8 m away and forming an angle of 73°. At the end of the learning phase, participants were asked to take a shortcut between the endpoints of the two legs of the triangle. To succeed, participants needed to integrate the distance and trajectory angles of the learned paths and then combine this information to infer the position of the endpoints in relation to each other. Even though their shortcuts were not accurate, participants went in the overall correct direction suggesting that they were able to create an allocentric spatial representation of the environment.

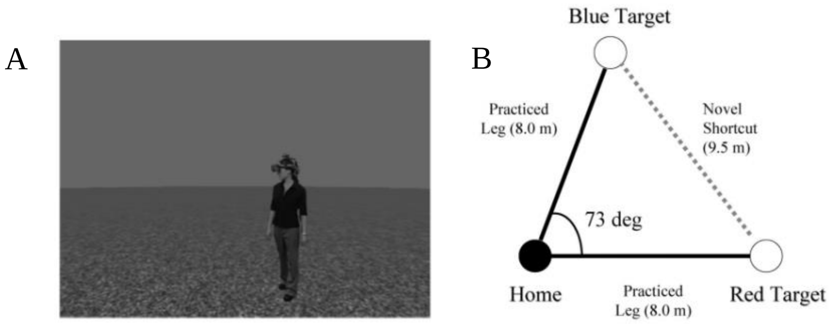

Figure 15. Experimental setup used by Foo et al. (2005). A. Desert world display. B. Illustration of the shortcut trial. During the shortcut trial, participants walked directly between the endpoints.

Only two studies investigated the capacity of young children to create a cognitive map in the absence of vision information. In a first experiment, Landau et al. (1981) and Landau et al. (1984) (which presented additional analyses) tested a congenitally blind 2.5-year-old girl named Kelli, 5 typically developing children from 2.10 to 3.9 years of age and 6 typically-developed adult undergraduate students. In their experiment, Kelli and the control blindfolded participants had to walk three paths connecting 4 different objects (a pillow, a basket of toys, a chair and a table) in a 2.44 m x 3.05 m room (Fig. 16). After this learning phase, participants were asked to walk to and return from the objects along 3 new paths they had never taken (shortcuts) in order to evaluate whether they had created a cognitive map of the environment. A total of 12 trials were administrated: the 3 new back and forth paths that were each repeated 2 times. The subjects' initial position and the position at the end of their trajectory were used to evaluate participants' performance. At the end of their each path, participants were considered successful if their final position fell within a 40° arc originating at the starting location and that contained the target. Kelli succeeded on 8 out of 12 trials, while typically developing children succeeded on an average of 7.4 out of 12 trials and young adults succeeded on an average of 10.8 trials out of 12 trials. However, individual results of the typically developing children were not provided, and thus we do not know about individual performance and variation at this age. Indeed, although a correct starting orientation on 10 of 12 trials sounds impressive, if the two "failed" trials were two of the three truly novel paths, and not the reversals or repeats of these paths, then these results may not provide sufficient support for the argument that children of this age can build cognitive maps in the absence of vision (Bennett, 1996). Moreover, the categorical measures used in Landau et al. (1984) ("successful" or "unsuccessful") provided no data about angles and distances taken by participants on the new paths and thus tell little about children and adults' accuracy in the task. It is therefore not entirely clear whether children were capable of integrating sufficiently precise information about angles and distances.

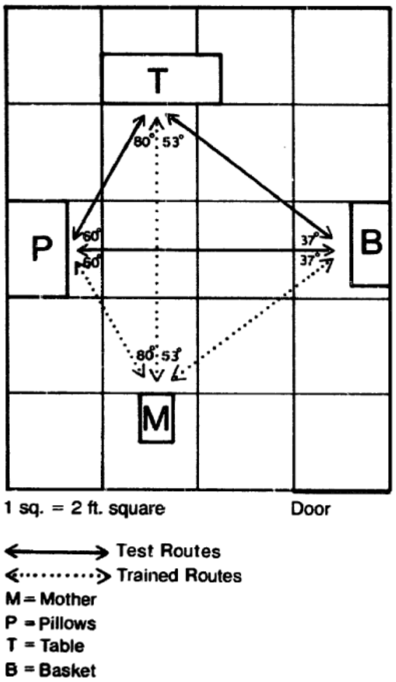

Figure 16. Experimental design of Landau et al. (1981) and Landau et al. (1984).

In a second experiment, Morrongiello et al. (1995) replicated Landau et al.'s study with a larger sample of typically developing children between 4.5 and 9 years of age. They used a similar sized room, but only tested each of the three novel paths once. They also included more measures of performance, including the participants' average distance from the target location, at both the beginning and the end of the novel paths taken. Based on all measures, 5- and 7-year-old children ended farther from the target than 9-year-olds, suggesting an improvement in spatial performance from 4 to 9 years of age. However, without an adult comparison group, it is not possible to know whether the 9-year-old children exhibited fully developed path integration capacities. Moreover, for all three novel paths the scores for the initial turn, the closest position to the target, and the final position relative to the target were averaged across all participants within each age group to yield a single estimate of performance for each age group. This procedure may have masked individual differences and obscured important information about potential errors or biases in the representation of the specific relations between environmental objects, both within and across age groups.

To conclude, the paradigm used in these studies (Landau et al., 1981; Landau et al., 1984; Morrongiello et al., 1995) is interesting because it enabled researchers to assess the capacity of subjects to form allocentric spatial representations in absence of visual information. These studies also show that this paradigm can be used with young children that have mental ages similar to individuals with WS and DS. Moreover, participants are navigating in a real-world environment and discovering common pieces of furniture. However, due to the lack of trial-by-trial data for children in both studies, it is difficult to unequivocally characterize the capacity of the participants to use path integration to build cognitive maps.

In my doctoral work, I used a paradigm that is similar to that used by Landau et al. (1981) and Morrongiello et al. (1995) to test the capacity of individuals with WS and DS to build a cognitive map in the absence of visual information. I compared their performance to that of typically developing children. Moreover, I tested typically developed adults between 20 and 30 years of age in order to investigate possible improvements of this capacity during normal development. I also analyzed each participant's performance on the novel shortcuts in order to provide individual estimates of the ability of individuals with WS, DS and typically developing children to create and use cognitive maps.

1.6. Experimental aims

Specific Aim 1. To assess low-resolution allocentric and egocentric spatial memory capacities in the presence of visual information in WS and DS

The first aim of my doctoral work was to assess the capacity of individuals with WS, DS and typically developing children and young adults to build allocentric and egocentric spatial representations in a real-world, controlled laboratory environment. For this aim, I tested the capacity of participants to remember one location among four potentially rewarded locations distributed in a 4 m X 4 m open-field arena. In the allocentric place learning condition, participants were required to learn and remember the reward location in relation to distal objects in the environment. In the egocentric response learning condition, participants had to learn that they could find the reward by performing a fixed motor response.

Because individuals with WS exhibit severe visuospatial impairments and are anecdotally described by parents and caregivers as having a very poor sense of orientation and ability to navigate, I predicted that participants with WS would exhibit impaired allocentric spatial memory. In contrast, based on the previous results of Banta Lavenex et al. (2015), I predicted that individuals with DS would exhibit basic allocentric spatial capacities, which allow them to encode the location of one reward within a low-resolution spatial representation of the environment.

Because previous studies have shown that individuals with WS and DS are capable of learning a sequence of egocentric left and right turns in both real-world and virtual environments, I predicted that individuals with WS and individuals with DS would exhibit basic egocentric response learning abilities.

Specific Aim 2. To assess the capacity of individuals with WS and DS to use path integration to construct egocentric and allocentric spatial representations in absence of vision

The second aim of my doctoral work was to characterize the capacity of individuals with WS, DS and typically developing children to use path integration to build egocentric and allocentric spatial representations. First, blindfolded participants were tested on their ability to return to a starting point after being led on straight and two-legged paths. Performance on this egocentric homing task will inform about the capacity of participants to walk straight and return to a starting point while blindfolded, as well as the level of precision that we may expect in the cognitive mapping task. Second, I evaluated the capacity of blindfolded participants to build and use an allocentric spatial representation in the absence of vision, in order to navigate between four objects placed in a large room. After an initial learning phase, participants were asked to walk directly to specific objects using novel paths (shortcuts), a hallmark of the capacity to create a cognitive map.

As discussed above, when memorizing objects and locations in large-scale environments in which individuals must move around, individuals have access to several sensory modalities including visual, vestibular and proprioceptive information. Previous studies assessing spatial capacities in WS tested their abilities with full access to visual information, sometimes with and sometimes without movement. These previous studies have reported severe spatial impairments in WS. However, the possibility that these impairments arise from altered dorsal visual stream processing, and thus impact only visuospatial processing, and not spatial processing in the absence of vision, cannot be ruled out. A preserved ability of WS individuals to use self-generated motion information to represent space in an allocentric manner will indicate that allocentric spatial capacities are relatively preserved in WS, and thus suggest that the impairments previously observed in other spatial tasks are due to the reliance on altered visual stream processing and are not the result of abnormal processing by the hippocampus-dependent memory system. In contrast, a failure of individuals with WS to use self-motion information to encode space in an allocentric manner will indicate that the allocentric memory system is impaired in WS, irrespective of the sensory input that is used to create the spatial representation. For DS, since Banta Lavenex et al. (2015) showed a preservation of low-resolution allocentric spatial capacities suggesting a preserved allocentric memory system in this syndrome, I predict that individuals with DS will perform relatively well in this task requiring them to use self-motion information to encode space in a low-resolution allocentric spatial representation, in absence of visual information.

2. EXPERIMENTAL PART

The participants, materials, tasks, procedures and results that constitute my doctoral thesis work are described in detail in the four peer-reviewed, published research articles that follow. I will therefore not describe this information elsewhere. The first two articles characterized the low-resolution allocentric spatial learning and egocentric response learning capacities in individuals with WS and DS. The third and fourth articles characterized the capacity of 5-9-year-old typically developing children, and individuals with WS and DS to use path integration in the absence of visual information in order to create a cognitive map of the environment.

2.1. Article 1: Dissociation of spatial memory systems in Williams syndrome

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RESEARCH ARTICLE

Dissociation of spatial memory systems in Williams syndrome

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Abstract

Williams syndrome (WS), a genetic deletion syndrome, is characterized by severe visuospatial deficits affecting performance on both tabletop spatial tasks and on tasks which assess orientation and navigation. Nevertheless, previous studies of WS spatial capacities have ignored the fact that two different spatial memory systems are believed to contribute parallel spatial representations supporting navigation. The place learning system depends on the hippocampal formation and creates flexible relational representations of the environment, also known as cognitive maps. The spatial response learning system depends on the striatum and creates fixed stimulus-response representations, also known as habits. Indeed, no study assessing WS spatial competence has used tasks which selectively target these two spatial memory systems. Here, we report that individuals with WS exhibit a dissociation in their spatial abilities subserved by these two memory systems. As compared to typically developing (TD) children in the same mental age range, place learning performance was impaired in individuals with WS. In contrast, their spatial response learning performance was facilitated. Our findings in individuals with WS and TD children suggest that place learning and response learning interact competitively to control the behavioral strategies normally used to support human spatial navigation. Our findings further suggest that the neural pathways supporting place learning may be affected by the genetic deletion that characterizes WS, whereas those supporting response learning may be relatively preserved. The dissociation observed between these two spatial memory systems provides a coherent theoretical framework to characterize the spatial abilities of individuals with WS, and may lead to the development of new learning strategies based on their facilitated response learning abilities.

KEYWORDS
genetic disorder, hippocampus, place learning, response learning, striatum

1 | INTRODUCTION

Williams syndrome (WS) is a genetic disorder caused by the deletion of ∼26 genes on the long arm of chromosome 7 resulting in overall mild to moderate intellectual disability (Ewart et al., 1993; Korenberg et al., 2000; Martens, Wilson, & Reutens, 2008). Individuals with WS exhibit an uneven cognitive profile with relative strengths in domains such as language production and face recognition, but severe deficits in visuospatial processing, including the ability to decipher, judge, recall and reconstruct the relationship between visually presented forms and objects (e.g., draw a house, replicate a block design, recall where an object was previously seen on a page, determine the orientation of a line) (Bellugi, Lichtenberger, Mills, Galaburda, & Korenberg, 1999; Martens et al., 2008; Mervis et al., 2000; Vicari, Bellucci, & Carlesimo, 2005). Other studies reported impairments in the abilities of individuals with WS to orient and navigate in a novel environment (Farran, Blades, Boucher, & Tranter, 2010), solve the radial arm maze (Foti et al., 2015; Mandolesi et al., 2009), effectuate efficient egocentric search tasks (Foti et al., 2011; Smith, Gilchrist, Hood, Tassabehji, & Karmiloff-Smith, 2009), and locate an object hidden on an array while using different spatial frames of reference (Nardini, Atkinson, Braddick, & Burgess, 2008). An important caveat concerning the described WS spatial profile, however, is the fact that none of the aforementioned studies investigating spatial orientation and navigation have employed learning and memory tasks which selectively assess the function of specific brain structures critical for spatial learning. In essentially all previous

TABLE 1 Participants

	Chronological age (years)				Mental age (years)			
	Mean	SD	Min	Max	Mean	SD	Min	Max
WS	21.5	10.6	8.1	43.8	5.9	1.0	4.5	7.6
TD	5.5	1.2	3.5	8.1	6.6	1.3	4.6	8.9

Chronological and mental ages for individuals with WS ($n = 18$) and typically developing (TD, $n = 19$) participants.

studies, performance could be significantly influenced by impairments in other cognitive processes required to solve the task (e.g., working memory, higher order linguistic competence, mental rotation or visualization), which may confound the estimation of spatial memory impairments in individuals with WS.

It is well established that there are two parallel but dissociable spatial memory systems that contribute to spatial navigation (Hartley, Maguire, Spiers, & Burgess, 2003; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003; McDonald and White, 1993; Packard and McGaugh, 1996; White and McDonald, 2002; White, Packard, & McDonald, 2013). Place learning depends on the hippocampal formation and creates flexible relational representations of the environment, also known as cognitive maps (O'Keefe and Nadel, 1978; Packard and McGaugh, 1996). Response learning depends on the striatum and creates fixed stimulus-response representations of behavioral performance, also known as habits (Packard and McGaugh, 1996). When a new environment is being learned, both the hippocampal and striatal learning systems are active (Devan, McDonald, & White, 1999; Ferbinteanu, 2016; Miyoshi et al., 2012; Voermans et al., 2004; Woolley et al., 2013). Nevertheless, studies have shown that both rats and humans rely predominantly on hippocampal place learning during the early stages of navigation, whereas striatal response learning becomes predominant as the environment and specific routes become familiar (Chang and Gold, 2003b; Hartley et al., 2003; Iaria et al., 2003; Jacobson, Gruenbaum, & Markus, 2012; Packard, 1999; Packard and McGaugh, 1996; Poldrack and Packard, 2003; Schmitzer-Torbert, 2007). In addition, experiments carried out in rats have shown that response learning is dominant and even facilitated when the hippocampus is inactivated and, reciprocally, place learning is dominant when the striatum is inactivated (Chang and Gold, 2003a; Packard and McGaugh, 1996; Schroeder, Wingard, & Packard, 2002). Altogether, these findings have led researchers to hypothesize that the interaction between the hippocampal place learning system and the striatal spatial response learning system is competitive, rather than cooperative, and that the use or activation of one system inhibits the use or activation of the other system (Chang and Gold, 2003a; Jacobson et al., 2012; Packard and Goodman, 2013; Schroeder et al., 2002; White and McDonald, 2002).

Thus, given our extensive knowledge and understanding of these two spatial memory systems, conspicuously absent from our assessment of the WS spatial profile is whether individuals with WS can succeed at the most basic forms of hippocampal place learning or stratial response learning, and how these two memory systems may interact and contribute to the observed spatial abilities, or impairments, of individuals with WS. Here we describe our experiments to assess these basic spatial capacities in individuals with WS and typically-developing (TD) children in the same mental age range.

2 | METHODS

2.1 | Participants

Participants were eighteen individuals with Williams syndrome (WS; clinical diagnostic made by FISH, a fluorescent in situ hybridization probe for the elastin gene in the WS critical region (Brewer, Morrison, & Tolmie, 1996); 10 males, 8 females; Table 1) and nineteen typically developing (TD) children (10 males, 9 females; Table 1).

Individuals with WS were recruited in Switzerland ($n = 9$) and in Italy ($n = 9$). No behavioral or performance differences were observed between the Swiss and the Italian participants with WS, and thus the data for these two populations were grouped for analysis and presentation. TD children having a chronological age similar to the mental ages of the individuals with WS were recruited and tested in Switzerland. TD children were reported by their parents to have been typically developing, and were neither born prematurely, nor had any suspected or diagnosed neurological conditions or learning disabilities. The mental age of all participants was determined using the Leiter International Performance Scale-Revised (Leiter-R; Subtests included in the Brief IQ from which MA is calculated are: Figure Ground, Form Completion, Sequential Order, and Repeated Patterns) (Roid and Miller, 1997). Mental age determination confirmed that the two groups overlapped on this measure (Table 1), and a *t* test confirmed that the two groups did not differ in mental age ($t(35) = 1.516$, $p = .138$). Two TD children (siblings) had strabismus that had been corrected, but both were diagnosed as lacking stereoscopic vision (i.e., depth perception). Because these two children behaved in a typical manner for the TD children, we included them in the study. The statistical analyses led to the same conclusions whether we included these two children or not. In sum, we did not exclude any recruited individuals with WS or TD children from our study.

Participants were tested on the place learning task and the response learning task on separate days, which were anywhere from 1 day to several months apart. Each session lasted approximately 45 minutes. All testing took place between 8:00 A.M. and 6:30 P.M. Human subjects research was approved by the Cantonal Ethics Commission for Human Research (Vaud, Switzerland; protocol no. 60/14), and was in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human

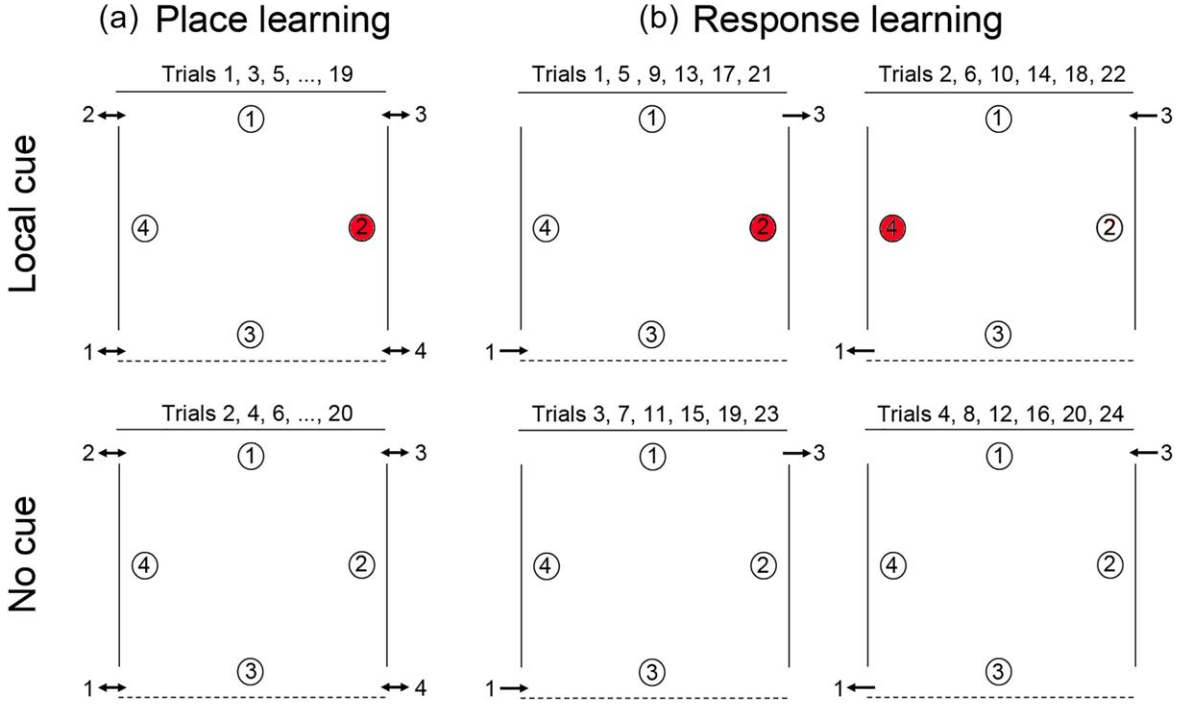

FIGURE 1 Schematic representation of the open-field arena used for testing place learning (a) and response learning (b). For place learning, the reward was always placed at the same location within the arena. For response learning, the reward could be found by performing the same motor response upon entering the arena [Color figure can be viewed at wileyonlinelibrary.com]

subjects in research. The participants (for some individuals with WS) or the parents of all participants gave informed written consent.

2.2 | Testing facilities

Nine individuals with WS and all of the TD children were tested at the University of Lausanne, Switzerland. Nine individuals with WS were tested in Fano, Italy. The main features of the testing facilities were consistent between the two sites. Testing took place within large rectangular rooms (8 m × 8 m in Lausanne and 8 × 7 m in Fano) containing many polarizing features such as doors, tables, chairs, wall posters, and so forth. Within the room was a 4 m × 4 m testing arena (Figure 1) that consisted of three walls made of suspended, opaque curtains (2 m high). Whereas the curtain on the back wall was 4 m wide, the curtains on the side walls extended only 3 m, so that there was a 50 cm gap at the front and the back of the wall, thus creating four entry points ("doors") through which participants passed in order to enter and exit the arena. The fourth (front) boundary of the arena was delineated by a rope extending to the two opposing sides of the arena, and suspended 30 cm off the ground. Exterior to the two side walls, the inter-trial waiting area was a corridor (2 m × 4 m) that contained two chairs with their backs to the arena and objects that were unique to each side. From within the arena, and from the inter-trial waiting area, participants had access to distant visual cues in front of the arena. Objects found in front of the arena (a table, chairs, one experimenter, camera, etc.) were placed 2 m away from the front of the arena.

The arena floors were uniform and thus provided no visual guidance cues. The testing arenas were void of all objects except for four white paper plates (18 cm in diameter) placed at the cardinal points in the arena (Figure 1). An inverted opaque plastic cup (7.5 cm in diameter, 6.5 cm high) was placed on each paper plate. A reward was placed under the inverted cup at one location. Participants had to lift or turn over the plastic cups to obtain the reward. Rewards were coins for individuals with WS and "treats" (e.g., Smarties®, Goldfish® crackers, pieces of breakfast cereal or pretzels) for TD children. Parents of TD children were queried with respect to alimentary allergies prior to testing, and children were asked whether there were any treats that they did not like. All testing was videotaped with a video camera located in front of the arena.

2.3 | General testing procedures

Testing involved a team of two experimenters. Experimenter 1 (E1) would stay with the participant throughout the testing session and would enter the arena with the participant, encourage the participant to search for the hidden reward, verbally praise the participant when a reward was found, remove cups from unrewarded locations as soon as they had been searched by a participant, direct the participant to the correct exit at the end of the trial, and occupy the participant during the inter-trial interval by reading to or conversing with the participant. Experimenter 2 (E2) was responsible for replacing the reward between trials, recording the data, and announcing the correct entry and exit doors to E1. Before testing began, participants viewed the arena with the four arranged plates (no inverted cups were present), from in front of the arena. While still in front of the arena, E1 showed the participant a reward item on a paper plate that she held in her hand. While the participant was watching, E1 would lower a plastic white cup over the reward to hide it. The participant would then be asked "Where is the treat/coin? Can you show me where it is?" When the participant lifted the cup to expose the reward, he/she would be verbally praised and told that it was his/hers to keep. Once the participant had been shown that a reward could be found underneath the plastic cup, the participant and E1 would go to the predetermined side of the arena where testing would begin. Once the participant was behind the curtain and occupied, E2 would hide a reward at the predetermined reward location.

In both the place and response learning tasks, participants completed two different types of trials: (1) Local cue trials, in which a local cue, specifically a red cup, covered the reward, whereas the three non-rewarded locations were covered with white cups (Figure 1). To find the reward, participants could search for the red cup or rely on place or response learning to identify the reward location (see below). This condition allowed us to assess the participants' motivation to search for the reward and their overall understanding of the task. (2) No cue trials, in which no local cue marked the reward location, as identical white cups covered all locations. In this case, participants could not discriminate between rewarded and never-rewarded locations based on local features, but instead had to rely on either a place learning strategy or a response learning strategy to identify the rewarded location. If participants did not find the reward on their first try, they were instructed to continue searching until they found the reward. Half of the participants completed the place learning task first, the other half performed the response learning task first. Analyses showed that performance was not influenced by whether participants completed the place learning task or the response learning task first.

2.4 | Place learning

Place learning was assessed by testing the ability of individuals with WS and TD children to learn and remember the location of one reward among four potentially rewarded locations (Figure 1a). For each participant one location in the arena was chosen as the goal location: for half of the participants location 4 was the designated goal, for the other half location 2 (locations 1 and 3, whose positions were distinct, were never goal locations). Each participant completed a total of 20 alternating local cue and no cue trials, with a 15-min break after the first 10 trials. There were four entries and exits to the arena. To preclude the use of egocentric and response strategies, participants were obliged to enter and exit the arena from a different door for every trial. Entry order was determined in a pseudo-random manner, with respect to the following conditions: (1) All entrances should be used an equal number of times in the two conditions (local and no cue conditions); (2) Participants may never enter the arena through a door which they had just exited on the immediately preceding trial (to preclude the use of egocentric strategies); (3) A no cue trial may never have the same entrance as the immediately preceding local cue trial; and (4) All entries must be made from the same side (right or left) that the participant just exited on the previous trial (i.e., participants were not moved from one side of the arena to the other between trials). At the end of the trial, E2 would point to the appropriate exit and E1 would guide the participant to that exit by pointing or by heading there first, therefore ensuring that the participant was on the appropriate side of the arena for the next trial. Participants were thus constantly moving about the arena from trial to trial, entering and exiting on different sides, and at the back or front of the arena. Moreover, no environmental landmarks, such as doors, windows or furniture, could be found adjacent to or directly behind any of the reward locations (with the exception of the red cups in the local cue condition). Consequently, in order to identify the reward location in the absence of the local cue, participants must rely on place learning: they must be able to learn and remember the reward location in relation to distal objects in the environment.

2.5 | Response learning

Response learning was assessed by testing the ability of individuals with WS and TD children to learn and remember the location of one reward. In this task, location 2 and location 4 were alternately rewarded. On all odd-numbered trials participants entered through door 1, location 2 was rewarded, and exited through door 3 (Figure 1b). On all even-numbered trials, participants entered through door 3, location 4 was rewarded, and exited through door 1. Participants thus had to learn that they could find the reward by performing a fixed motor response from the entrance point. Alternating pairs of trials in presence of a local cue marking the rewarded location and pairs of trials without the local cue allowed us to test the participants' motivation and general understanding of the task, and their ability to solve the task using a response learning strategy, respectively. Each participant completed pairs of Local cue trials and pairs of No cue trials in alternace (2 local cue trials followed by 2 no cue trials for a total of 24 trials total), with a 15 minute break after the first 12 trials. Response learning proceeded as follows: Trials 1, 5, 9, 13, 17, 21 with Local Cue: Enter door 1, location 2 rewarded, exit door 3. Trials 2, 6, 10, 14, 18, 22 with Local Cue: Enter door 3, location 4 rewarded, exit door 1. Trials 3, 7, 11, 15, 19, 23 with No Cue: Enter door 1, location 2 rewarded, exit door 3. Trials 4, 8, 12, 16, 20, 24 with No Cue: Enter door 3, location 4 rewarded, exit door 1. Thus, from trial-to-trial the location of the reward changed in relation to the global environment, but remained constant relative to the door just used by the participant to enter the arena. Consequently, in order to identify the reward location in the absence of the local cue, participants must rely on response learning: They must be able to learn to associate the reward location with a fixed motor response from the door used to enter the arena.

2.6 | Verbal instructions and feedback

For the first local cue trial of both the place and response learning tasks, as participants first entered the arena, E1 would ask the participant "Where do you think the reward is hidden?" For each subsequent trial, upon entering the arena, E1 would simply prompt the participant by saying "Show me where the reward is hidden." To determine unequivocally whether individuals with WS could succeed at place learning when given access to coherent visual, vestibular, and proprioceptive information, and to make sure that task comprehension was not an issue, after individuals with WS and TD children found the reward on the first local cue trial of the place learning task, E1 explained that the reward would always be found at this exact same location (while pointing at the rewarded plate with the red cup hidden from view). This same explanation was repeated to individuals with WS that did not identify the rewarded location for the first five local cue and no cue trials (or until they became annoyed, told E1 that they remembered the rule, and asked E1 to stop repeating that instruction). In contrast, TD individuals were given this verbal reinforcement only following the first two trials (i.e., one local cue and one no cue trial). For the response learning task, the experimenter gave no explanation to the participants about finding the reward in any particular location since the premise behind response learning is that individuals rely on a stimulus-response "habit" ("I do this"), and thus the rule is the solution. Note that for the place learning task, the rule ("always here") is not the same as the solution (i.e., using place learning to identify where "here" is). Thus, although participants were told the rule, they would not be able to follow this rule if they were not capable of place learning.

2.7 | Data analysis

We performed General Linear Model (GLM) analyses to compare the number of correct first choices (i.e., choosing the reward location as their first choice upon entering the arena) that participants made on the last eight trials (thus omitting the first two local cue and no cue learning trials in the place learning task and the first four learning trials in the response learning task), between groups (WS vs. TD), between conditions (Local cue vs. No cue) and between spatial tasks (Place learning vs. Response learning). Post-hoc analyses were performed with unpaired *t* tests when the ANOVA F ratio was significant and thus controlling for Type I error rate. Significance level was set at $p < 0.05$ for all analyses.

Above chance performance in the place and response learning tasks was determined for each individual with a nonparametric Wilcoxon signed-rank test comparing the number of correct first choices (visiting a rewarded location) and the number of incorrect first choices (visiting a nonrewarded location) for the last eight place and response learning trials. We normalized the number of correct and incorrect choices based on the probability to make those choices: the number of correct choices was divided by one and the number of incorrect choices was divided by three. The number of individuals with WS and TD children who solved one, two or neither of these tasks were compared with the log-likelihood ratio for contingency tables.

3 | RESULTS

To characterize the place learning and response learning abilities of WS and TD individuals, we analyzed the proportion of correct choices (i.e., choosing the reward location as their first choice upon entering the arena) in both the place learning and response learning tasks, in presence or absence of a local cue (a red cup) marking the reward location. A global GLM analysis revealed differences between experimental groups ($F_{(1,35)} = 5.501$, $p = 0.025$; TD children > WS individuals) and cue conditions ($F_{(1,35)} = 72.264$, $p < 0.001$; Local cue > No cue), but no interaction between groups and cue conditions ($F_{(1,35)} = 0.000$, $p = 0.995$). Importantly, there was no difference between the two types of spatial learning tasks (Place learning vs. Response learning; $F_{(1,35)} = 1.445$, $p = 0.237$), but a significant interaction between spatial tasks and experimental groups ($F_{(1,35)} = 15.367$, $p < 0.001$), and between cue conditions, spatial tasks and experimental groups ($F_{(1,35)} = 37.183$, $p < 0.001$).

3.1 | Local cue

When a red cup marked the goal location (Figure 2a), there was no difference in performance between place learning and response learning tasks ($F_{(1,35)} = 1.112$, $p = 0.299$) and no interaction between spatial tasks and experimental groups ($F_{(1,35)} = 0.224$, $p = 0.639$). Overall, TD children made slightly more correct choices than WS individuals ($F_{(1,35)} = 4.724$, $p = 0.037$; TD: $M = 0.95$ SE = 0.04; WS: $M = 0.83$, SE = 0.04). Within group comparisons revealed that TD children made more correct choices in the place learning task than in the response learning task ($t_{(18)} = 2.157$, $p = 0.045$; Place learning: $M = 0.99$, SE = 0.01; Response learning: $M = 0.91$, SE = 0.04), whereas WS individuals did not differ in the number of correct choices made in the place learning and response learning tasks ($t_{(17)} = 0.303$, $p = 0.765$; Place: $M = 0.84$, SE = 0.05; Response: $M = 0.81$, SE = 0.09). Although TD children made more correct choices than WS individuals in the place learning task with the local cue ($t_{(35)} = 2.940$, $p = 0.006$), TD children and WS individuals did not differ in the response learning task with the local cue ($t_{(35)} = 1.10$, $p = 0.279$). In sum, in the presence of a red cup marking the reward location, although both groups performed well above chance (WS: $t_{(17)} = 11.749$, $p < 0.001$; TD: $t_{(18)} = 81.492$, $p < 0.001$), TD children performed slightly better than WS individuals in the place learning task, and WS individuals performed as well as TD children in the response learning task.

3.2 | No cue

When the reward location was not marked by a local cue (Figure 2b), there was no overall difference in performance between place learning and response learning tasks ($F_{(1,35)} = 1.142$, $p = 0.293$), and the difference between experimental groups failed to reach significance ($F_{(1,35)} = 4.089$, $p = 0.051$). However, there was an interaction between spatial learning tasks and experimental groups ($F_{(1,35)} = 30.059$, $p < 0.001$). TD children made more correct choices in the place learning task than in the response learning task ($t_{(18)} = 5.561$, $p < 0.001$; Place learning: $M = 0.95$, SE = 0.03; Response learning: $M = 0.49$, SE = 0.08). In contrast, WS individuals made more correct choices in the response learning task than in the place learning task ($t_{(17)} = -2.697$, $p = 0.015$; Place learning: $M = 0.45$, SE = 0.06; Response learning: $M = 0.76$, SE = 0.08). Importantly, TD children made more correct choices than WS individuals in the place learning task without local cue ($t_{(35)} = 7.295$, $p < 0.001$), whereas WS individuals made more correct choices than TD children in the response learning task without local

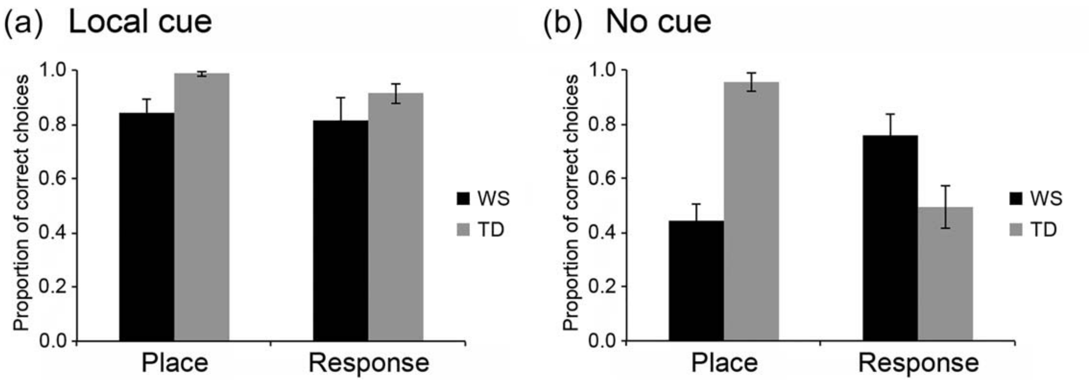

FIGURE 2 Proportion of correct choices (i.e., choice of the rewarded location as the first choice upon entering the arena; Mean ± SEM) made by individuals with WS ($N = 18$) and TD children ($N = 19$) in the place learning and response learning tasks, in presence (a) or absence (b) of a local cue marking the reward location

cue ($t_{(35)} = -2.344$, $p = 0.025$). In sum, WS individuals performed better than TD children in the response learning task when no local cue marked the reward location.

3.3 | Within group comparisons

Within group comparisons of performance in the four experimental conditions confirmed the contrasting behavioral patterns observed for TD children and WS individuals in the place learning and response learning tasks. TD children made more correct choices in the place learning task with the local cue than they did in the response learning task with a local cue, and more correct choices in both of these tasks than in the response learning task without a local cue ($F_{(3,18)} = 28.744$, $p < 0.001$; Place learning with local cue > Response learning with local cue > Response learning without local cue; all $p < 0.045$). In addition, TD children made more correct choices in the place learning task without a local cue than in the response learning task without a local cue ($p < 0.001$). In contrast, TD children did not differ in the number of correct choices in the place learning task with and without the local cue ($p = 0.262$). The performance of WS individuals also differed between testing conditions ($F_{(3,17)} = 8.354$, $p < 0.001$). However, in contrast to TD children, WS individuals made fewer correct choices in the place learning task without the local cue than in all three other tasks (all $p < 0.015$), which did not differ from each other (all $p > 0.370$).

In sum, and contrary to TD children, WS individuals performed worse in the place learning task in absence of the red cup than they did in the place learning task when this local cue marked the goal location. In contrast, in the response learning task, WS individuals performed as well in the absence of the local cue as they did when the local cue marked the reward location.

3.4 | Individual analyses

To evaluate the evolution of performance across trials in the place learning and response learning tasks, in the absence of a local cue marking the rewarded location, we determined the percentage of participants in each group who found the reward as their first choice upon entering the arena for each trial. Place learning appeared to be the default strategy for TD children, since about 90% chose the correct location within the first block of two trials in the place learning task (Figure 3a) and increased to nearly all participants across the remaining blocks of trials. In contrast, only about 50% of individuals with WS

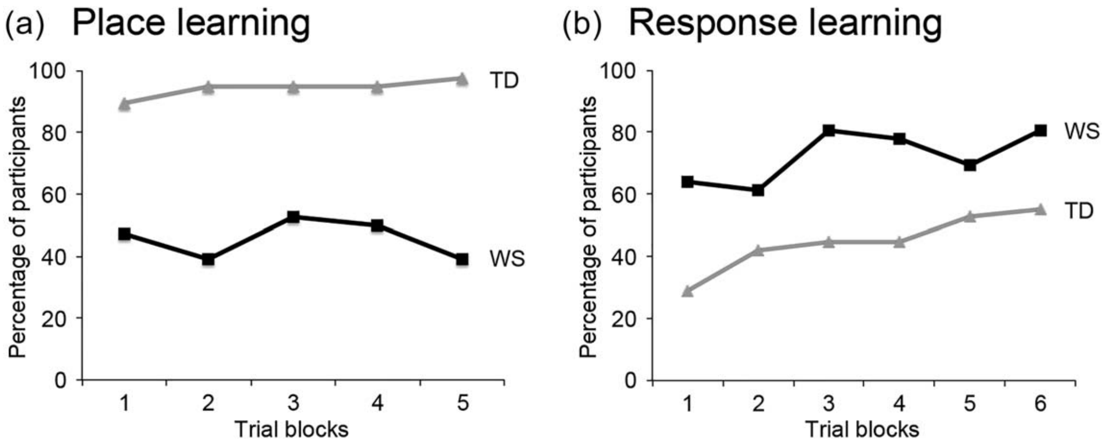

FIGURE 3 Percentage of individuals with WS and TD children in the same mental age range who found the reward as their first choice upon entering the arena, in the place learning (a) and response learning (b) conditions, in absence of a local cue

chose the correct location within the first block of two trials in the place learning task, and as a group their performance did not improve across the remaining trials (Figure 3b).

The opposite pattern of results was observed in the response learning task (Figure 3b). Response learning appeared to be the default strategy for individuals with WS, since more than 60% of participants with WS chose the correct reward location as their first choice in the first block of trials, and more than 80% did so in the last block of trials in the response learning task. In contrast, less than 30% of TD children chose the correct location within the first block of trials (Figure 3b), and although their performance improved across the subsequent blocks of trials, they never reached the same levels of performance as individuals with WS.

Finally, we determined how many individuals with WS and TD children performed above chance level, and therefore demonstrated their ability to solve either the place learning or response learning tasks when no local cue marked the reward location (Table 2). The number of participants who solved one, two or neither of the tasks differed between groups (Log likelihood ratio test: $X^2_{(3)} = 29.95$, $p < 0.0001$). These analyses yielded four main findings: (1) Thirteen of eighteen individuals with WS performed above chance level on the response learning task, whereas only three of nineteen TD children did. Interestingly, multiple pieces of evidence (including response latency, error types, children's verbal reports, and additional probe trials) indicated that two additional TD children performed above chance in the response learning task, but did so by using a trial-unique place learning strategy. These TD children recalled where they had found the reward on the previous trial (i.e., location 2 or 4), and since the two locations were alternately rewarded, chose the opposite location. Consequently, we did not consider these two children as being successful in the response learning task. Two other TD children attempted to use the same strategy to solve the response task but failed due to their poor recall of the location rewarded on the immediately preceding trial. It is important to note that individuals with WS could not have succeeded at the response learning task using this type of trial-unique place learning strategy since they were incapable of place learning even over repeated trials. (2) Of the thirteen individuals with WS who exhibited above chance performance in the response learning task, only one solved the place learning task. (3) Whereas eighteen of nineteen TD children performed above chance in the place learning task, only three individuals with WS did. (4) Among the three individuals with WS who demonstrated place learning, only one was able to solve the response learning task. Altogether, these analyses of individual performance further support the view that impairments in place learning facilitate response learning in individuals with WS, and that the ability to exhibit place learning impedes the ability to exhibit response learning in both individuals with WS and TD children.

4 | DISCUSSION

We found that individuals with WS exhibited a dissociation in their spatial learning abilities subserved by two parallel spatial learning and memory systems. As compared to TD children, place learning performance was severely impaired in individuals with WS, whereas their spatial response learning performance was facilitated. These findings suggest that place learning and response learning may interact competitively to control the behavioral strategies normally used to support human spatial navigation. These findings further suggest that the neurobiological pathways supporting place learning may be affected by the genetic deletion responsible for WS, whereas the neurobiological pathways supporting response learning may be relatively preserved. The dissociation observed between these two spatial memory systems provides a coherent theoretical framework to characterize the spatial abilities of individuals with WS, and may ultimately lead to the development of new learning strategies in other modalities (Foerde, Knowlton, & Poldrack, 2006), based on their facilitated response learning abilities.

4.1 | Hippocampal place learning

Place learning has been shown to be dependent on the hippocampal formation in rodents, monkeys and humans (Banta Lavenex, Colombo, Ribordy Lambert, & Lavenex, 2014; Lavenex, Amaral, & Lavenex, 2006; Morris, Garrud, Rawlins, & Okeefe, 1982). In WS, some aspects of hippocampal physiology, morphology and function exhibit abnormalities (Haas et al., 2014; Meyer-Lindenberg, Mervis, & Berman, 2006; Meyer-Lindenberg et al., 2005). In accordance, a few studies have suggested that there are deficits in hippocampus-dependent spatial processing in individuals with WS, but because the tasks used previously were often complex and may have required the use of extraneous cognitive processes (i.e., comprehension of complex verbal instructions, mental rotation and working memory (Farran et al., 2010; Mandolesi et al., 2009; Nardini et al., 2008)), it was not entirely clear whether place learning per se was impacted in WS. Our findings provide unequivocal evidence that hippocampus-dependent place learning is severely impaired, if not abolished, in a majority of individuals with WS. Indeed, 70% of the indivuals with WS that we tested were incapable of solving our task, which can be considered the most basic of place

TABLE 2 Individual performance

	Place Yes; Response No	Place Yes; Response Yes	Place No; Response No	Place No; Response Yes
WS individuals	2	1	3	12
TD children	15	3	1	0

Number of individuals with WS ($n = 18$) and TD children ($n = 19$) who performed above chance level in the place learning and/or the response learning tasks in absence of a local cue.

learning tasks (e.g., not confounded by extraneous cognitive processes), and which can be solved by a majority of typically developing children from 24 months of age, and by 95% of all typically developing children by 36 months of age (Ribordy, Jabes, Banta Lavenex, & Lavenex, 2013; Ribordy Lambert, Lavenex, & Banta Lavenex, 2015).

In contrast to our findings of severe place learning impairments, it has been reported that individuals with WS can succeed at using the geometry of their environment to reorient in some conditions (Ferrara and Landau, 2015; Lakusta, Dessalegn, & Landau, 2010). Geometric reorientation has been shown to be impaired by hippocampal lesion in rats (McGregor, Hayward, Pearce, & Good, 2004). In humans, fMRI studies have correlated boundary use, or the combined use of boundary and feature cues, with increased hippocampal activation (Doeller, King, & Burgess, 2008; Sutton, Joanisse, & Newcombe, 2010), lending further support for the role of the hippocampus in geometric reorientation. Importantly, the experimental paradigm for assessing geometric reorientation in individuals with WS is theoretically less confounded by the extraneous cognitive processes described above, suggesting that the task can assess the function of specific brain structures critical for spatial learning. The question thus arises as to how two presumably hippocampus-dependent tasks give rise to different findings in individuals with WS, with their geometric reorientation performance relatively similar to that of TD children, but their place learning abilities essentially abolished?

It is possible, if not likely, that these two tasks are subserved by different parallel pathways or subsystems within the medial temporal lobe. In animals, neuroanatomical and electrophysiological evidence suggests that external sensory information regarding visuospatial feature information enters the hippocampus via a different pathway than internally-generated spatial information (Lavenex and Amaral, 2000; Lavenex, Suzuki, & Amaral, 2002; Lavenex, Suzuki, & Amaral, 2004). Specifically, in non-human primates, the perirhinal and rostral entorhinal cortices (i.e., perirhinal and lateral entorhinal cortices in rodents) convey visual feature or object information to the hippocampus, whereas the parahippocampal cortex, and the intermediate and caudal subdivisions of the entorhinal cortex (i.e., postrhinal and medial entorhinal cortices in rodents) convey visuospatial scene information to the hippocampus. Furthermore, electrophysiological evidence in rodents suggests that self-generated movement information, which contributes to the control of head-direction cells found in the presubiculum, parasubiculum and retrosplenial cortex, the activity of which are integrally involved in real-world place learning, may also enter the hippocampus via the medial entorhinal cortex (i.e., caudal entorhinal cortex in primates) (Knierim, Neunuebel, & Deshmukh, 2014). Because individuals must be disoriented prior to testing (Ferrara and Landau, 2015; McGregor et al., 2004), the geometric disorientation paradigm makes self-generated movement information unreliable and incongruous with the visual information that becomes available once the blindfold placed on the individual's eyes is removed. For individuals subjected to a disorientation procedure, only the information concerning local cues and visual scenes is reliable to guide successful reorientation towards geometrically equivalent corners, a behavior which may be considered akin to view matching. Indeed, it has been proposed that geometric disorientation tasks may be solved by view matching (Cheng, 2008; Ferrara and Landau, 2015), and do not require the individual to maintain a continuous sense of his/her location within the environment. We hypothesize that such capacities, which are relatively preserved in WS, may be subserved by the intermediate entorhinal cortex to hippocampus pathway (Chareyron, Banta Lavenex, Amaral, & Lavenex, 2017).

In contrast, the performance of individuals with WS in our place learning task, a task which requires participants to keep track of their own movements in the environment and which apparently cannot be solved by view matching in individuals with WS, is severely impaired. We hypothesize that such capacities may be subserved by the caudal entorhinal cortex to hippocampus pathway. As we previously suggested for the normal development of spatial memory abilities in typically developing children (Lavenex and Banta Lavenex, 2013), distinct hippocampal circuits may underlie the expression of specific and dissociable “hippocampus-dependent” memory processes. It thus stands to reason that during abnormal development, the functional integrity of these distinct hippocampal circuits may be differentially affected. Nevertheless, regardless of whether separate hippocampal circuits are ultimately implicated in solving these two different tasks, our data show that place learning requiring the coherent integration of visual, vestibular and proprioceptive information is severely impaired in individuals with WS.

4.2 | Striatal response learning

Individuals with WS exhibited facilitated response learning abilities. Individuals with WS performed better than TD children from the very first trials in the response learning task. In contrast, striatal response learning appeared to be inhibited in TD children. Although response learning emerges earlier (well before 2 years of age) than place learning in TD infants (Acredolo, 1978; Cornell and Heth, 1979; Newcombe, Huttenlocher, Bullock Drummey, & Wiley, 1998; Ribordy, Jabes, Banta Lavenex, & Lavenex, 2013), our study shows that by 4 years of age incidental response learning is extremely difficult. Although the three TD children who were able to solve our response learning task fell into the older half of our sample, we have observed children up to 12 years of age fail on this response learning task. Moreover, as described in the results, two additional TD children performed above chance level in the response learning task by using a trial-unique place learning strategy, i.e., recalling that only two locations were ever rewarded, and choosing the opposite of that which was rewarded on the preceding trial. However, this strategy was slower (participants took on average twice as long to choose a first location), more difficult (participants complained that the task was difficult), and prone to errors (although they succeeded statistically, they made more errors than children who employed a response learning strategy). Two other TD children attempted to use the same strategy to solve the response task but failed due to the poor recall of which location was rewarded on the immediately preceding trial. Note that individuals with WS could not have succeeded at the response learning task using a trial-unique place learning strategy since most individuals were incapable of place learning even over repeated trials. Finally, it is important to recognize that whereas we chose to compare the performance of individuals with WS and typically-developing children in the same mental age range, our findings are not dependent on this specific choice of comparison group. Our main finding, that individuals with WS exhibit a dissociation between place and response learning is valid regardless of the control group used. Moreover, our results further confirm the idea that mental age is not necessarily predictive of performance on tasks other than those used to determine mental age, or else individuals with WS would have succeeded at place learning and failed at response learning. Instead, our results support the hypothesis that cognitive capacities are domain-dependent, and composite scores such as IQ and mental age cannot necessarily predict performance on tasks which rely on specific brain areas and specific cognitive processes.

Structural brain imaging using tensor-based morphometry has shown that the volume of the dorsal striatum, including the caudate nucleus and the putamen, is reduced in individuals with WS (Chiang et al., 2007). In accordance, an fMRI study has shown that adult individuals with WS exhibit slower response times accompanied by reduced activity in the caudate nucleus, as compared to chronological age-matched controls, when performing a response inhibition task (Mobbs et al., 2007). Considering the evidence of neuroanatomical and functional impairments in the caudate nucleus, our findings of not only preserved but facilitated striatal response learning may seem surprising. However, as for the differences between geometric reorientation and place learning, these apparent inconsistencies may be reconciled by considering specific subsystems within the striatum (Yin and Knowlton, 2006), and the fact that inhibition learning and spatial response learning may implicate different striatal systems (Eagle and Robbins, 2003; Featherstone and McDonald, 2004; Liljeholm and O'Doherty, 2012). Thus, whereas some striatal abnormalities appear to translate into impairments in response inhibition in individuals with WS, our behavioral data suggest that they may not preclude individuals with WS from exhibiting facilitated striatal response learning, which may depend on other relatively preserved striatal pathways.

4.3 | Competitive interaction

According to the theory of functional incompatibility (Sherry and Schacter, 1987), parallel memory systems subserving processes such as place and response learning may have evolved because adaptations inherent in one spatial memory system make it ineffective at solving other types of spatial memory problems. The findings that the hippocampal- and striatal-dependent memory systems may interact in a competitive manner suggest that, depending on the circumstances, either place learning or response learning will predominate, effectively silencing the opposing learning system. In contrast, a recent study described a seemingly cooperative relationship between hippocampal and striatal activity in individuals with Huntington's disease (HD), a genetically-determined neurodegenerative disorder impacting primarily the striatum (Voermans et al., 2004). Across participants, greater dysfunction of the caudate nucleus in HD was associated with a relative increase in hippocampal activity which enabled HD participants to perform as well as controls on a trial-unique route recognition task performed in a virtual environment. Furthermore, in control participants the authors observed increased interaction between the hippocampus and striatum (as compared to HD patients) during route recognition. These data were interpreted to suggest that the hippocampal and striatal systems work cooperatively to influence navigational strategies (Voermans et al., 2004). However, cooperative interaction may have been suggested by the findings only because (1) a hippocampus-dependent learning strategy may compensate for the gradual dysfunction of a striatum-dependent learning strategy and (2) the performance of individuals with HD was similar to that of controls (e.g., facilitation was not observed). In contrast, our current behavioral findings in individuals with WS suggest that not only can a striatum-based response strategy not be used to solve a place learning task in case of hippocampal impairment, but impaired place learning turns individuals with WS into super response learners. In contrast to TD children in whom place learning was predominant, and indeed interfered with their ability to exhibit response learning, the response strategy appeared to be the default mode for individuals with WS.

In agreement with our findings, results from another group of children with a neurodevelopmental learning disorder, ADHD, suggest that the normal balance between place and response learning can be shifted (Robaey, McKenzie, Schachar, Boivin, & Bohbot, 2016). Children with and without ADHD were trained to criteria on a virtual 8-arm radial arm maze surrounded by numerous distal visual cues, and which could be solved by relying on either place or response strategies. The strategy that children relied upon was determined by their performance on a probe trial in which there were no visible landmarks. Whereas only 20% of the control children exhibited perfect performance on the probe trial, indicating that they were relying on response learning during the training phase, 35% of children that exhibited one or more ADHD symptoms did (Robaey et al., 2016). Taken together with our findings, these results suggest that response learning may be preferentially expressed in individuals with a variety of neurodevelopmental learning disorders with differing etiologies.

Finally, it is important to consider whether experience might play a role in defining the Williams spatial profile. For example, might experience act to permanently shift the balance from a system that should normally rely on place learning (during typical development) to one that may rely predominantly on response learning (during atypical development, such as in WS). Is place learning completely impaired in most individuals with WS, or is it possible, for example, that hippocampal development is only delayed in young children with WS, and that due to this delay parents and children begin to rely on striatal-dependent strategies, which serve to further strengthen their reliance on these strategies and weaken dependence on hippocampal-dependent strategies. We showed that TD children were unable to access explicitly the solution to the response learning task, although previous evidence suggests that they likely possess the solution. Is it possible that individuals with WS are the exact opposite of the TD children, possessing the solution to the place learning task but unable to access it? Although this explanation seems doubtful, one possible way to address this question is to compare individuals with WS with other groups of individuals with neurodevelopmental disorders who may also show delayed maturation of the hippocampal formation and hippocampal-dependent memory processes to see whether they also show permanent impairment of place learning capacities.

4.4 | The WS spatial memory profile

Our findings provide a coherent theoretical framework to characterize the spatial abilities of individuals with WS. Individuals with WS are severely impaired on spatial tasks that require the individual to keep track of self-generated movement in order to define his location and the location of other objects in the environment, in an allocentric spatial relational representation (i.e., in relation to other locations and landmarks in the environment). In contrast, our study shows that individuals with WS are capable of using visual guidance (a.k.a. landmark or beacon guidance) to learn and remember the location of a goal since they were able to find the reward when it was covered by a red cup. Finally, our results show that most individuals with WS exhibit preserved and even superior capacities to learn and remember a goal location based on previously experienced motor trajectories.

5 | CONCLUSIONS

The dissociation of the hippocampal-dependent place learning system and the striatal-dependent response learning system in individuals with WS and TD children provides evidence supporting three fundamental findings: First, it reveals a competitive interaction between human spatial memory systems. Second, it demonstrates that a discrete hemizygous gene deletion can lead to a shift in the reliance on two learning and memory systems, which may serve to define the cognitive impairments and preserved abilities of affected individuals. Third, it provides a coherent theoretical framework to characterize the real-world spatial abilities of individuals with WS, showing that spatial abilities necessitating place learning are impaired, whereas spatial abilities subserved by response learning are facilitated.

Our findings emphasize the fact that although structural and functional evidence of abnormalites in atypically developing brains are informative, they may not always be sufficient to predict the presence or severity of cognitive deficits in tasks normally dependent on those brain regions; atypically developing brains are not the same as typically-developed mature brains with acquired damage (Karmiloff-Smith, 2013). Nevertheless, careful investigations of fundamental cognitive processes in atypically-developing individuals may help to determine the contribution of a limited number of genes to the expression of complex human behaviors.

Importantly, the competitive interaction between the hippocampal and striatal learning systems has been shown in human studies outside the spatial domain: namely on probabilistic classification learning (Poldrack et al., 2001) and simple classification learning tasks (Foerde et al., 2006). Accordingly, the functional dissociation between hippocampus-dependent and striatum-dependent learning in individuals with WS may lead to the development of new learning strategies based on their facilitated response learning abilities.

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2.2. Article 2: Low-resolution place and response learning capacities in Down syndrome

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Low-Resolution Place and Response Learning Capacities in Down Syndrome

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Down syndrome (DS), the most common genetic cause of intellectual disability, results from the partial or complete triplication of chromosome 21. Individuals with DS are impaired at using a high-resolution, allocentric spatial representation to learn and remember discrete locations in a controlled environment. Here, we assessed the capacity of individuals with DS to perform low-resolution spatial learning, depending on two competing memory systems: (1) the place learning system, which depends on the hippocampus and creates flexible relational representations of the environment; and (2) the response learning system, which depends on the striatum and creates fixed stimulus–response representations of behavioral actions. Individuals with DS exhibited a preservation of the low-resolution spatial learning capacities subserved by these two systems. In place learning, although the average performance of individuals with DS was lower than that of typically developing (TD) mental age (MA)-matched children and TD young adults, the number of individuals with DS performing above chance level did not differ from TD children. In response learning, the average performance of individuals with DS was lower than that of TD adults, but it did not differ from that of TD children. Moreover, the number of individuals with DS performing above chance level did not differ from TD adults, and was higher than that of TD children. In sum, whereas low-resolution place learning appears relatively preserved in individuals with DS, response learning appears facilitated. Our findings are consistent with the hypothesis that the neural pathways supporting low-resolution place learning and response learning are relatively preserved in DS.

Keywords: allocentric, egocentric, spatial memory, multiple memory systems, Down syndrome, dissociation

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INTRODUCTION

Down syndrome (DS), resulting from a partial or complete triplication (trisomy) of chromosome 21, is the most common genetic cause of intellectual disability, with an incidence of 1 in 625–1,000 live births (Bittles et al., 2006; de Graaf et al., 2017). Adults with DS have IQs ranging from 30 to 70 and a typical mental age (MA) ranging from 5 to 9 years of age (Vicari et al., 2005, 2006). Despite a global mental retardation, individuals with DS show a unique cognitive profile compared to other genetic disorders. Individuals with DS exhibit specific difficulties in the verbal domain, including poor language abilities (Chapman et al., 1991; Chapman, 1997; Abbeduto et al., 2003) and impairments in verbal short-term memory (Jarrold and Baddeley, 1997), especially in maintaining phonological information over a short delay (Raitano Lee et al., 2010). By contrast, their visuo-spatial memory ("*where*" *memory*) is reported as relatively preserved. For example, individuals with DS exhibit a performance similar to that of MA-matched typically developing (TD) children in learning where pictures are presented on a piece of paper (Vicari et al., 2005) and on the Corsi block-tapping task (Wang and Bellugi, 1994; Jarrold and Baddeley, 1997; Numminen et al., 2001; Laws, 2002). However, not all non-verbal capacities are spared. Individuals with DS tend to neglect the internal details of stimuli, such as in the Delis hierarchical processing task, and instead exhibit a bias toward the global features of those stimuli (Bellugi et al., 1999), but see D'Souza et al., 2016. Difficulties in memorizing and recognizing pictures of objects ("*what*" *memory)* have also been reported in DS (Vicari, 2001; Vicari et al., 2005).

Germane to the current study, previous investigations of spatial memory in DS mainly assessed small-scale visuo-spatial capacities. Research has shown, however, that performance on small-scale spatial tasks do not correlate with performance on large-scale spatial tasks, particularly those in which participants must move around (Quaiser-Pohl et al., 2004; Hegarty et al., 2006; Farran et al., 2010). Evaluating the large-scale spatial capacities of individuals with DS is important because spatial deficits may limit their everyday functioning and autonomy. Nevertheless, when evaluating spatial learning and memory capacities, it is important to consider the influence that other cognitive processes, including but not limited to, verbal comprehension (of task rules, etc.), working memory, executive functions, and visual imagery, may have on performance. Moreover, it is fundamental to recognize that there are different types of dissociable spatial memory systems that may interact and contribute to guiding behavior, and thus impact overall task performance (Banta Lavenex and Lavenex, 2009; Banta Lavenex et al., 2015; Bostelmann et al., 2017).

In the current study, we investigated the ability of individuals with DS to rely on two different spatial memory systems in order to identify one discrete location among four possible locations in a controlled environment: (1) the place learning system, responsible for creating allocentric spatial representations or cognitive maps, and which has been shown to depend on the integrity of the hippocampus in rats, monkeys, and humans (O'Keefe and Dostrovsky, 1971; O'Keefe and Nadel, 1978; Morris et al., 1982; Banta Lavenex et al., 2006; Banta Lavenex et al., 2014); and (2) the response learning system, responsible for creating fixed stimulus–response representations of behavioral actions also known as habits, and which has been shown to depend on the dorsal striatum in rats and humans (Packard et al., 1989; Packard and McGaugh, 1996; Yin and Knowlton, 2006).

Place Learning

Place learning refers to an individual's ability to learn and remember locations in an allocentric spatial frame of reference. In this representation, locations are encoded in relation to other objects or locations in the environment (i.e., in a viewpoint-independent manner), thus enabling the creation of a cognitive map of the environment (Tolman, 1948; O'Keefe and Nadel, 1978; Banta Lavenex et al., 2014). For example, imagine a teacher's desk that can be described in allocentric terms as both in front of the class and in the center of the room; importantly, the desk maintains its relations to other fixed objects irrespective of where a student is sitting in the classroom. The ability of individuals with DS to use place learning has been previously assessed in virtual environments as a specific test for "hippocampus-dependent" memory. For example, Pennington et al. (2003) employed a virtual Morris water maze task, a classic task for investigating place learning in rodents (Morris et al., 1982), in which individuals had to learn the position of a target within a virtual room containing distal visual cues. During a probe trial without the actual target, individuals with DS spent less time searching in the vicinity of the target location, as compared to TD children, thus suggesting an impairment in hippocampus-dependent spatial learning in DS. However, in a subsequent study including a larger group of participants, Edgin et al. (2010) failed to find a difference between individuals with DS- and MA-matched TD children, raising questions about the usefulness or reliability of this task to characterize the spatial cognitive profile of individuals with DS.

In another virtual reality study, Courbois et al. (2013) tested the ability of 10 individuals with DS to take a novel route (i.e., shortcut between two previously traveled routes), as a means of assessing their ability to build a cognitive map. Seven of the individuals with DS were able to learn two initial routes (i.e., three did not), by either memorizing ordered sequences of landmarks and actions to be taken (e.g., go to the bridge and turn right, then go to the tower and turn left, etc.) or by using a beacon-following strategy moving toward a series of landmarks (e.g., go toward the bridge, look around and find the tower, then go toward the tower, etc.). A third possible strategy not considered by the authors was for participants to learn a sequence of turns (see response learning, below). Eventually, only two of the seven individuals with DS who had learned the routes were able to take a shortcut between the start and end locations. Overall, these results suggest that individuals with DS may have relatively preserved route learning abilities, but greater difficulty in representing the configural or spatial relationships between landmarks constituting the environment, i.e., building an allocentric spatial representation of the environment that subserves successful place learning.

Although spatial tasks conducted in virtual reality tend to approximate real-world tasks more closely than standard tabletop neuropsychological tests, their ethological validity has been questioned (Banta Lavenex and Lavenex, 2009; Taube et al., 2013). In the real world, different sensory modalities (including visual, vestibular, and proprioceptive information) provide information that is coherent. This information is integrated by the brain, including the hippocampus, to construct reliable representations of an individual's experiences. By contrast, in virtual reality studies, different inputs derived from different sensory modalities are often incoherent. In that context, Banta Lavenex et al. (2015) investigated the place learning capacities of adult individuals with DS- and MA-matched TD children in a spatial learning task carried out in a real-world, controlled environment. Participants had to locate three rewards among

12 potentially rewarded locations arranged on three nested square arrays within a 4 m × 4 m testing arena. Individuals with DS made fewer correct choices before erring, visited more locations to find the three rewards, and performed fewer errorless trials than MA-matched TD children. However, task performance varied among individuals with DS, and 50% of the individuals with DS performed above chance level. Interestingly, these individuals were able to choose preferentially the rewarded location located on the outer array, which could be identified using a low-resolution topological representation of the environment (Poucet and Benhamou, 1997). Only two individuals with DS (out of 20) were able to reliably identify the other two rewarded locations located on the middle and inner arrays, which required the ability to build a high-resolution spatial representation of the environment. These previous results thus suggest that low-resolution place learning may be relatively preserved in individuals with DS (e.g., as compared to TD children), whereas high-resolution place learning may be more impacted (e.g., as compared to TD children). Data in rodents and humans suggest that low-resolution topological coding and high-resolution metric coding implicate different hippocampal circuits, respectively, the CA1 field of the hippocampus and the dentate gyrus-CA3 field (Gilbert et al., 2001; Gilbert and Kesner, 2006; Lavenex and Banta Lavenex, 2013). Our behavioral data in individuals with DS therefore suggest that the dentate gyrus-CA3 functional circuit may be more systematically impaired, whereas CA1 function may be significantly impaired in only about half of individuals with DS. However, because participants had to remember three locations among 12 possible locations, it is not clear whether task performance was also impacted by the number of locations to be remembered (i.e., memory load). Consequently, it remains to be determined whether, as a group, individuals with DS are able to perform place learning for a single location, using a low-resolution topological representation of the environment.

Response Learning

The response learning system creates fixed stimulus–response representations of behavioral actions, also known as habits (Packard and McGaugh, 1996). This system has been shown to be subserved by the dorsal striatum in rats and humans (Packard et al., 1989; Packard and McGaugh, 1996; Yin and Knowlton, 2006). When learning a new environment, both place learning and response learning strategies are implicated (Devan et al., 1999; Voermans et al., 2004; Miyoshi et al., 2012; Woolley et al., 2013; Ferbinteanu, 2016). However, it is often reported that during the early stages of navigation both rats and humans predominantly rely on hippocampal place learning, whereas response learning strategies become more prominent as the environment and specific routes become familiar, such as when the same route is taken repeatedly (Packard and McGaugh, 1996; Packard, 1999; Chang and Gold, 2003b; Hartley et al., 2003; Iaria et al., 2003; Poldrack and Packard, 2003; Schmitzer-Torbert, 2007; Jacobson et al., 2012).

As discussed above, the ability of individuals with DS to learn a route in a virtual environment was reported as relatively preserved. Individuals with DS were able to learn the routes and did not need significantly more trials than MA-matched TD children to reach criterion (Courbois et al., 2013). Given the very short routes to be learned in that study (only two turns for each route; right, left for the first route; left, right for the second route), individuals with DS may have learned a sequence of turns along the routes, while paying very little attention to landmarks around the routes and without integrating the two routes into an allocentric spatial frame of reference (see place learning, above). To our knowledge, only one study specifically assessed response learning in individuals with DS in a real-world environment (Mangan, 1992). The experimental setup consisted of a round platform (3.65 m in diameter) containing 11 symmetrically arranged holes that could hide rewards. The response learning task required 16–28 months old individuals with DS and TD children to always turn in the same direction on the platform to find the reward. For example, after watching the reward being hidden in one of the four holes surrounding the center hole (and always the same hole for any given child), the child was moved to the center of the platform. From here, if s/he turned to the right, for example, s/he would always find the rewarded hole. Although children with DS needed more trials than TD children to solve the task, they were able to find the reward in a final probe trial, following a 1-min delay between when the object was hidden and when the child was allowed to search. These results suggested that individuals with DS are capable of response learning from 16 months of age. Note that the same participants were tested on a place learning task, but consistent with the results of other studies describing the emergence of place learning between 21 and 25 months of age (Newcombe et al., 1998; Ribordy Lambert et al., 2013; Ribordy Lambert et al., 2015), neither DS nor TD children were able to exhibit reliable place learning. The inability of individuals with DS to exhibit place learning was thus inconclusive.

Parallel Spatial Learning Systems

Even though "hippocampus-dependent" place learning and "striatum-dependent" response learning both contribute to spatial navigation, it has been hypothesized that the interaction between the two systems is competitive, rather than cooperative, and that the use or activation of one system inhibits the use or activation of the other system (Schroeder et al., 2002; White and McDonald, 2002; Chang and Gold, 2003b; Jacobson et al., 2012; Packard and Goodman, 2013). Importantly, studies in rats have demonstrated that response learning is dominant and even facilitated (i.e., more easily expressed) when the hippocampus is inactivated. By contrast, place learning is dominant when the striatum is inactivated (Packard and McGaugh, 1996; Schroeder et al., 2002; Chang and Gold, 2003b).

In that context, Bostelmann et al. (2017) tested individuals with Williams syndrome (WS), a genetic disorder associated with hippocampal abnormalities (Meyer-Lindenberg et al., 2005, 2006; Haas et al., 2014), using two basic spatial memory tasks designed to resemble the work carried out in rodents (Schroeder et al., 2002; White and McDonald, 2002; Chang and Gold, 2003b; Jacobson et al., 2012; Packard and Goodman, 2013). In the place learning task, individuals with WS exhibited severe impairments in comparison to MA-matched TD children. By contrast, in the response learning task, individuals with WS exhibited better performance than MA-matched TD. In the context of the above-described results from the lesion studies carried out in rats (Packard and McGaugh, 1996; Schroeder et al., 2002; Chang and Gold, 2003b), the performance of individuals with WS suggested that the impairment of the "hippocampus-dependent" place learning system is accompanied by the facilitation of the "striatum-dependent" response learning system in WS. It thus stands to reason that impaired hippocampal function in individuals with DS, as evidenced by deficits in high-resolution hippocampus-dependent spatial learning (Banta Lavenex et al., 2015), may result in a facilitation of response learning.

Aim of the Study

The aim of the current study was to assess the capacity of individuals with DS to perform low-resolution spatial learning, based on two dissociable memory systems: (1) the place learning system, which depends on the hippocampus and creates flexible relational representations of the environment; and (2) the response learning system, which depends on the striatum and creates fixed stimulus–response representations of behavioral actions.

We hypothesized that the majority of individuals with DS should exhibit performance similar to that of MA-matched TD children and thus to succeed at a low-resolution place learning task. However, since aspects of their place learning abilities are nevertheless impaired, suggesting hippocampal dysfunction, individuals with DS should perform better than MA-matched TD children in a low-resolution response learning task.

MATERIALS AND METHODS

Participants

Participants were 27 individuals with DS (13 males, 14 females), 19 typically developing children (10 males, 9 females), and 21 typically developed young adults (10 males, 11 females) (**Table 1**). Individuals with DS were recruited in Switzerland (*n* = 5) and in Italy (*n* = 22). All TD children and TD adults were recruited in Switzerland. Since no behavioral or performance differences were observed between the Swiss and the Italian participants with DS the data for these two populations were grouped for analysis and presentation. The parents and/or caregivers of participants with DS were asked whether the individual exhibited any possible signs of age-related dementia. None of our participants was signaled as showing any signs of dementia onset.

TABLE 1 | Participants.

	Chronological age (years)				Mental age (years)			
	Mean	**SD**	**Min**	**Max**	**Mean**	**SD**	**Min**	**Max**
DS	23.4	7.7	15.0	43.5	5.6	0.7	4.7	7.0
TD-C	5.5	1.2	3.5	8.1	6.6	1.3	4.7	8.7
TD-A	21.0	2.0	18.3	25.5	–	–	–	–

Chronological and mental ages for individuals with DS (n = 27; NB: the MA for three individuals with DS was not available), typically developing children (TD-C, n = 19), and typically developed young adults (TD-A, n = 21).

Typically developing children with a chronological age similar to the MAs of the individuals with DS were recruited and tested in Switzerland. The MA of all TD children and 24 of 27 participants with DS was determined using the Leiter International Performance Scale-Revised (Leiter-R; Subtests included in the Brief IQ from which MA is calculated are: Figure Ground, Form Completion, Sequential Order, and Repeated Patterns) (Roid and Miller, 1997). TD children were reported by their parents to have been typically developing, and were neither born prematurely, nor had any suspected or diagnosed neurological conditions or learning disabilities. Two TD children (siblings) had strabismus that had been corrected, but both were diagnosed as lacking stereoscopic vision (i.e., depth perception). Since these two children behaved in a typical manner for the TD children, we included them in the study. The statistical analyses led to the same conclusions whether we included these two children or not. In sum, we did not exclude any recruited individuals with DS or TD children from our study. The TD adult group was not specifically matched for chronological age with our DS participants, although the mean age of the two groups did not differ statistically. TD adults reported to have been typically developing, and were neither born prematurely, nor had any suspected or diagnosed neurological conditions or learning disabilities. The results of the TD children were previously published in Bostelmann et al., 2017.

Participants were tested on the place learning task and the response learning task anywhere from 1 day to several months apart. Each session lasted approximately 45 min. Testing took place between 8:00 a.m. and 6:30 p.m. Human subjects research was approved by the Cantonal Ethics Commission for Human Research (Vaud, Switzerland; protocol no. 60/14), and was in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects in research. The participants (TD adults and some individuals with DS) or the parents of the TD children and the participants with DS gave informed written consent.

Testing Facilities

Five individuals with DS, and all the TD children and TD adults were tested at the University of Lausanne, Switzerland. Twenty-two individuals with DS were tested in Nardò, Italy. The main features of the testing facilities were consistent between the two sites. Testing took place within large rectangular rooms (8 m × 8 m in Vaud and 16 m × 10 m in Nardò) containing many polarizing features such as doors, tables, chairs, wall posters, etc. Within the room was a 4 m × 4 m testing arena (**Figure 1**) that consisted of three walls made of suspended, opaque curtains (2 m high). Whereas the curtain on the back wall was 4 m wide, the curtains on the side walls extended only 3 m, so that there was a 50 cm gap at the front and the back of the wall, thus creating four entry points ("doors") through which participants passed in order to enter and exit the arena. The fourth (front) boundary of the arena was delineated by a rope extending to the two opposing sides of the arena, and suspended 30 cm off the ground. Exterior to the two side walls, the inter-trial waiting area was a corridor

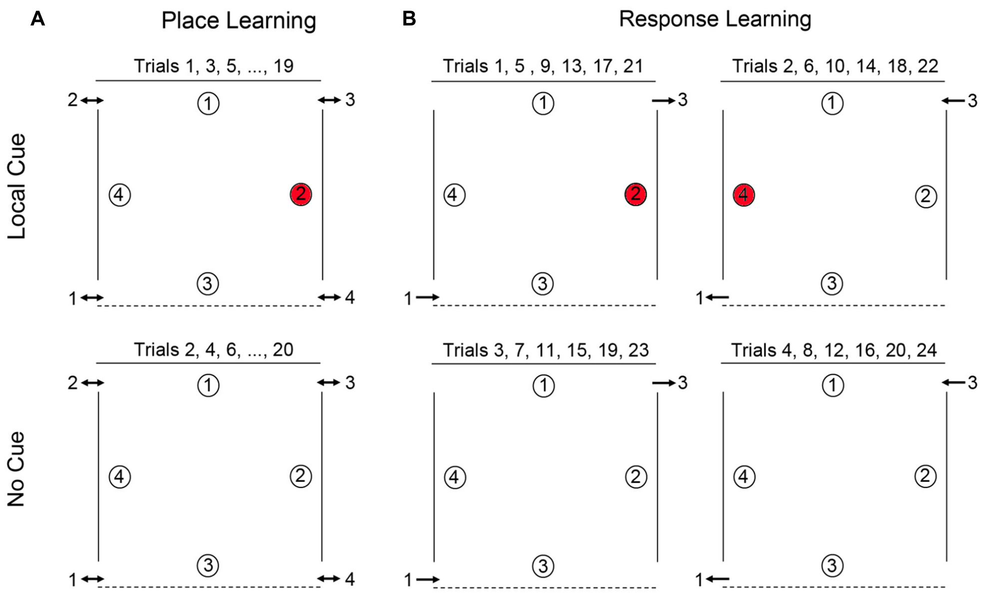

FIGURE 1 | Schematic representation of the open-field arena used for testing place learning **(A)** and response learning **(B)**. For place learning, the reward was always placed at the same location within the arena (location 2 for 50% of the participants and location 4 for the other 50% of the participants). For response learning, the reward (at either location 2 or location 4 on alternate trials) could be found by performing the same motor response upon entering the arena.

(2 m × 4 m) that contained two chairs with their backs to the arena and objects that were unique to each side. From within the arena, and from the inter-trial waiting area, participants had access to distant visual cues in front of the arena. Objects found in front of the arena (a table, chairs, one experimenter, camera, etc.) were placed 2 m away from the front of the arena.

The arena's floor was uniform and thus provided no visual guidance cues. The testing arena was empty except for four white paper plates (18 cm in diameter) placed at the cardinal points in the arena (**Figure 1**). An inverted opaque plastic cup (7.5 cm in diameter, 6.5 cm high) was placed on each paper plate. A reward was placed under the inverted cup at one location. Participants had to lift or turn over the plastic cups to obtain the reward. Rewards were coins for individuals with DS and TD adults, and "treats" (e.g., Smarties®, Goldfish® crackers, pieces of breakfast cereal or pretzels) for TD children. TD adults and parents of TD children were queried with respect to alimentary allergies prior to testing, and children were asked whether there were any treats that they did not like, which would be excluded as rewards during their testing session. All testing was videotaped with a video camera located in front of the arena.

General Testing Procedures

For individuals with DS and TD children, testing involved a team of two experimenters. Experimenter 1 (E1) would stay with the participant throughout the testing session and would enter the arena with the participant, encourage the participant to search for the hidden rewards, verbally praise the participant when a reward was found, remove cups from unrewarded locations as soon as they had been searched by a participant, direct the participant to the correct exit at the end of the trial, and occupy the participant during the inter-trial interval by reading to or conversing with the participant. Experimenter 2 (E2) was responsible for replacing the reward between trials, recording the data, and announcing the correct entry and exit doors to E1. Before testing began, participants viewed the arena with the four arranged plates (no inverted cups were present), from in front of the arena. While still in front of the arena, E1 showed the participant a reward item on a paper plate that she held in her hand. While the participant was watching, E1 would lower a plastic white cup over the reward to hide it. The participant would then be asked "Where is the treat/coin? Can you show me where it is?" When the participant lifted the cup to expose the reward, s/he would be verbally praised and told that it was hers/his to keep. Once the participant had been shown that a reward could be found underneath the plastic cup, the participant and E1 would go to the predetermined side of the arena where testing would begin. Once the participant was behind the curtain and occupied, E2 would hide a reward at the predetermined reward location. For TD adults, only experimenter E2 was present, and the participants were directed to the correct entrances when E2 called out a number that hung next to the entrance on the outside of the arena, or when E2 pointed to the specific exit when they were inside the arena.

In both the place and response learning tasks, participants completed two different types of trials: (1) *Local cue trials*, in which a local cue, specifically a red cup, covered the reward, whereas the three non-rewarded locations were covered with white cups (**Figure 1**). To find the reward, participants could search for the red cup or rely on place or response learning to identify the reward location (see below). This condition allowed us to assess the participants' motivation to search for the reward and their overall understanding of the task. (2) *No cue trials*, in which no local cue marked the reward location, as identical white cups covered all locations. In this case, participants could not discriminate between rewarded and never-rewarded locations based on local features, but instead had to rely on either a place learning strategy or a response learning strategy to identify the rewarded location. Half of the participants performed the place learning task first, the other half performed the response learning task first. Analyses showed that performance was not influenced by whether participants completed the place learning task or the response learning task first.

Place Learning

Place learning was assessed by testing the ability of individuals with DS, TD children, and TD adults to learn and remember the location of one reward among four potentially rewarded locations (**Figure 1A**). For each participant, one location in the arena was chosen as the goal location: for half of the participants, location 4 was the designated goal, for the other half location 2 (locations 1 and 3, whose positions were distinct, were never goal locations). Each participant completed a total of 20 alternating local cue and no cue trials, with a 15-min break after the first 10 trials (*NB*: TD adults did not receive a break). There were four entries and exits to the arena. In order to preclude the use of egocentric and response strategies, participants were obliged to enter and exit the arena from a different door for every trial, and could never enter through a door they had just exited through on the immediately preceding trial. Entry order was determined in a pseudo-random manner, with respect to the following conditions: (1) all entrances should be used an equal number of times in the two conditions (local and no cue conditions); (2) participants may never enter the arena through a door which they had just exited on the immediately preceding trial (to preclude the use of egocentric strategies); (3) a no cue trial may never have the same entrance as the immediately preceding local cue trial; and (4) all entries must be made from the same side (right or left) that the participant just exited on the previous trial (i.e., participants were not moved from one side of the arena to the other between trials). At the end of the trial, E2 would point to the appropriate exit and E1 would guide the participant to that exit by pointing or by heading there first, therefore, ensuring that the participant was on the appropriate side of the arena for the next trial. Participants were thus constantly moving about the arena from trial to trial, entering and exiting on different sides, and at the back or front of the arena. Moreover, no environmental landmarks, such as doors, windows, or furniture, could be found adjacent to or directly behind any of the reward locations (with the exception of the red cups in the local cue condition). Consequently, in order to identify the reward location in the absence of the local cue, participants must rely on place learning: they must be able to learn and remember the reward location in relation to distal objects in the environment.

Response Learning

Response learning was assessed by testing the ability of individuals with DS, TD children, and TD adults to learn and remember the location of one reward. In this task, location 2 and location 4 were alternately rewarded. On all odd numbered trials participants entered through door 1, location 2 was rewarded, and exited through door 3 (**Figure 1B**). On all even-numbered trials, participants entered through door 3, location 4 was rewarded, and exited through door 1. Participants thus had to learn that they could find the reward by performing a fixed motor response from the entrance point. Each participant completed pairs of local cue trials and pairs of no cue trials in alternation (2 local cue trials followed by 2 no cue trials for a total of 24 trials total), with a 15-min break after the first 12 trials. Response learning proceeded as follows: Trials 1, 5, 9, 13, 17, and 21, with Local Cue: enter door 1, location 2 rewarded, exit door 3. Trials 2, 6, 10, 14, 18, and 22, with Local Cue: enter door 3, location 4 rewarded, exit door 1. Trials 3, 7, 11, 15, 19, and 23, No Cue: enter door 1, location 2 rewarded, exit door 3. Trials 4, 8, 12, 16, 20, and 24, No Cue: enter door 3, location 4 rewarded, exit door 1. Thus, from trial-to-trial, the location of the reward changed in relation to the global environment, but remained constant relative to the door just used by the participant to enter the arena. Consequently, in order to identify the reward location in the absence of the local cue, participants must rely on response learning: they must be able to learn to associate the reward location with a fixed motor response from the door used to enter the arena.

Verbal Instructions and Feedback

For the first local cue trial of both the place and response learning tasks, as participants first entered the arena, E1 would ask the participant "Where do you think the reward is hidden?". For each subsequent trial, upon entering the arena, E1 would simply prompt the participant by saying "Show me where the reward is hidden". In order to determine unequivocally whether individuals with DS could succeed at place learning when given access to coherent visual, vestibular and proprioceptive information, and to preclude poor task comprehension from negatively influencing performance, after individuals with DS, TD children, and TD adults found the reward on the first two trials (one local cue trial and one no cue trial) of the place learning task, E1 explained that the reward would always be found at this exact same location (while pointing at the rewarded plate with the red cup hidden from view). This same explanation was repeated to individuals with DS that did not identify the rewarded location for up to the first five local cue and no cue trials (or until they became annoyed, told E1 that they remembered the rule, and asked E1 to stop repeating that instruction). For the response learning task, the experimenter gave no explanation to the participants about finding the reward in any particular location since the premise behind response learning is that individuals rely on a stimulus–response "habit" ("I do this"), and thus the rule is the solution. Note that for the place learning task, the rule ("always here") is not the same as the solution (i.e., using place learning to identify where "here" is). Thus, although participants were told the rule, they would not be able to follow this rule if they were not capable of place learning (i.e., identifying the target location relative to distal objects and locations in the environment).

Data Analysis

We performed general linear model (GLM) analyses to compare the number of correct first choices (i.e., choosing the reward location as their first choice upon entering the arena) that participants made on the last eight trials (thus omitting the first two local cue trials and the first two no cue trials in the place learning task, and the first two pairs of trials – the first two pairs of local cue trials and the first two pairs of no cue trials – in the response learning task), between groups (DS individuals, TD children, and TD adults), between conditions (local cue vs. no cue), and between spatial tasks (place learning vs. response learning). All statistical analyses were performed with the SPSS 21.0 software. *Post hoc* analyses were performed with the Fisher-least significant difference test when the ANOVA *F* ratio was significant, thus controlling for Type I error rate (Carmer and Swanson, 1973). Significance level was set at $P < 0.05$ for all analyses. We report effect size with η_p^2 [partial eta squared: SSeffect/(SSeffect + SStotal); the sum of squares of the effect divided by the total sum of squares + the sum of squares of the effect; as reported by SPSS 21.0] for ANOVAs, as well as Cohen's ds [difference between means/pooled standard deviation; or ds = t^*sqrt($1/n1 + 1/n2$)] for unpaired t-tests and Cohen's *dz* (*dz* = *t*/ sqrt(*n*)) for paired samples *t*-tests (Lakens, 2013).

The data on the number of correct choices suggested that individuals with DS and TD children exhibited a bimodal performance distribution. The majority of individuals with DS made very few or no errors on the place learning task, whereas a number of individuals made very few or no correct choices. This suggests that the average number of correct choices alone may not be sufficient to represent task performance. To provide additional information, we compared the number of individuals who performed above chance on each task across the three groups. Above chance performance in the place and response learning tasks was determined for each individual with a non-parametric Wilcoxon signed-rank test comparing the number of correct first choices (visiting a rewarded location) and the number of incorrect first choices (visiting a non-rewarded location) for the last eight place and response learning trials. Since an analysis of choices for all individuals, both those that passed and those that did not pass, showed that errors were distributed across the three incorrect locations (and were not restricted to the opposite location), we normalized the number of correct and incorrect choices based on the probability to make those choices: the number of correct choices was divided by one and the number of incorrect choices was divided by three. Importantly, when calculated as such, this level of above chance performance is equivalent to making six correct first choices on the last eight trails (i.e., 75% correct). The number of individuals with DS, MA-matched TD children, and TD adults who solved one, two, or neither of these tasks were compared with the log-likelihood ratio for contingency tables (Zar, 1999).

RESULTS

In order to characterize the place learning and response learning capacities of individuals with DS, MA-matched TD children, and TD adults, we analyzed the proportion of correct choices (i.e., choosing the reward location as their first choice upon entering the arena) in both the place learning and response learning tasks, in presence or absence of a local cue (a red cup) marking the reward location (**Figure 2**). A global GLM analysis revealed differences between experimental groups [$F_{(2,64)} = 8.460$, $P = 0.001$, $\eta_p^2 = 0.209 = 0.209$, power = 0.958; TD adults > TD children = DS individuals] and cue conditions [$F_{(1,64)} = 33.199$, $P < 0.001$, $\eta_p^2 = 0.342$, power = 1.000; Local cue > No cue], as well as an interaction between groups and cue conditions [$F_{(2,64)} = 6.058$, $P = 0.004$, $\eta_p^2 = 0.159$, power = 0.870]. There was also a difference between the two types of spatial tasks [place learning vs response learning: $F_{(1,64)} = 18.680$, $P < 0.001$, $\eta_p^2 = 0.226$, power = 0.989]. Moreover, there were significant interactions between cue conditions and spatial tasks [$F_{(1,64)} = 21.334$, $P < 0.001$, $\eta_p^2 = 0.250$, power = 0.995], between spatial tasks and experimental groups [$F_{(2,64)} = 6.050$, $P = 0.004$, $\eta_p^2 = 0.159$, power = 0.870], and between cue conditions, spatial

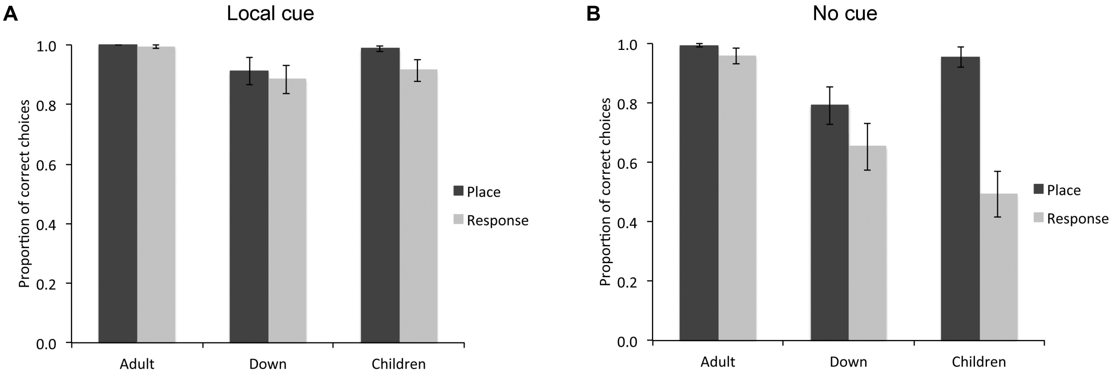

FIGURE 2 | Proportion of correct choices (i.e., choice of the rewarded location as the first choice upon entering the arena; mean ± SEM) made by individuals with DS ($n = 27$), TD children ($n = 19$), and TD adults ($n = 21$) in the place learning and response learning tasks, in presence **(A)** or absence **(B)** of a local cue marking the reward location.

tasks, and experimental groups [$F_{(2,64)}$ = 7.306, P = 0.001, η^2_p = 0.186, power = 0.927].

Local Cue

When a red cup marked the goal location (**Figure 2A**), the difference between groups just failed to reach significance [$F_{(2,64)}$ = 3.046, P = 0.054, η^2_p = 0.087, power = 0.570], although individuals with DS (M = 0.899, SE = 0.026) made fewer correct choices than TD adults (M = 0.997, SE = 0.030; P = 0.017). There was no difference in performance between place learning and response learning tasks [$F_{(1,64)}$ = 2.314, P = 0.133, η^2_p = 0.035, power = 0.322] and no interaction between spatial tasks and experimental groups [$F_{(2,64)}$ = 0.653, P = 0.524, η^2_p = 0.020, power = 0.155]. In the place learning task with a local cue, there was no difference between groups [$F_{(2,64)}$ = 2.356, P = 0.103, η^2_p = 0.069, power = 0.460]. In the response learning task with a local cue, there was no significant difference between groups [$F_{(2,64)}$ = 2.246, P = 0.114; η^2_p = 0.066, power = 0.441].

Within group comparisons revealed that TD children made more correct choices in the place learning task than in the response learning task [$t_{(18)}$ = 2.158, P = 0.045, Cohen's dz = 0.495; place learning: M = 0.987, SE = 0.009; response learning: M = 0.915, SE = 0.037). The performance of TD adults [$t_{(20)}$ = 1.000, P = 0.329, Cohen's dz = 0.218) and individuals with DS [$t_{(26)}$ = 0.536, P = 0.596, Cohen's dz = 0.103] did not differ between the place learning and response learning tasks.

In sum, in the presence of a red cup marking the reward location, although TD adults, TD children and individuals with DS performed well above chance, TD children made more correct choices in the place learning task than in the response learning task, whereas no difference was found between the two tasks for the DS group, or the TD adult group.

No Cue

When the reward location was not marked by a local cue (**Figure 2B**), there was a difference between experimental groups [$F_{(2,64)}$ = 9.619, P < 0.001, η^2_p = 0.231, power = 0.977], a difference between place learning and response learning tasks [$F_{(1,64)}$ = 24.492, P < 0.001, η^2_p = 0.277, power = 0.998], and an interaction between spatial learning tasks and experimental groups [$F_{(2,64)}$ = 8.119, P = 0.001, η^2_p = 0.202, power = 0.951]. In the place learning task without a local cue, there was a difference between groups [$F_{(2,64)}$ = 5.489, P = 0.006, η^2_p = 0.146, power = 0.834]. TD adults (M = 0.994, SE = 0.049) and TD children (M = 0.955, SE = 0.051) performed similarly (P = 0.579), and made more correct choices than individuals with DS (M = 0.793, SE = 0.043; both P < 0.05). Note that if we consider only the performance of the individuals performing above chance level (including 21/21 TD adults, 21/27 individuals with DS, and 18/19 TD children), the overall statistical difference between groups remained [$F_{(2,57)}$ = 3.186, P = 0.049, η^2_p = 0.101, power = 0.587]. Specifically, individuals with DS (M = 0.953, SE = 0.018) made fewer correct choices than TD adults (M = 0.994, SE = 0.006; P = 0.02), but their performance did not differ from that of TD children (M = 0.987, SE = 0.009; P = 0.067).

In the response learning task without a local cue, there was a difference between groups [$F_{(2,64)}$ = 10.730, P < 0.001, η^2_p = 0.251, power = 0.987]. TD adults (M = 0.959, SE = 0.071) performed overall better than individuals with DS (M = 0.654, SE = 0.062) and TD children (M = 0.495, SE = 0.074; both P < 0.01), but individuals with DS performed similarly to TD children (P = 0.173). Note that if we consider only the performance of the individuals performing above chance level (including 17/21 TD adults, 15/27 individuals with DS, and only 3/19 TD children), there was no difference between groups [$F_{(2,32)}$ = 0.419, P = 0.662, η^2_p = 0.025, power = 0.112; DS individuals: M = 0.992, SE = 0.008; TD adults: M = 0.978, SE = 0.016; TD children: M = 1.000, SE = 0.000].

The performance of TD adults did not differ between place learning and response learning tasks [$t_{(20)}$ = 1.305, P = 0.207, Cohen's dz = 0.284; place learning: M = 0.994, SE = 0.006; response learning: M = 0.959, SE = 0.026]. Similarly, the performance of individuals with DS did not differ between the two learning tasks [$t_{(26)}$ = 1.650, P = 0.111, Cohen's dz = 0.317; place learning: M = 0.793, SE = 0.063; response learning: M = 0.654, SE = 0.079]. By contrast, TD children made more correct choices in the place learning task than in the response learning task [$t_{(18)}$ = 5.561, P < 0.001, Cohen's dz = 1.275; place learning: M = 0.955, SE = 0.033; response learning: M = 0.495, SE = 0.078].

In sum, as a group, in the place learning task without a local cue, individuals with DS made fewer correct choices than TD children and TD adults. In the response learning task without a local cue, individuals with DS made fewer correct choices than TD adults, but performed similarly to TD children. TD children performed better in the place learning task than in the response learning task, whereas individuals with DS performed similarly in both tasks.

Within Group Comparisons Across All Conditions

Within group comparisons of performance in the four experimental conditions confirmed the contrasting behavioral patterns observed for individuals with DS, TD children, and TD adults, in the place learning and response learning tasks.

The performance of TD adults did not differ between the four experimental conditions [$F_{(3,60)}$ = 1.864, P = 0.145, η^2_p = 0.085, power = 0.460].

Typically developing children made more correct choices when the local cue was present in the place learning task than in the response learning task, and more correct choices in both of these conditions than in the response learning task without the local cue [$F_{(3,54)}$ = 28.748, P < 0.001, η^2_p = 0.615, power = 1.000; place learning with local cue > response learning with local cue > response learning without local cue; all P < 0.05]. In addition, without the local cue, TD children made more correct choices in the place learning task than in the response learning task (P < 0.001). By contrast, TD children did not differ in the number of correct choices in the place learning task with and without the local cue (P = 0.263).

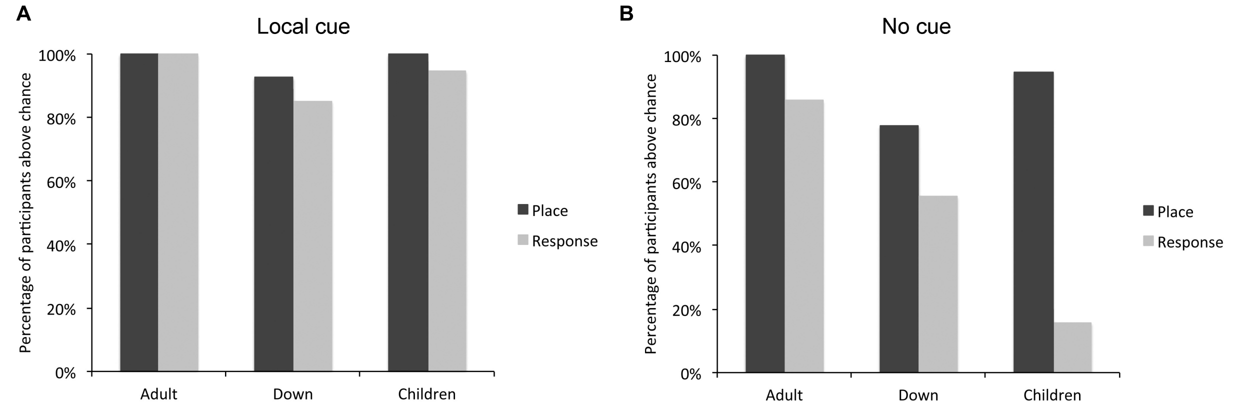

FIGURE 3 | Percentage of individuals with DS (n = 27), TD children (n = 19), and TD adults (n = 21) who performed above chance level in the place learning and response learning tasks, in presence **(A)** or absence **(B)** of a local cue marking the reward location.

The performance of individuals with DS also differed between testing conditions [$F_{(3,78)} = 5.393$, $P = 0.002$, $\eta_p^2 = 0.172$, power = 0.924]. Individuals with DS made more correct choices in the place learning task with the local cue than in the place learning and response learning tasks without the cue (both $P < 0.05$). In addition, individuals with DS made more correct choices in the response learning task with the cue than in the response learning task without the cue ($P = 0.003$).

In sum, contrary to TD children and TD adults, individuals with DS made fewer correct choices in the place learning task without the local cue than with the local cue. In the response learning task, TD children and individuals with DS made fewer correct choices in the absence of the local cue than when the local cue marked the reward location.

Individual Analyses

We also determined how many individuals with DS, TD children, and TD adults performed above chance level, and therefore demonstrated their ability to solve either the place learning or response learning tasks, in presence or absence of the local cue (**Figure 3**). In the presence of the local cue, the number of participants who performed above chance level in the place learning and response learning tasks did not differ between groups [log likelihood ratio test: $X^2_{(2)} = 0.040$, $P = 0.980$]. Moreover, there was no difference in the number of participants who successfully performed the place learning or response learning task within each group [TD adults: $X^2_{(1)} = 0$, $P = 1$; individuals with DS: $X^2_{(1)} = 0.763$, $P = 0.382$; TD children: $X^2_{(1)} = 1.413$, $P = 0.234$].

By contrast, in absence of the local cue, the number of participants who succeeded (i.e., performed above chance level) at the place learning and response learning tasks differed between groups [log likelihood ratio test: $X^2_{(2)} = 7.059$, $P = 0.029$]. The number of individuals with DS who succeeded at the place learning and response learning tasks did not differ [$X^2_{(1)} = 3.043$, $P = 0.081$]. By contrast, more TD children succeeded at the place learning task than the response learning task [$X^2_{(1)} = 27.848$, $P < 0.0001$], and more TD adults succeeded at the place learning task than the response learning task [$X^2_{(1)} = 4.390$, $P = 0.037$]. For TD adults, the difference was due to the fact that whereas all TD adults succeeded at place learning, three reported using a conditional place strategy to solve the response task (i.e., they remembered which location was rewarded last and chose the opposite location) and one simply failed to identify the rewarded locations consistently. The other 17 TD adults both succeeded at the task and reported using a response strategy. By definition, the use of a response strategy implies that the participant does not use a cognitive place strategy to identify the rewarded location; instead, they recall only the rule "when I am here, I go there." In sum, whereas more TD children (and TD adults) succeeded at the place learning task compared to the response learning task, this difference was not significant in DS.

In addition, we further determined how many individuals with DS, TD children, and TD adults demonstrated their ability to solve both, either or none of the place learning or response learning tasks when no local cue marked the reward location, in order to assess whether the ability to complete one task may be associated with the inability to complete the other task (**Table 2**).

The number of participants who solved both, either or none of the two tasks differed between groups [log likelihood ratio test: $X^2_{(6)} = 27.159$, $P < 0.001$]. In the place learning task, the number of participants who performed above chance level differed between groups [$X^2_{(2)} = 8.425$, $P = 0.015$]. Fewer individuals with DS performed above chance level than TD

TABLE 2 | Individual performance.

	Place Yes Response Yes	**Place Yes Response No**	**Place No Response Yes**	**Place No Response No**
DS individuals	13	8	2	4
TD children	3	15	0	1
TD adults	17	4	0	0

Number of individuals with DS (from n = 27), TD children (from n = 19), and TD adults (from n = 21), who performed above chance level in the place learning and/or the response learning tasks in absence of the local cue.

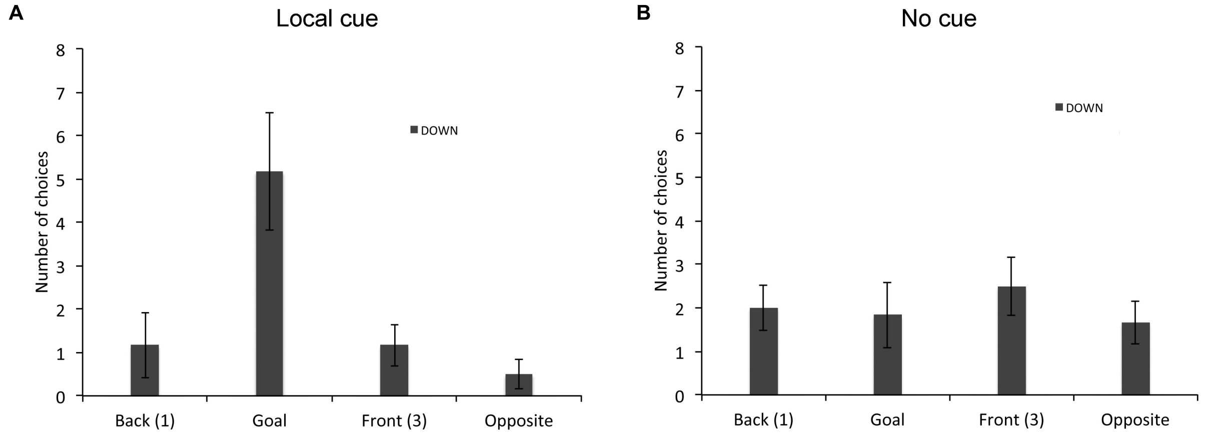

FIGURE 4 | Proportion of choices (goal location (2), opposite location (4), back location (1), or front location (3), as the first choice upon entering the arena; mean +/− SEM) made by individuals with DS, who did not perform above chance level the place learning task, in presence **(A)** or absence **(B)** of a local cue marking the reward location.

adults [$X^2_{(1)} = 7.566$, $P = 0.006$]. TD children did not differ from TD adults [$X^2_{(1)} = 1.517$, $P = 0.218$] or individuals with DS [$X^2_{(1)} = 2.795$, $P = 0.094$]. In the response learning task, the number of participants who performed above chance level differed between groups [$X^2_{(2)} = 18.627$, $P < 0.001$]. Fewer TD children performed above chance level than TD adults [$X^2_{(1)} = 18.427$, $P < 0.001$] and individuals with DS [$X^2_{(1)} = 7.908$, $P < 0.005$]; the difference between individuals with DS and TD adults failed to reach significance [$X^2_{(1)} = 3.559$, $P = 0.059$].

In sum, the analyses of individual performance suggest that TD adults can succeed at both place and response learning, whereas TD children are preferentially place learners and have difficulty with response learning. By contrast, individuals with DS exhibit an intermediate pattern, with place learning capacities similar to those of TD children, but response learning capacities similar to those of TD adults.

Choice Analyses

Finally, we analyzed the types of choices made by individuals who did not perform above chance level in the place or response learning task in absence of the local cue. In the place learning task, since all TD adults performed the task and only one of the 19 TD children did not succeed without the local cue, we restricted this analysis to the six individuals with DS who did not perform above chance level in absence of the local cue (**Figure 4**). A repeated-measures GLM analysis revealed no main effect of locations [$F_{(3,15)} = 2.283$, $P = 0.121$, $\eta_p^2 = 0.313$, power = 0.465], but a significant interaction between locations and cue conditions [$F_{(3,15)} = 5.445$ $P = 0.010$, $\eta_p^2 = 0.521$, power = 0.857]. In presence of the local cue (**Figure 4A**), the six individuals with DS chose preferentially the goal location over the opposite location [$F_{(3,15)} = 5.000$, $P = 0.013$, $\eta_p^2 = 0.500$, power = 0.824; goal > opposite: $P = 0.031$]. By contrast, in absence of the local cue (**Figure 4B**), individuals with DS did not discriminate between the four locations [$F_{(3,15)} = 0.255$, $P = 0.856$, $\eta_p^2 = 0.049$, power = 0.088], suggesting that as a group they exhibited no consistent pattern of behavior (e.g., a response strategy would result in the "opposite" location being chosen on 50% of the trials, whereas a "first cup seen" strategy would result in locations 1 ("Back") and 3 ("Front") each being chosen 50% of the time).

In the response learning task (**Figure 5**), we compared the choices of individuals with DS (*n* = 12) and TD children (*n* = 16) that did not perform above chance. A repeated-measures GLM analysis revealed a main effect of locations [$F_{(3,72)} = 27.999$, $P < 0.001$, $\eta_p^2 = 0.538$, power = 1.000], an interaction between groups and locations [$F_{(3,72)} = 2.876$, $P = 0.042$, $\eta_p^2 = 0.107$, power = 0.664] and an interaction between conditions and locations [$F_{(3,72)} = 60.626$, $P < 0.001$, $\eta_p^2 = 0.716$, power = 1.000]. The analysis of the choices of individuals with DS revealed a main effect of locations [$F_{(3,33)} = 7.639$, $P = 0.001$, $\eta_p^2 = 0.410$, power = 0.977], and an interaction between locations and cue conditions [$F_{(3,33)} = 22.822$ $P < 0.001$, $\eta_p^2 = 0.675$, power = 1.000]. In presence of the local cue (**Figure 5A**), individuals with DS chose preferentially the goal location over the other three locations [$F_{(3,13)} = 22.317$, $P < 0.001$, $\eta_p^2 = 0.670$, power = 1.000; all $P < 0.01$). By contrast, in absence of the local cue (**Figure 5B**), individuals with DS did not discriminate between the four locations [$F_{(3,33)} = 1.955$, $P = 0.140$, $\eta_p^2 = 0.151$, power = 0.458]. The analysis of the choice of TD children also revealed a main effect of locations [$F_{(3,39)} = 32.364$, $P < 0.001$, $\eta_p^2 = 0.713$, power = 1.000], and an interaction between locations and cue conditions [$F_{(3,39)} = 41.139$, $P < 0.001$, $\eta_p^2 = 0.760$, power = 1.000]. In presence of the local cue (**Figure 5A**), TD children chose preferentially the goal location over the other three locations, which did not differ from each other [$F_{(3,39)} = 109.792$, $P < 0.001$, $\eta_p^2 = 0.894$, power = 1.000; all $P < 0.001$]. By contrast, in absence of the local cue (**Figure 5B**), TD children did not discriminate between the four locations [$F_{(3,39)} = 1.058$, $P = 0.378$, $\eta_p^2 = 0.075$, power = 0.264].

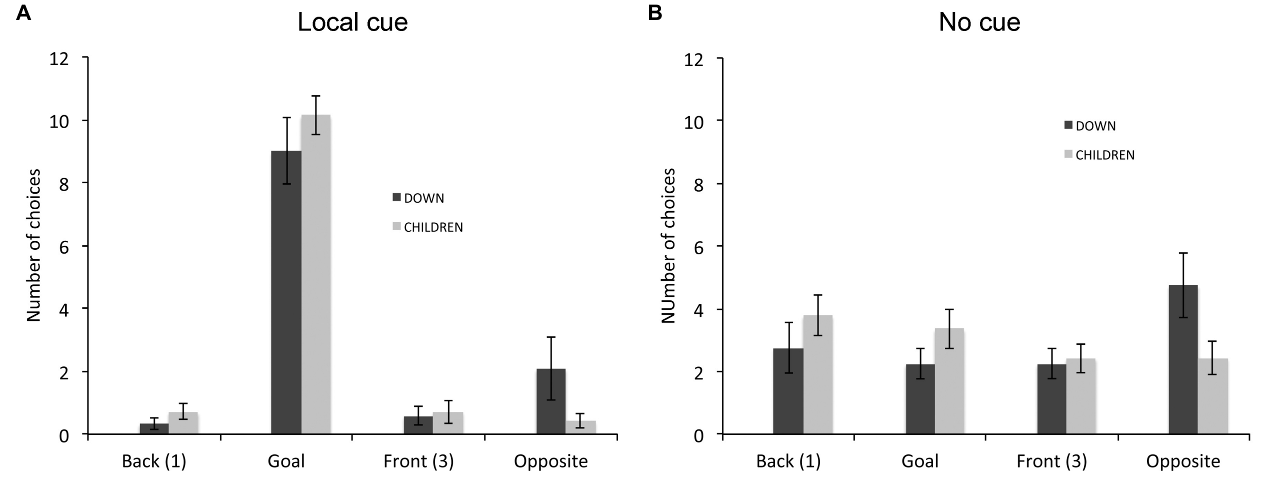

FIGURE 5 | Proportion of choices (goal location (2), opposite location (4), back location (1), or front location (3), as the first choice upon entering the arena; mean ± SEM) made by individuals with DS and TD children, who did not perform above chance level the response learning task, in presence **(A)** or absence **(B)** of a local cue marking the reward location.

In sum, in the place learning task, although the average number of correct choices made by individuals with DS was lower than those made by MA-matched TD children and TD young adults, the number of individuals with DS who performed above chance level did not differ from TD children, suggesting a relative preservation of low-resolution place learning abilities in DS. In the response learning task, the average performance of individuals with DS was lower than that of TD adults, but it did not differ from that of TD children. Moreover, the number of individuals with DS who performed the response learning task above chance level did not differ from TD adults, and was higher than that of TD children, suggesting a slight enhancement of low-resolution response learning abilities in DS.

DISCUSSION

We investigated the capacities of individuals with DS to solve low-resolution, place learning and response learning tasks, which are thought to be subserved by two different functional brain networks. Individuals with DS exhibited relatively preserved low-resolution place learning capacities and somewhat facilitated response learning capacities, as compared to TD children. Together with our previous findings of severe impairments in high-resolution place learning capacities in DS (Banta Lavenex et al., 2015), and our previous findings of severe impairments in low-resolution place learning and facilitated response learning in WS (Bostelmann et al., 2017), our current findings support the hypothesis that impairments in some components of the "hippocampus-dependent" place learning system may facilitate "striatum-dependent" response learning.

Place Learning Capacities in DS

First, it is important to emphasize that all participants from the three different groups (individuals with DS, MA-matched TD children and TD adults) were able to discriminate the rewarded location in presence of the local cue, in both the place learning and response learning tasks. This finding shows that individuals with DS (1) understood the objectives of the task; (2) could initiate and sustain a selective search; and (3) inhibit searching unrewarded locations when they knew the location of the hidden reward. In the place learning task, when no local cue marked the reward location, as a group individuals with DS made fewer correct choices, as compared to both TD children and TD adults. However, since six of 27 individuals with DS made numerous errors and 21 individuals with DS performed above chance and made very few errors, treating all individuals with DS as a homogeneous group may not be most appropriate way to describe their capacities. Indeed, when considering only the individuals who performed above chance level, although individuals with DS made fewer correct choices than TD adults, their performance did not differ from that of TD children. Moreover, the average number of correct choices may not be the most appropriate indicator of group performance. By contrast, we found that the number of individuals with DS who performed the place learning task above chance level was not significantly different from TD children. Altogether, these findings suggest that although individuals with DS did not reach the performance level of TD adults, they exhibited a relative preservation of low-resolution place learning, with 21/27 of individuals with DS exhibiting capacities similar to those of MA-matched TD children.

By contrast, we have previously shown that individuals with DS were severely impaired, as compared to MA-matched TD children, in a high-resolution place learning task in which participants had to find three rewards among twelve potentially rewarded locations (Banta Lavenex et al., 2015). Indeed, only 50% of the individuals with DS in that study performed above chance level. Moreover, these individuals choose preferentially the rewarded location located on the outer array, which could be identified by using a low-resolution topological representation of the environment (Poucet and Benhamou, 1997). TD children, on the other hand, consistently showed that they were able to identify the other two rewarded locations located on the middle and inner arrays, which required the ability to build a high-resolution spatial representation of the environment. Only two individuals with DS (10%) were able to reliably identify the two rewarded locations on the middle and inner arrays. Our previous findings thus differ from those of the present study in which we found that 78% of the individuals with DS were capable of succeeding at a low-resolution place learning task.

We believe that the overall pattern of results exhibited by individuals with DS as compared to TD children and adults, rather than any single measure, is informative for deciphering the relative preservation or impairment of their spatial learning and memory capacities. The majority of individuals with DS demonstrate relatively preserved low-resolution place learning capacities (similar to TD children, but impaired as compared to TD adults), but severely impaired high-resolution place learning capacities (as compared to TD children). These behavioral findings support the hypothesis that some specific hippocampal circuits may be particularly impacted in DS. Indeed, different functional pathways within the hippocampal formation are thought to contribute to complementary but partially dissociable spatial coordinate systems (Rolls and Kesner, 2006). A direct projection from the entorhinal cortex to CA1 is thought to be able to subserve basic allocentric spatial processing (Brun et al., 2002; Lavenex and Banta Lavenex, 2013). By contrast, imaging studies in humans, neurophysiological studies in rats, and computational models, have established that the dentate gyrus, together with its connections to CA3, subserve a process known as pattern separation (Kesner, 2007; Bakker et al., 2008), which subserves the discrimination of spatial locations that are close to one another (Kesner, 2007; Morris et al., 2012). In accordance with this hypothesis, disrupting the CA3 input to CA1 results in decreased spatial tuning of CA1 place cells (Brun et al., 2002; Nakashiba et al., 2008), suggesting the necessity of the dentate gyrus to CA3 functional circuit for building high-resolution spatial representations, even though it is not required for building low-resolution spatial representations. The fact that individuals with DS have relatively preserved low-resolution place learning capacities, but impaired high-resolution place learning capacities suggest that the function of CA1 may be relatively preserved, whereas the function of the dentate gyrus/CA3 region may be more generally and severely impaired. Indeed, although structural MRI studies have reported smaller hippocampal volumes in children (Pinter et al., 2001) and adults (Raz et al., 1995; Aylward et al., 1999) with DS, neuropathological findings suggest possibly greater abnormalities in the dentate gyrus (Contestabile et al., 2010). Non-invasive functional studies, as well as detailed post-mortem neuropathological studies will be needed to provide additional evidence necessary to answer this question.

Response Learning Capacities in DS

The second aim of our study was to assess low-resolution response learning capacities in DS. When no cue indicated the location of the reward, individuals with DS exhibited a response learning performance that was intermediate between those of MA-matched TD children and TD adults. As a group, in the response learning task without the local cue, individuals with DS made fewer correct choices than TD adults, but their performance was not significantly different from that of MA-matched TD children. However, as for place learning, the group of DS individuals exhibited a bimodal performance, again suggesting that the average number of correct responses may not be the most appropriate indicator of group performance. Accordingly, when we consider the individual performance, more individuals with DS performed above chance level (15/27; 56%) than TD children (3/19; 16%). As discussed previously (Bostelmann et al., 2017) response learning appears to be inhibited in 3.5- to 8-year-old TD children. Although response learning may emerge as early as 6 months of age, and earlier than place learning during both typical and atypical development (Acredolo, 1978; Cornell and Heth, 1979; Mangan, 1992; Newcombe et al., 1998; Ribordy Lambert et al., 2013), once TD children start exhibiting basic place learning capacities around 2 years of age (Newcombe et al., 1998; Ribordy Lambert et al., 2013), incidental spatial response learning, as tested under these experimental conditions, appears to become extremely difficult for TD children. By contrast, our data show that response learning appears to be more easily expressed in individuals with DS as compared to TD children with the same MA.

Finally, it is important to consider the impact of the different instructions given for the different tasks. Since individuals with DS were hypothesized to show greater deficits in hippocampal-dependent tasks such as place learning, in order to try to assure that any deficits that we observed were due to deficits in place learning alone, and not to other parasitic cognitive processes (e.g., lack of comprehension of the goals of the task), we gave as much instruction as possible. This means that for the place learning task participants were told that the reward "can always be found here." However, if the hippocampus is impaired and unable to support allocentric spatial processing, this instruction alone would not enable the participant to find the rewarded location. By contrast, for the response learning task, telling the participant to "go this way" would be providing the solution to the problem. Importantly, our results show that for response learning task, even given the more apparent difficulty of the task due to the lack of verbal instructions: (1) more individuals with DS passed than did TD children; and (2) the number of individuals with DS passing the place learning task did not differ from the number of DS individuals passing the response learning task. Together, these results suggest that response learning is truly facilitated in this group of individuals.

In light of experiments carried out in rats which have shown that response learning is dominant and even facilitated when the hippocampus is inactivated (Packard and McGaugh, 1996; Schroeder et al., 2002; Chang and Gold, 2003a), we hypothesize that impaired "hippocampus-dependent" place learning may facilitate "striatum-dependent" response learning. Our previous study in individuals with DS revealed severe impairments of high-resolution place learning capacities, but suggested a relative preservation of low-resolution place learning capacities (Banta Lavenex et al., 2015). Our current results confirm the relative preservation of low-resolution place learning capacities, as well as a facilitation of response learning in individuals with DS, as compared to MA-matched TD children. Using the same paradigm as in the current study, we previously showed that severe impairments in low-resolution place learning are accompanied by a large facilitation of response learning in WS (Bostelmann et al., 2017), another genetic neurodevelopmental disorder affecting the hippocampal formation (Meyer-Lindenberg et al., 2005; Meyer-Lindenberg et al., 2006). Interestingly, results from a previous study performed in children with ADHD also suggested that the normal interaction between place and response learning may be altered (Robaey et al., 2016). In their study, children were trained on a virtual 8-arm radial maze that was surrounded by visual cues that appeared in the distance. The task could be solved by employing either a response or a place learning strategy. The strategy used by children during training was assessed in a probe trial without any visible landmarks. Twenty percent of the control children exhibited perfect performance on the probe trial, indicating that they were relying on response learning during the training phase. By contrast, 35% of children that exhibited one or more ADHD symptoms exhibited perfect performance on the probe trial, indicating a greater reliance on response learning (Robaey et al., 2016).

Taken together, the findings from these different studies indicate that response learning may be more easily expressed in individuals with a variety of neurodevelopmental learning disorders associated with abnormal hippocampal function. A comparison of the performance of individuals with WS and individuals with DS leads us to further hypothesize that greater impairments in “hippocampus-dependent” place learning may be associated with greater facilitation of “striatum-dependent” response learning.

Not All Space Is Created Equal

The current findings confirm that spatial memory is not a unitary process. As discussed previously (Banta Lavenex and Lavenex, 2009; Banta Lavenex et al., 2015; Bostelmann et al., 2017), it is critical to recognize that there are different types of spatial learning and memory systems, subserved by different functional brain networks, which may interact and contribute to guiding behavior, and thus impact overall task performance. Consequently, it is necessary to perform a detailed and systematic evaluation of spatial memory processes in order to define a comprehensive and coherent profile of spatial cognitive abilities, which may help to infer the specific cognitive processes and underlying neurobiological substrates that may be impacted or preserved in DS, as well as in other neurodevelopmental or acquired neurological disorders.

In a study by Pennington et al. (2003) utilizing a virtual Morris water maze, evidence of “hippocampus-dependent” spatial memory impairments in DS was inferred from the fact that during a probe trial without the target object, individuals with DS ($n = 18$; 11–19 years old) spent significantly less time searching for the object in the correct quadrant (16% of the duration of the probe trial) than MA-matched TD children (30%; $n = 18$; individually matched to individuals with DS). In a subsequent study, however, Edgin et al. (2010) failed to show a difference in search time between individuals with DS (27%; $n = 55$; 7–38 years old) and MA-matched TD children (21%; $n = 36$). The fundamental features of the task were designed to replicate the features of the original task developed for rats (Morris, 1981). Children used a joystick to navigate in the virtual arena. Each participant completed four visible-target practice trials, after which the target became invisible and the child was instructed to move around the arena until the target was found. After five trials in this condition, the child was presented with a probe trial during which the target would not appear. The child was prompted to continue searching for the target for a total of 90 sec. Although this task may be adequate to demonstrate global impairments in “hippocampus-dependent” place learning following complete hippocampal lesions, as was shown in rats (Morris et al., 1982; Brun et al., 2002), it is not necessarily adequate to reveal the dysfunction of distinct hippocampal regions. Indeed, rats or mice with CA3 dysfunction are able to acquire the task and exhibit clear recognition of the training quadrant (Brun et al., 2002; Nakashiba et al., 2008). Our current findings, together with the results of our previous study (Banta Lavenex et al., 2015), revealed significant variability in the place learning abilities of individuals with DS, which can nevertheless be characterized by largely preserved low-resolution place learning capacities and severely impaired high-resolution place learning capacities. This pattern of results is thus consistent with the absence of significant differences in the performance of the virtual water maze (Edgin et al., 2010), which would only require low-resolution place learning capacities to discriminate the trained quadrant during the probe trial.

Two other studies by Courbois et al. (2013) and Purser et al. (2015) revealed significant impairments in route learning in virtual environments in individuals with DS. Courbois et al. (2013) concluded that individuals with DS were able to learn specific routes, but they were unable to integrate information about these routes into a configurational representation of the environment. Purser et al. (2015) concluded that individuals with DS exhibited a large deficit in route learning, but the exact nature of this deficit was not clearly identified. This kind of representation was also defined by Purser et al. (2015), as configural knowledge, which consists of layout information about an environment that incorporates the relations, including the distance and direction, between features in that environment. These definitions are consistent with the definition of place learning, which refers to an individual’s ability to learn and remember locations in an allocentric spatial frame of reference, in which locations are encoded in relation to other objects or locations in the environment (i.e., in a viewpoint-independent manner), allowing the construction of a cognitive map of one’s environment (Tolman, 1948; O’Keefe and Nadel, 1978; Banta Lavenex et al., 2014). We would like to argue that the characterization of place learning as being “hippocampus-dependent” (O’Keefe and Nadel, 1978) needs to be further qualified to take into account the functions of distinct hippocampal circuits (Rolls and Kesner, 2006; Lavenex and Banta Lavenex, 2013). Our current results, together with the results of Banta Lavenex et al. (2015), suggest that we can already distinguish between (1) low-resolution, topological representations of the environment, and (2) high-resolution spatial representations that include precise metric information. There are certainly a number of other functions associated with distinct hippocampal regions and/or circuits that should be further studied. Thus, it will particularly important to continue investigating different types of "hippocampus-dependent" cognitive processes and not consider possible discrepancies between experimental results as inconsistencies, but rather as useful information regarding the functionality of specific neurobiological substrates subserving these processes.

Accordingly, it is important to think about the implications of using virtual reality paradigms in order to evaluate the ability of individuals with DS to create allocentric representations of the environment. We do not want to argue that virtual reality should never be used, but researchers should be aware of, and discuss, the possible implications of having limited or no access to certain types of information normally available in the real world. For example, when navigating in a real-world environment, participants have access to nearly 130° of visual flow. By contrast, in virtual reality tasks, participants often perceive an atypical reduced point of view. Indeed, computer screens are normally 41 cm wide and displayed directly in front of the subject at a distance of about 61 cm, yielding a field of view of approximately 37° (Tan et al., 2006). Note that newer technologies using, for example, VR goggles or full room displays, may enable a greater immersion in the virtual environment. However, when navigating in the real world, subjects rely not only on visual information, such as landmarks and visual flow, but also on vestibular and proprioceptive information. Altogether, these different inputs contribute to the creation of allocentric representations (Etienne and Jeffery, 2004). Accordingly, removing vestibular and proprioceptive information decreases spatial memory performance in humans (Ruddle and Lessels, 2006). Similarly, the response properties of hippocampal place cells are less specific when vestibular and proprioceptive information is removed, and only visual information is available (Matsumura et al., 1999; Ravassard et al., 2013). It is thus likely that the place learning capacities of individuals with DS in virtual reality paradigms may be negatively impacted by (1) abnormally limited visual information, and (2) the absence of, or more accurately, the presence of contradictory information provided by the vestibular and proprioceptive systems. Consistent with this view, in the study by Courbois et al. (2013), even TD children had serious difficulties solving the virtual reality task, since only five out of nine children could take the shortcut. By contrast, our study provided evidence that a majority of individuals with DS, as well as nearly all MA-matched TD children, were capable of creating a basic allocentric representation of the environment to find one reward location among four possible locations, in a 4 m × 4 m arena, in which participants had access to coherent visual, vestibular and proprioceptive information. Alternatively, and in contrast to previous studies carried out in virtual environments, it would be important to also determine whether individuals with DS are able to build an allocentric spatial representation of the environment, or cognitive map, in absence of visual information, by relying uniquely on self motion-generated vestibular and proprioceptive information.

CONCLUSION

Although our previous study showed that high-resolution place learning is severely impacted in individuals with DS, the current study shows that low-resolution place learning may be relatively preserved in these individuals. Consistent with the theory of a competitive interaction between "hippocampus-dependent" place learning and "striatum-dependent" response learning, response learning appears facilitated in individuals with DS, as compared to MA-matched TD children. Altogether, these findings also suggest that the neural pathways supporting high-resolution place learning may be relatively more impacted in DS, whereas the neural pathways supporting low-resolution place and response learning may be relatively preserved.

AUTHOR CONTRIBUTIONS

PBL and PL were responsible for the conception and design of the work, acquisition, analysis and interpretation of the data, and drafting of the manuscript. MB was responsible for the design of the work, acquisition, analysis and interpretation of the data, and drafting of the manuscript. LM was responsible for data acquisition. FC and DM were responsible for data acquisition and manuscript drafting. SV was responsible for conception of the work and manuscript drafting.

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Conflict of Interest Statement: 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.

2.3. Article 3: Children five-to-nine years old can use path integration to build a cognitive map without vision

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Children five-to-nine years old can use path integration to build a cognitive map without vision

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ABSTRACT

Although spatial navigation competence improves greatly from birth to adulthood, different spatial memory capacities emerge at different ages. Here, we characterized the capacity of 5–9-year-old children to use path integration to build egocentric and allocentric spatial representations to navigate in their environment, and compared their performance with that of young adults. First, blindfolded participants were tested on their ability to return to a starting point after being led on straight and two-legged paths. This egocentric homing task comprising angular and linear displacements allowed us to evaluate path integration capacities in absence of external landmarks. Second, we evaluated whether participants could use path integration, in absence of visual information, to create an allocentric spatial representation to navigate along novel paths between objects, and thus demonstrate the ability to build a cognitive map of their environment. Ninety percent of the 5–9-year-old children could use path integration to create an egocentric representation of their journey to return to a starting point, but they were overall less precise than adults. Sixty-four percent of 5–9-year-old children were capable of using path integration to build a cognitive map enabling them to take shortcuts, and task performance was not dependent on age. Imprecisions in novel paths made by the children who built a cognitive map could be explained by poorer integration of the experienced turns during the learning phase, as well as greater individual variability. In sum, these findings demonstrate that 5–9-year-old children can use path integration to build a cognitive map in absence of visual information.

1. Introduction

Although spatial competence improves greatly from birth to adulthood, different spatial capacities emerge at different ages during development (Lavenex & Banta Lavenex, 2013; Newcombe & Huttenlocher, 2000). Egocentric spatial capacities emerge first in the newborn, and dominate the child's spatial world for at least the first six months (Acredolo & Evans, 1980; Acredolo, 1978; Bremner, 1978). Between 8.5 and 12 months, infants become capable of using cues or landmarks to remember spatial locations (Acredolo & Evans, 1980; Bremner, 1978; Bushnell, McKenzie, Lawrence, & Connell, 1995), and can use landmarks that are close to a goal to recall that location (Lew, Bremner, & Lefkovitch, 2000). At the same time, infants demonstrate that they can also track their position relative to landmarks following simple positional changes that provoke changes in vestibular and optic flow inputs, such as translation along a straight line or rotational displacements (Cornell & Heth, 1979; Keating, McKenzie, & Day, 1986; Landau & Spelke, 1988; McKenzie, Day, & Ihsen, 1984). From 12 months of age, children can track their position relative to landmarks following more

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complex positional changes involving translation and rotation, i.e., when they move to a new location and change heading simultaneously (Acredolo & Evans, 1980; Acredolo, 1978; Acredolo, Adams, & Goodwyn, 1984; Bremner, Knowles, & Andreasen, 1994; Lew et al., 2000; Newcombe, Huttenlocher, Drummey, & Wiley, 1998). Finally, by 18 months of age, children can track the direction and the magnitude of their own rotational displacements in the absence of visual cues, a capacity fundamental to path integration (Rieser & Heiman, 1982; Rider & Rieser, 1988). The culmination of this early period of spatial competence improvement occurs around 20 months of age when the capacity to form viewpoint-independent, allocentric spatial representations of the environment begins to emerge in children, with reliable expression being observed in children 24 months of age and older (Newcombe et al., 1998; Ribordy Lambert, Lavenex, & Banta Lavenex, 2016; Ribordy, Jabès, Banta Lavenex, & Lavenex, 2013).

In a recent review, Newcombe (2019) provided an extensive description of empirical data supporting these incremental and hierarchical developmental profiles in children. Surprisingly, cognitive mapping abilities were described as emerging last and extremely tardively: "*In line with research on normative development, 12 years of age may be the time not only when cognitive maps become widely evident but also when the adult variation pattern stabilizes.*" (p. 6). It has also been reported that the integration of visual and self-motion information to support small-scale navigation may not be present in 4- to 8-year-old children (Nardini, Jones, Bedford, & Braddick, 2008), and that viewpoint-independent allocentric strategies are either lacking or rudimentary in children under 6 years of age (Nardini, Thomas, Knowland, Braddick, & Atkinson, 2009). However, these assessments contrast with experimental evidence showing that allocentric spatial processing emerges by two years of age in children (Newcombe et al., 1998; Ribordy et al., 2013), and that 3-year-old children benefit from external "room" landmarks to identify a toy's location in an array of cups (Nardini, Burgess, Breckenridge, & Atkinson, 2006), as well as findings from previous studies describing the cognitive mapping abilities of children between 2.5 and 9 years of age (Landau, Gleitman, & Spelke, 1981; Landau, Spelke, & Gleitman, 1984; Morrongiello, Timney, Humphrey, Anderson, & Skory, 1995). Evaluation of the literature on the development of spatial capacities suggests that there may be two main reasons why the relevance of these previous findings has been overlooked. First, there may be some confusion about the concept of cognitive maps and its relation to the concept of allocentric spatial representations. Indeed, although the studies by Landau et al. (1981, 1984) and Morrongiello et al. (1995) clearly investigated cognitive mapping in children, and by inference the studies of Newcombe et al. (1998), Ribordy et al. (2013) and Ribordy Lambert, Lavenex, and Banta Lavenex (2015) also studied cognitive mapping, none of these publications used this term explicitly. Second, there may be some doubts concerning the validity and reliability of the results presented in the studies of Landau et al. (1981, 1984) and Morrongiello et al. (1995), which may have led some scholars to consider these results as insufficient evidence of cognitive mapping abilities in children. In this article, we will address both of these reasons, the former theoretically and the latter with empirical data, in an attempt to clarify the issue and establish a consistent age at which cognitive mapping abilities emerge in children.

1.1. Allocentric spatial representations are cognitive maps

Tolman (1948) first coined the term cognitive map and described it as "*a tentative map, indicating routes, paths and environmental relationships which finally determines what responses, if any, the animal will finally release*". O'Keefe and Nadel (1978) concept of a cognitive map was consistent with Tolman's definition, although they further proposed that cognitive maps possessed Euclidean properties, specifically exact directional and distance information. Recent views suggest that spatial cognitive maps represent the relationships between world elements such as objects, environmental landmarks and locations, which may support flexible behavior (Behrens et al., 2018); this view is consistent with Tolman's conceptualization, and the one that we adopt here. Although the use of the term allocentric spatial representation is more recent, it is now well-accepted by experimental psychologists and neuroscientists alike that in the spatial domain, the terms allocentric representations and cognitive maps are synonymous (McNaughton, Battaglia, Jensen, Moser, & Moser, 2006; Nadel & Hardt, 2004), and that both refer specifically to viewpoint-independent representations of the relations between different objects in the environment (Golledge, Klatzky, & Loomis, 1996; Langston et al., 2010; McNaughton et al., 2006; O'Keefe & Nadel, 1978; Ruddle & Lessels, 2006; Spiers & Barry, 2015; Wang, Chen, & Knierim, 2019; Wills, Cacucci, Burgess, & O'Keefe, 2010). Thus, animals that are capable of building allocentric spatial representations are capable of using these representations to navigate between objects in their environment in a flexible manner, and take novel, never before experienced routes or shortcuts, to navigate to a desired destination. Indeed, the ability to take novel routes has come to be regarded as hallmark evidence to infer the existence of cognitive maps.

It is also well-established that cognitive maps are subserved by a distributed network of neurons and neural systems in the medial temporal lobe that include head-direction cells, grid cells and place cells (Lavenex & Banta Lavenex, 2013; McNaughton et al., 2006; Newcombe, 2019; Taube, 2007; Wang et al., 2019). Moreover, anatomical and electrophysiological evidence in rats and monkeys (Jabès, Banta Lavenex, Amaral, & Lavenex, 2011; Langston et al., 2010; Lavenex, Banta Lavenex, & Amaral, 2004, 2007; Lavenex, Sugden, Davis, Gregg, & Banta Lavenex, 2011; Wills et al., 2010) and behavioral evidence in rats, monkeys and humans (Langston et al., 2010; Lavenex & Banta Lavenex, 2006, 2013; Newcombe et al., 1998; Ribordy et al., 2013; Wills et al., 2010) indicate that the spatial memory processes dependent on these neural systems emerge concomitantly with the functional maturation of different cell types and circuits in the medial temporal lobe.

In sum, evidence for the use of allocentric spatial representations can be taken as evidence of the ability to build cognitive maps. To date, however, the ability of children to use allocentric spatial representations has mainly been assessed by testing their ability to use visual cues to learn and remember the location of one to several hidden rewards. Although this evidence should be sufficient for concluding that these children are capable of building cognitive maps, such experiments do not provide hallmark evidence for the ability to take shortcuts. In contrast, aside from the studies by Landau et al. (1981, 1984) and Morrongiello et al. (1995), whose results may be considered inconclusive, children's ability to use path integration to build cognitive maps in the absence of visual information has been much less studied.

1.2. Path integration can be used to build cognitive maps

Path integration is the ability to use self-motion information generated by one's own body movement (i.e., idiothetic cues) to keep track of one's position in space (Etienne, Maurer, & Séguinot, 1996; Mittelstaedt, 1999; Mittelstaedt & Mittelstaedt, 1980), and is generally described as a mechanism that predominates when visual information is minimized or absent. For path integration, the estimation of both direction and distance is required. In absence of visual flow information, angular displacements (rotations) are estimated primarily based on vestibular information from the semi-circular canals, and linear displacements (translations) are estimated primarily based on proprioceptive information, but also from information pertaining to linear acceleration transmitted by the otolith organs found in the vestibular labyrinth of the inner ear (Etienne & Jeffery, 2004; Etienne et al., 1996; Taube, 2007). Efferent copies of motor commands complement vestibular and proprioceptive information in the estimation of both rotations and translations (Taube, 2007), and contribute to the coding of spatial location by hippocampal neurons (Foster, Castro, & McNaughton, 1989). As an individual moves along a path in their environment, information about rotations and translations must be integrated continuously in order to calculate their position with respect to the journey's starting point. Although path integration does enable an individual to return to a starting point, path integration should not be equated to "homing". Path integration is a neural computational process and homing is just one behavior supported by this process (Savelli & Knierim, 2019). Importantly, and contrary to navigational processes employing vision, path integration is an imprecise process in which error is accrued with every step (translational displacement) and every turn (rotational displacement), unless or until external cues can be used as landmarks to (re) calibrate the path integration system (Allen, 2004; Etienne & Jeffery, 2004; Etienne et al., 1996; Fujita, Klatzky, Loomis, & Golledge, 1993; Klatzky et al., 1990; Loomis et al., 1993; McNaughton et al., 1996). Thus, when using path integration, external sensory information from the environment such as familiar visual, tactile or olfactory stimuli must be provided at least occasionally in order to confirm or update the individual's position and correct for cumulated error (Etienne & Jeffery, 2004; McNaughton et al., 1996; Savelli & Knierim, 2019).

Path integration can be used to construct either egocentric or allocentric spatial representations of the environment (Alyan & McNaughton, 1999; Etienne et al., 1996, 1998; Jayakumar et al., 2019; McNaughton et al., 1996, 2006). Egocentric representations encode objects or goal locations in relation to the subject's body (e.g., on my left) or via a sequence of body-centered actions (e.g., turn right, walk ten steps, turn left). Egocentric representations constructed from path integration lack contextual spatial information that can place an individual in a particular place in relation to environmental landmarks. When moving, an individual's self-motion information is constantly and automatically encoded and updated. When the individual is ready to return home, a direct return trajectory can be derived which can support homing behavior even in the absence of specific contextual spatial information concerning the surrounding environment. Most often, studies of path integration have been limited to assessing performance on homing tasks in the absence of vision. In triangle completion tasks, for example, physiologically blind or blindfolded sighted participants are guided along a trajectory with two legs connected by an angle of a particular size, and then asked to return to the starting point using the most direct route. In this case, the memory representation that is created is the location of a fixed reference point in relation to one's body, and thus includes the direction and distance to this reference point (Loomis et al., 1993; Loomis, Klatzky, & Golledge, 2001). Humans and a wide variety of species, such as ants, rodents, dogs and hamsters demonstrate the ability to return to a starting point via the most direct path after being led or locomoting independently along a path that includes one or more turns (Corlett, Patla, & Williams, 1985; Fujita et al., 1993; Giovannini, Jacomuzzi, Bruno, Semenza, & Surian, 2009; Klatzky et al., 1990; Loomis et al., 1993; Mittelstaedt & Mittelstaedt, 1980; Muller & Wehner, 1988; Seguinot, Cattet, & Benhamou, 1998; Seguinot, Maurer, & Etienne, 1993; Smith, McKeith, & Howard, 2013).

Path integration also plays a fundamental role in the formation of allocentric spatial representations of the environment (McNaughton et al., 1996, 2006), which include the relative positions of objects and locations within the environment, as well as in coding the individual's position with respect to those environmental landmarks (Etienne & Jeffery, 2004; Jayakumar et al., 2019; Savelli & Knierim, 2019). Indeed, the same information about direction and distance traveled by an individual between different objects' locations contributes to the definition of the position of those objects in relation to each other, within a representation of the environment that is independent of the observer's position (Jayakumar et al., 2019; McNaughton et al., 1996). Importantly, path integration is not used only when external landmarks are unavailable; it is a continuously operating, automatic process that integrates with landmark processing (Savelli & Knierim, 2019; Tcheang, Bulthoff, & Burgess, 2011). In fact, whenever possible, both systems are used concurrently since they normally provide coherent, complementary information to help the individual orient, update its position and navigate (Jayakumar et al., 2019; Tcheang et al., 2011). Path integration is thus used to build allocentric representations of the relationships between external landmarks, while at the same time the external landmarks help to correct for cumulated error and calibrate the path integration system (McNaughton et al., 1996). In humans, behavioral studies have shown that both blindfolded and physiologically blind adults are capable of forming allocentric spatial representations of the explored environment (Giudice, 2018; Passini & Proulx, 1988). Altogether, these findings indicate that path integration contributes to building cognitive maps in humans.

1.3. Can children build cognitive maps without visual information?

Several studies have shown that 3–4-year-old children can use path integration in the presence or absence of vision to spatially update their position and keep track of locations and objects in their environment following self-movement (Rieser & Heiman, 1982; Rider & Rieser, 1988; Rieser & Rider, 1991; Bremner et al., 1994). In contrast, only two studies have investigated the capacities of blind or blindfolded children to build cognitive maps using path integration in the absence of vision (Landau et al., 1981, 1984; Morrongiello et al., 1995), and the theoretical implications of their results have sometimes been overlooked when considering how to interpret the evidence from experiments designed to assess the spatial capacities of young children (Nardini et al., 2009; Negen, Heywood-Everett, Roome, & Nardini, 2018; Newcombe, 2019). This may be due to conceptual discrepancies, or to the assumption that such advanced spatial capacities cannot be present in young children who perform poorly in virtual environments or in real-world paradigms that dissociate or remove relevant spatial cues (Broadbent, Farran, & Tolmie, 2014; Buckley, Haselgrove, & Smith, 2015; Bullens, Klugkist, & Postma, 2011; Nardini et al., 2008). However, it may also be due to some weaknesses with these two previous studies that make assessing the validity and reliability of their data difficult.

Landau et al. (1981, 1984) tested a congenitally blind 2.5-year-old girl (Kelli), and five typically developing (TD) children (from 2 years and 10 months to 3 years and 9 months of age), as well as six TD adults. In their paradigm, Kelli and blindfolded TD partipants were led along several paths connecting four different objects in a 2.44 m × 3.05 m room. Participants were then asked to walk novel, direct paths between the objects. A total of 12 "novel" path trials were administrated: each of the three new paths (there and back) was repeated twice (thus, three novel paths, three repeated paths, and six reversed paths). To estimate performance on each trial, the experimenters recorded the subjects' position 60 cm after they started along their path, and again at the end of their path. After 60 cm, Kelli was facing toward the correct goal location on 11 out of 12 trials. TD children exhibited similar performance with correct orientation on an average of 10 out of 12 trials. At the end of their path, participants were considered successful if their final position fell within a 40° segment originating at the starting location and containing the target. Kelli succeeded on 8 out of 12 trials, and TD children succeeded on an average of 7.4 out of 12 trials. However, individual results of the TD children were not provided, and thus we do not know about individual performance and variation at this age. Indeed, although a correct starting orientation on 10 of 12 trials sounds impressive, if the two "failed" trials were two of the three truly novel paths, and not the reversals or repeats of these paths, then these results may not provide sufficient support for the argument that children of this age can build cognitive maps in the absence of vision (Bennett, 1996). Moreover, given the small size of the experimental room, it is surprising that Kelli only succeeded at reaching the target on 8 of 12 trials, after heading in the correct direction on 11 trials. Finally, adults exhibited superior performance as compared to children, with their original orientation correct on an average of 11.5 out of 12 trials and their final position correct on an average of 10.8 out of 12 trials. In sum, because Kelli and the other children succeeded on approximately two-thirds of the paths, Landau et al. (1981) concluded that "*this blind child, and sighted controls, know about some of the metric properties of space, probably Euclidean properties*." Although these findings are suggestive that children from 2.5 years of age can use path integration to build a cognitive map without vision, given the lack of detailed data concerning individual children's trial-by-trial performance, these findings must be verified.

Morrongiello et al. (1995) replicated Landau et al.'s study with a larger sample of TD children from 4.5 to 9 years of age. In contrast to Landau et al. (1984), Morrongiello et al. (1995) were unable to test 12 children younger than 4.5 years of age because they refused to wear the opaque goggles that blocked vision for the duration of the task and/or refused to walk alone while wearing the goggles or other blindfolds. They used a similar sized room (3.6 m × 4.8 m), but because the repetition of novel trials may enable learning and thus may not be used as evidence demonstrating the ability to make novel shortcuts, Morrongiello et al. (1995) only tested each of the three novel paths once. They also included more measures of performance, including the participants' average distance from the target location, at both the beginning and the end of the novel paths taken. Based on all measures, 5- and 7-year-olds were farther from the target than 9-year-olds, suggesting an improvement in spatial performance from 4 to 9 years of age. Thus, whereas Landau et al. (1984) concluded that children from 2 years of age were indeed capable of creating an Euclidean representation of space, Morrongiello et al. (1995) concluded that the capacity to produce novel paths is not fully mature in 5-year-old children, but rather continues to improve until at least 9 years of age. However, without an adult comparison group, it is not possible to know whether the 9-year-old children exhibited fully-developed path integration capacities. Moreover, for all three novel paths the scores for the initial turn, the closest position to the target, and the final position relative to the target were averaged across all participants within each age group to yield a single estimate of performance for each age group. This procedure may have masked individual differences and obscured important information about potential errors or biases in the representation of the specific relations between environmental objects, both within and across age groups. Finally, even though Morrongiello et al. (1995) provided more specific measures of performance to test children's ability to represent the Euclidean properties of space, they did not answer the question as to how many children were capable of building a cognitive map and at what age that capacity may emerge.

In sum, the lack of trial-by-trial data for individual children in these two studies makes their results difficult to scrutinize and assess by the independent reader, thus possibly explaining why these studies may sometimes be overlooked. Moreover, from the data reported it is not possible to determine whether children's inaccuracies in novel path construction were due to: (1) errors in the topological representation of the relationships between objects, which would suggest that basic low-resolution allocentric spatial capacities are not yet capable of being formed in absence of vision, or (2) imprecisions in the Euclidean coding of angle and distance information, which would suggest that although basic allocentric spatial capacities are present, these capacities are still continuing to mature with respect to their precision and resolution (Ribordy Lambert et al., 2015, 2016).

1.4. Aim of this study

The aim of this study was to characterize the capacity of 5–9-year-old children to use path integration to home and to build cognitive maps supporting navigation in their environment. To assess the level of maturation of these capacities in young children, we also tested young adults on the same tasks. First, blindfolded participants were tested on their ability to return to a starting point after being led on straight and two-legged paths. Performance on this homing task that involved only simple angular and linear displacements allowed us to evaluate children's path integration capacities in absence of external landmarks and the necessity to build a cognitive map. Second, we evaluated whether participants could use path integration, in absence of visual information, to build a cognitive map. Similar to the studies by Landau et al. (1981, 1984) and Morrongiello et al. (1995), participants in our study had to navigate between four different objects placed in an 8 m × 8 m room. After an initial phase where blindfolded participants learned some of the spatial relations between objects by walking between those objects, participants were then asked to walk directly to specific objects using three novel paths (shortcuts), and then to reverse that route. In order to provide an accurate description of each participant's capacity to encode the spatial relations between the different objects, each path was analyzed and reported separately for each participant. Accuracy measures (angles and distances) as well as dispersion measures (variability of the angles taken) were calculated to describe the participants' performance. By assessing the data from both the homing and the cognitive mapping tasks, we were able to determine: (1) whether 5–9-year-old children can build a cognitive map in the absence of vision, and if so, what percentage of children do so and at what age; (2) whether children who can build cognitive maps exhibit imprecisions in Euclidean coding, as compared to adults; and (3) whether imprecisions in Euclidean coding are due to a poor integration of the experienced angles and distances in an allocentric representation, or a poor ability to reproduce the correct turn angles and walk straight for the correct distance when blindfolded.

2. Methods

2.1. Participants

Twenty-eight typically developing children (15 girls; average age: 6.9 years, SD: 1.4 years, min: 4.8 years, max: 9.7 years) and twenty-three typically developed young adults (12 women; average age: 22.2 years, SD: 2.7 years, min: 19.3 years, max: 30.3 years) participated in both the homing and cognitive mapping tasks (Experiments 1 and 2, respectively). Children were recruited via personal connections, and via email postings on social networks and to the university community. Children were reported by their parents to have been typically developing, and were neither born prematurely, nor had any suspected or diagnosed neurological conditions or learning disabilities. Adults were undergraduate students enrolled in the Bachelor of Psychology at the University of Lausanne and received course credit for their participation.

The two experiments took place on separate days, which were anywhere from one day to a few months apart. Participants were assessed on the homing task during their first visit and on the cognitive mapping task during their second visit. Each experiment lasted about 45 min and took place Mondays through Saturdays, between 8:00 A.M. and 6:30 P.M. Human subjects research was approved by the Cantonal Ethics Commission for Human Research (Vaud, Switzerland; protocol no. 60/14), and was in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects in research. Adult participants or children's parents gave informed written consent.

2.2. Testing facilities and general procedures

Testing took place within an 8 m × 8 m room (Fig. 1). During the homing task (Fig. 1A and B), the room was devoid of any objects. Construction tape that was undetectable when it was walked on was placed on the floor, 1.5 m from each of the walls that constituted the four corners of the room. At the corner closest to the entry door, the tape was arranged to represent a house, which was designated as "home", i.e., the position to which participants were instructed to always return on each trial. In the other three corners of the room, the tape formed a small "x" surrounded by a square that served as a visual landmark for the experimenter when guiding the participants. Participants were filmed with a camera placed in the far corner of the room opposite the corner containing the home. During the cognitive mapping task (Fig. 1C), the testing room contained four real-sized pieces of furniture. Each object was placed against the center of a wall: a bench (0°), a shelf (90°), a chair (180°) and a table (270°). Participants were filmed with a camera placed in the corner of the room between the bench and the table.

In both tasks, children were rewarded with small food rewards (e.g., Smarties®, Goldfish® crackers, gummy bears, pieces of

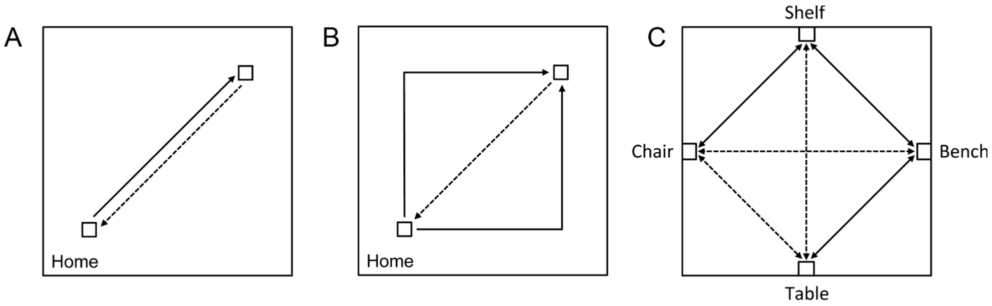

Fig. 1. Schematic representation of the experimental design carried out in an 8 m × 8 m testing room. Solid lines indicate guided trajectories; dashed lines indicate direct paths that participants were verbally requested to make. (A) Homing task, straight paths: 7 m straight line guided trajectory, 7 m return path. (B) Homing task, angled paths: 10 m angular guided trajectory with a right or left turn (5 m + 5 m), and 7 m return path. (C) Allocentric task: Guided routes (solid) and novel routes (dashed) between four objects. The paths between the bench and the chair, and between the table and the shelf were 7 m long; the other paths were 5 m long.

breakfast cereal or pretzels, etc.). One reward was given for each completed trial (a walked trajectory) and was not based on performance accuracy. Children's parents were queried with respect to alimentary allergies, and children were asked whether there were any treats that they did not like.

Visual information was eliminated with a “sleeping mask” blindfold individually adjusted to the subject's head and face at the start of each trial for the homing task, and before entering the room for the allocentric task. A black scarf was tied around the mask and the participant’s head to ensure that they could not see any light. Two experimenters tested children. Experimenter 1 (E1) would guide the child, and Experimenter 2 (E2) recorded the data. For adults, E1 was responsible for both guiding the participants and recording the data. For children and adults, E1 walked next to or behind the participant, close enough to provide non-specific verbal encouragement (e.g., “You’re doing great!”, regardless of performance) and to assure their security when they were walking independently (e.g., to prevent them from walking into walls or objects), but far enough so as not to interfere with the participant’s movements.

2.3. *Specific testing procedures*

2.3.1. *Homing task*

Participants were tested on their ability to return to a starting point (“home”) after being led along a predetermined route. Before beginning, participants were told that they would be guided along some paths while blindfolded, and that it was their job to try to return to the starting point as precisely as possible at the end of each guided route. Participants were instructed that once they thought that they were at the home position they were to stop walking and remain stationary. Each participant performed a total of 20 trials without vision. Half of the trials consisted of a linear route of 7 m (Fig. 1A), and the other half of the trials consisted of a 10 m route with a 90° left or right turn in the middle (Fig. 1B). The trials were given in the following order: Straight path Session 1: 5 × 7 m linear route, guided by the left arm; Two-legged path Session 1: 5 × 10 m route with a 90° right turn at the halfway point, guided by the left arm; Straight path Session 2: 5 × 7 m linear route, guided by the right arm; Two-legged path Session 2: 5 × 10 m route with a 90° left turn at the halfway point, guided by the right arm. At the end of each guided route, and while still facing in the direction of the outbound travel, E1 released the participant’s arm and instructed them to “go home” (i.e., to the starting point). Although participants had been instructed to stop walking once they estimated that they had arrived at home, if participants were approaching a wall and did not show signs of stopping, E1 gently placed a hand on the participant to stop them. Once participants were stationary, they could take off the blindfold, look where they were positioned in the room, and then return to the starting position (home) in order to prepare for the next trial. To ensure that all participants understood the task, prior to the beginning of each session they experienced a practice trial during which they were led through the guided part of the path without the blindfold, their arm released at the end of the guided path, and then asked to “go home”. All trials began from the same starting point. A trial was terminated when a participant stopped alone or when the experimenter stopped the participant just before a wall.

2.3.2. *Cognitive mapping task*

Participants were tested on their ability to take novel paths (shortcuts) to navigate to previously visited locations marked by four large objects placed in the 8 m × 8 m room (Fig. 1C). Prior to entering the room, participants were told that they were going to be blindfolded, and that they would then explore our laboratory’s living room. Participants were never told the goal of the experiment, or that they would have to remember the position of the objects in the room or navigate to those objects using novel routes. Although all participants were familiar with the empty room from having participated in the homing task, they were blindfolded prior to entering the room for the cognitive mapping task, and thus never saw the objects or their positions in the room. Once blindfolded, participants were led into the room and were guided to the bench where they were asked to sit down. Importantly, although the bench was located on the far-right wall relative to the entry door, some participants may not have had explicit knowledge of its position in the room; it could just as easily be perceived as being on the far wall opposite the door.

2.3.2.1. Learning phase. Participants were taught the routes between (1) the bench and the shelf, (2) the shelf and the chair, and (3) the bench and the table, always in this same order for each participant (solid lines in Fig. 1C; Supplementary Material 1). Accordingly, at the beginning of each trial, participants were positioned so that they were either sitting straight on the bench or chair, or so that their back was touching the shelf or the table, and their feet pointing straight forward. For each route to be learned, children were guided by the arm round-trip between the two objects twice by E1, then asked to make the round-trip alone one time, then guided through two more round-trips, and finally asked to make two more round-trips alone. For each route to be learned, adults were guided by the arm round-trip between the two objects twice by E1, then asked to make the round-trip alone twice. Each time participants reached an object by themselves or guided by E1, E1 named the object and participants were asked to touch the object or sit on it, for the chair and the bench.

In non-guided learning trials, if a participant came within 30 cm of the target object, E1 would gently take her/his arm and guide her/him into contact with the object, so that the participant would not startle or injure her/himself colliding with the object, thus terminating the trial. If the participant was in the correct quadrant of the room (tape markings on the floor outlined this zone), but not within 30 cm of the target object, the participant was allowed to continue walking until s/he came within 30 cm of a wall, at which point E1 gently stopped the participant and guided her/him to the target object. If a participant began walking in the wrong direction and after travelling 4 m was not in the correct quadrant, E1 would gently stop her/him and guide her/him back to the starting object, and then begin escorting the participant through the next two guided trials. This behavior was demonstrated only by a few children and only during their first one or two non-guided trial(s) of certain routes.

2.3.2.2. Testing phase. Participants ended the learning phase sitting on the bench, and immediately began the testing phase from this position. Participants were asked to walk alone and directly to objects, which would require them to take novel paths or shortcuts to these objects. First, E1 asked participants to walk directly from the bench to the chair (i.e., "now, go alone directly to the chair"). Once sitting in the chair, they were asked to walk directly to the table. Once their back was to the table, they were asked to walk directly to the shelf. Then, the participants were instructed to perform the three reverse routes: from the shelf to the table (i.e., "now, go alone directly to the table"), from the table to the chair, and from the chair to the bench. In the testing phase, each trial and data collection terminated when a participant either: (1) came within 30 cm of the target, at which point E1 gently guided the participant to the object, or (2) came within 30 cm of a wall, at which point E1 gently stopped the participant and guided her/him to the target object.

2.4. Data collection

Participants' movements and trajectories were recorded with the Noldus TrackLab system (Wageningen, The Netherlands). Participants wore a vest on which a radio frequency-emitting Ultra-Wide Band tag was affixed to each shoulder. The system collected the X and Y coordinates of each tag at a frequency of 4.75 Hz. The smoothed averaged X and Y coordinates of the two tags were computed to plot the location of the participant's head on a 2D representation of the room. Each trajectory was then transferred to the ImageJ program (NIH, USA), and retraced to measure the distance and angle information for the different parts of each individual trajectory.

We used several measures to quantify participants' performance on each trial: (1) The initial heading, defined as the angular difference between the ideal path and the participant's path one meter after starting their journey. (2) The final heading, defined as the angular difference between the ideal path and the participant's path after the participant either stopped alone (homing task), reached the target object (cognitive mapping task), or was stopped by E1 (homing and cognitive mapping tasks). (3) The distance to target, defined as the shortest distance between the participant's final position and home (homing task) or the target object (cognitive mapping task). For the homing task, the five trials of each session in absence of vision were averaged to obtain one single value for each of these measures (1–3) for each participant. For the cognitive mapping task, the six novel paths were analyzed separately.

We also provided an overall measure of task performance: (4) "Pass" or "Fail". For the homing task, we estimated whether subjects passed or failed by determining whether their average end location was within the quadrant of the room that included the outbound journey's starting point (home), as defined by the two perpendicular bisectors of the room's walls. In the cognitive mapping task, we estimated whether subjects passed or failed each of the three novel paths and the three reverse paths. To be considered as passing, the end point of the participant's trajectory had to be within the same quadrant as the target object, as defined by the two diagonals bisecting the room. This defined the area of the room in which participants were closer to the target object than any other object. We did not use a more restrictive criterion, e.g., within an arbitrary distance to the target, because we did not expect (Loomis et al., 1993), nor did we find, that either adults or children could exhibit perfect performance and always come within contact-distance of the object at the end of their trajectory. Indeed, path integration is an imprecise mechanism, in which error is accrued with every step and every turn (Etienne & Jeffery, 2004). Path integration appears only capable of guiding an individual to a general area, but not necessarily to an exact location. Our data confirm this, showing that not all adults reached the goal objects precisely.

2.5. Data analysis

For angular measures of direction, we used circular statistics computed in Excel following the formulas described in Zar (1999). We performed one-sample tests for the mean angle (Zar, 1999; p.620) to determine whether each group's average initial or final heading followed a mean heading that deviated from zero° (0° was considered as the perfect angle). We considered a 99% confidence interval to define a significant departure from the ideal direction. Age group comparisons were performed with the two-sample Watson-Williams tests for angular measures (Zar, 1999; p.625).

To quantify the variability for individual participants, we computed the angular deviation for each participant ($r = \text{sqrt}(\sin(\alpha)^2 + \cos(\alpha)^2)$, where α is the average angle for each subject within a session), and then calculated the average angular deviation for each group. Statistical analyses of the angular deviation and the distance to target were performed with the SPSS 25.0 software. We used General Linear Model analyses with age groups as a between-subject factor and test sessions or trials as repeated measures to analyze the distance to target, and the individual variability (r) of initial and final headings. We used independent samples t-tests to compare age groups within one session or trial. We used Pearson's r correlations to evaluate the relations between children's age and performance.

3. Results

3.1. Homing task: Straight outbound paths

3.1.1. "Pass" or "Fail"

Fig. 2 shows the average end locations of adults and children who were asked to return to "home" after being led blindfolded on a straight 7 m path, thus ideally requiring a 180° turn and a 7 m straight walk to return to the starting point. For Session 1, 22/23 adults (Fig. 2A; participant A56 failed) and 26/28 children (Fig. 2B; participants C36 and C167 failed) had an average end location in the quadrant of the room where the home was located and were thus considered to have passed the homing task. For Session 2, 23/23

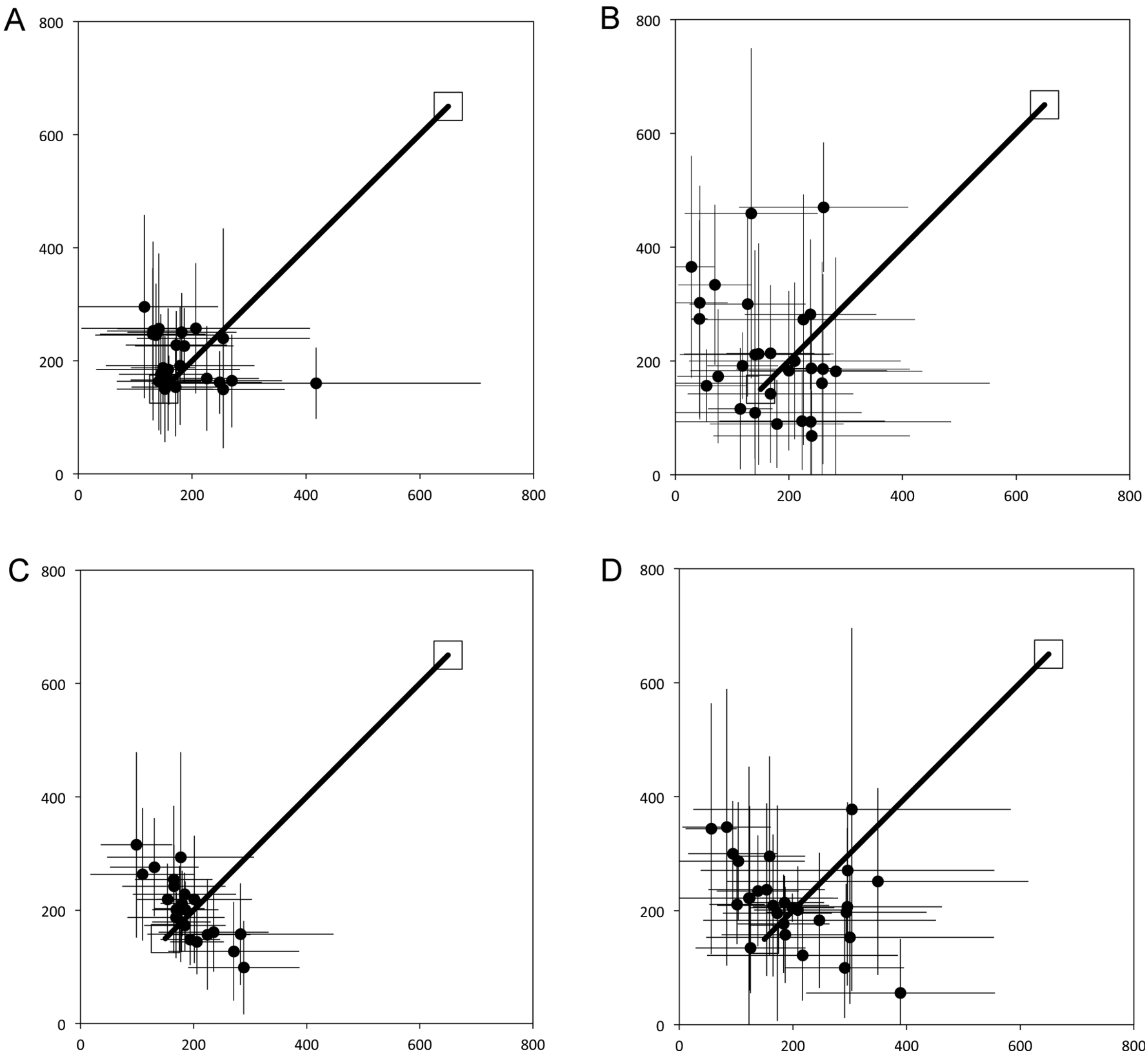

Fig. 2. Average end location of individual participants' return paths, following a straight 7 m outward path in the homing task. The horizontal and vertical error bars represent the standard deviation for each individual across one session. The solid line indicates the outward straight path. The top right square indicates the starting point of the return path. The bottom left square indicates "home". (A) Adults, Session 1. (B) Children, Session 1. (C) Adults, Session 2. (D) Children, Session 2. Room size: 800 cm × 800 cm.

adults (Fig. 2C) and 28/28 children (Fig. 2D) had an average end location in the quadrant of the room where the home was located and were thus considered to have passed the task.

3.1.2. Average distance from home

There were differences between age groups ($F_{(1,49)} = 17.461$, $p < 0.001$) and sessions ($F_{(1,49)} = 4.538$, $p = 0.038$), but no interaction between age groups and sessions ($F_{(1,49)} = 0.090$, $p = 0.766$). In both sessions, children's average distance between their end location and home was greater than the adults' (Session 1: adults: 145 ± 12 cm, children: 202 ± 13 cm, $t_{(49)} = 3.140$, $p = 0.003$; Session 2: adults: 120 ± 9 cm, children: 184 ± 13 cm, $t_{(49)} = 3.768$, $p < 0.001$). The average distance from home was shorter in Session 2 than in Session 1 when both groups were considered together, but the difference between sessions was not significant when each group was considered separately (adults: $t_{(22)} = 1.646$, $p = 0.114$; children: $t_{(27)} = 1.359$, $p = 0.185$). For children, the average distance between the participant's end location and home did not correlate with age (Session 1: Pearson's $r = -0.060$, $n = 28$, $p = 0.760$; Session 2: Pearson's $r = -0.198$, $n = 28$, $p = 0.313$). It is important to note, however, that children often did not stop on their own and E1 stopped children more often than adults because they were approaching a wall (out of 10 trials; adults: 0.68 ± 0.14 trials; children: 3.96 ± 0.49 trials; $t_{(48)} = 5.735$, $p < 0.001$).

3.1.3. Initial heading

Following a straight 7 m outward path, neither the adults' nor the children's group average initial heading, after turning and walking one meter, differed from the ideal heading; the children's group average initial heading did not differ from that of adults (Supplementary Material 2). In contrast, children's angular deviation was greater than adults' in both sessions, showing that children's initial heading was more variable than that of adults. Accordingly, the within-subject variability in initial heading was higher in children than in adults ($F_{(1,49)} = 4.885$, $p = 0.032$); it did not differ between Sessions 1 and 2 ($F_{(1,49)} = 1.731$, $p = 0.194$) and there was no interaction between groups and sessions ($F_{(1,49)} = 0.974$, $p = 0.328$).

3.1.4. Final heading

Following a straight 7 m outward path, neither the adults' nor the children's group average final heading differed from the ideal heading; the children's group average final heading did not differ from that of adults (Supplementary Material 3). In contrast, children's angular deviation was greater than adults' in both Sessions 1 and 2, showing that children's final heading was overall more variable than that of adults (as was observed for the initial heading). Accordingly, the within-subject variability in final heading was higher in children than in adults ($F_{(1,49)} = 7.631$, $p = 0.008$); it did not differ between Sessions 1 and 2 ($F_{(1,49)} = 0.057$, $p = 0.813$) and there was no interaction between groups and sessions ($F_{(1,49)} = 1.751$, $p = 0.192$).

3.1.5. Heading correlations

Children's average of the unsigned angle after one meter correlated negatively with age in Session 1 (Pearson's $r = -0.507$, $n = 28$, $p = 0.006$) and Session 2 (Pearson's $r = -0.377$, $n = 28$, $p = 0.048$), indicating a decrease in angular error with age. Interestingly, however, although children's initial heading correlated with their final heading in Session 1 (Pearson's $r = 0.731$, $n = 28$, $p < 0.001$) and Session 2 (Pearson's $r = 0.858$, $n = 28$, $p < 0.001$), the average of the unsigned final heading angle did not correlate with children's age in Session 1 (Pearson's $r = -0.069$, $n = 28$, $p = 0.729$), and the correlation just failed to reach the predefined level of statistical significance in Session 2 (Pearson's $r = -0.350$, $n = 28$, $p = 0.068$).

3.2. Homing task: two-legged angled paths

3.2.1. "Pass" or "Fail"

Fig. 3 shows the average end locations of adults and children who were asked to return "home" after being led blindfolded on a two-legged path of 10 m, with a 90° right turn after 5 m (Session 1) or a 90° left turn after 5 m (Session 2), thus ideally requiring a 135° right (Session 1) or 135° left (Session 2) turn at the end of the guided path, and a 7 m straight walk to return home. Although participants could also turn "the long way around" requiring an ideal turn of 225° to the left (Session 1) or to the right (Session 2), in Session 1 only three children turned left one time each, and in Session 2 only two children turned right one time and one child turned right two times (for a total of only seven "long way" turns, out of 280 turns). No adult turned left in Session 1, and only one adult turned right one time in Session 2.

For Session 1, 23/23 adults (Fig. 3A) and 26/28 children (Fig. 3B; participants C52 and C53 failed) had an average end location in the quadrant of the room where the home was located and were thus considered to have passed. For Session 2, 23/23 adults (Fig. 3C) and 25/28 children (Fig. 3D; participants C36, C39 and C50 failed) had an average end location in the quadrant of the room where the home was located and were thus considered to have passed the task.

3.2.2. Average distance from home

There were differences between groups ($F_{(1,49)} = 15.281$, $p < 0.001$), but no difference between sessions ($F_{(1,49)} = 0.062$, $p = 0.804$), and no interaction between groups and sessions ($F_{(1,49)} = 0.552$, $p = 0.461$). In both sessions, children's average distance between their end location and home was greater than the adults' (Session 1: adults, 138 ± 8 cm, children, 191 ± 14 cm, $t_{(49)} = 3.056$, $p = 0.004$; Session 2: adults, 132 ± 10 cm, children, 203 ± 19 cm, $t_{(40.896)} = 3.268$, $p = 0.002$). Children's average distance between their end location and home did not correlate with age in Session 1 (Pearson's $r - 0.138$, $n = 28$, $p = 0.483$). In contrast, the average distance between the children's end location and home correlated negatively with age in Session 2 (Pearson's $r = - 0.610$, $n = 28$, $p = 0.001$). These results were linked to both an improvement of the performance of older children and a worsening of the performance of younger children in Session 2. As was the case for straight outbound paths, E1 stopped children more often than adults because they were approaching a wall (out of 10 trials; adults: 0.55 ± 0.17 trials; children: 4.14 ± 0.51 trials; $t_{(48)} = 6.082$, $p < 0.001$).

3.2.3. Initial heading

Following a two-legged 10 m angled outward path, the adults' group average heading after turning and walking one meter toward home did not differ from the ideal heading (Supplementary Material 4). In contrast, the children's group average initial heading differed from the ideal heading in both Sessions 1 and 2. Moreover, for both sessions, children's average initial heading differed from the adults'. The observed angular deviation was also greater for children. Accordingly, the within-subject variability in the initial heading was higher in children than in adults ($F_{(1,49)} = 9.623$, $p = 0.003$); it did not differ between sessions ($F_{(1,49)} = 1.037$, $p = 0.313$) and there was no interaction between groups and sessions ($F_{(1,49)} = 0.331$, $p = 0.568$). Altogether, these data indicate that children had more difficultly integrating the 90° turn in the middle of the guided path, as compared to adults, and as compared to the straight path with no turn to be integrated, thus deriving a less accurate and less precise turn angle than the one needed to return home. Importantly, children's initial headings following both the paths with the 90° left turn and the 90° right turn revealed that children tended to under-rotate their initial rotation to start the return path.

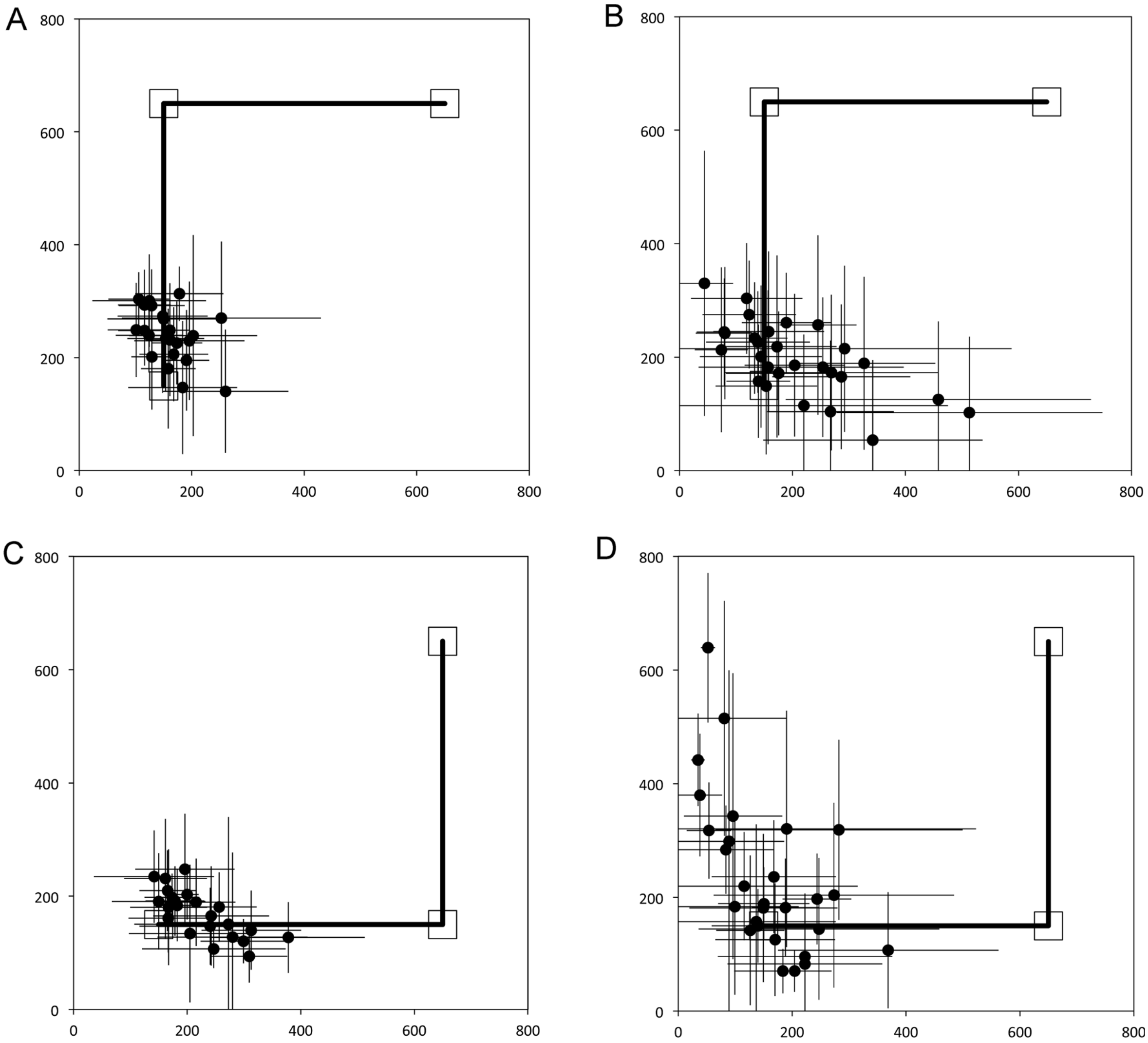

Fig. 3. Average end location of individual participants' return paths, following a two-legged 10 m angled outward journey in the homing task. The horizontal and vertical error bars represent the standard deviation for each individual across one session. The solid line indicates the outward angled path. The top right square indicates the starting point of the return path. The bottom left square indicates "home". (A) Adults, Session 1. (B) Children, Session 1. (C) Adults, Session 2. (D) Children, Session 2. Room size: 800 cm × 800 cm.

3.2.4. Final heading

Following a two-legged 10 m outward journey, the children's group average final heading did not differ from the ideal heading in either Session 1 or 2, but it differed from the adult's group average final heading in Session 2 (Supplementary Material 5; the difference just failed to reach the predefined level of statistical significance in Session 1). The adults' average final heading did not differ from the ideal heading in Session 1, but it was different from the ideal heading in Session 2, despite the rather small deviation from the ideal path. Children's angular deviation was greater than the adults' angular deviation in Session 1, but the difference failed to reach the predefined level of statistical significance in Session 2. Accordingly, the within-subject variability in final heading was higher in children than in adults ($F_{(1,49)} = 8.535$, $p = 0.005$); it did not differ between sessions ($F_{(1,49)} = 0.112$, $p = 0.739$) and there was no interaction between groups and sessions ($F_{(1,49)} = 0.389$, $p = 0.536$). Altogether, the final heading indicates that on average both adults and children walked in the direction of their starting point (home) after a two-legged 10 m path with a 90° angle, but the children's performance was overall more variable that the adults'.

3.2.5. Headings correlations

Children's average of the unsigned angles after one meter did not correlate with age in either Session 1 (Pearson's $r = -0.165$, $n = 28$, $p = 0.402$) or Session 2 (Pearson's $r = -0.253$, $n = 28$, $p = 0.193$). Children's initial heading correlated with their final heading in Session 1 (Pearson's $r = 0.794$, $n = 28$, $p < 0.001$) and in Session 2 (Pearson's $r = 0.865$, $n = 28$, $p < 0.001$). The average of the unsigned final heading angle did not correlate with children's age in Session 1 (Pearson's $r = 0.025$, $n = 28$,

$p = 0.900$) or Session 2 (Pearson's $r = -0.369$, $n = 28$, $p = 0.053$), at the predefined level of statistical significance.

3.3. Homing task: Results summary

Altogether, the results from the homing task show that both children and adults can succeed in returning to the area where the starting point of a walking journey was located after being led blindfolded on straight or two-legged outward paths, but on average, children end up significantly farther from home than adults. Moreover, and in contrast to adults, when children must integrate a turn (as in the two-legged path), their initial heading (after turning and walking one meter) is less accurate (compared to adults and to the ideal heading) and more variable (compared to adults) than when they must simply turn 180° after walking a straight outward path. Importantly, this relatively poorer performance appears to be at least partially due to the children's diminished capacity to integrate the 90° turn in the middle of the two-legged path, rather than solely due to their capacity to turn accurately, since the ideal 180° turn needed to return home following the straight path is greater than the ideal 135° angle needed to return home following the two-legged path (i.e., turning error is cumulative, and larger angular displacements should incur larger errors (Loomis et al., 1993)). Knowing that children as young as 4.8 years of age were capable of using path integration to build an egocentric spatial representation supporting homing behavior, we next evaluated whether these same children were capable of using path integration to build an allocentric spatial representation to take shortcuts, the hallmark of cognitive mapping abilities.

3.4. Cognitive mapping task

3.4.1. "Pass" or "Fail"

After having been blindfolded and guided along three selected paths between four different objects located in an 8 m × 8 m room (Fig. 1; Supplementary Material 1), participants were asked to make six direct never-traveled trajectories between these objects, the first three being entirely novel paths and the last three being their reverse paths. Figs. 4 and 5 show the individual end location, for each adult and each child, for each trajectory. Between 91% and 100% of the adults exhibited passing performance by ending in the quadrant that contained the target object on each trial (Bench to Chair: 21/23; Chair to Table: 23/23; Table to Shelf: 23/23; Shelf to Table: 23/23; Table to Chair: 23/23; Chair to Bench: 22/23). Between 57% and 86% of the children exhibited passing performance by ending in the quadrant that contained the target object on each trial (Table 1; Bench to Chair: 16/28; Chair to Table: 20/28; Table to Shelf: 22/28; Shelf to Table: 23/28; Table to Chair: 24/28; Chair to Bench: 22/28).

We considered that a reasonably stringent criterion to define overall successful performance in the cognitive mapping task would require participants to succeed on at least four of the six novel paths, including the two paths with a 45° angle (i.e., Chair to Table, and Table to Chair). We reasoned that successful performance on the two paths with a 45° angle was necessary in order to claim the existence of a cognitive map, since successful performance on all of the other novel routes could be achieved by adopting a strategy of simply walking straight from the object at the beginning of the path, and that such a strategy might be adopted by participants who had not constructed a cognitive map of the spatial relationships between the four objects' locations. Indeed, as shown below in the paragraph on initial heading, our data confirmed this. When applying these criteria, 23/23 adults (100%) and 18/28 children (64%; Table 1) were able to travel to the target objects using novel paths, therefore demonstrating that they had built a cognitive map using path integration and could use this map to successfully navigate between the four objects without vision.

Importantly, the ability of children to construct a cognitive map did not correlate with age, between 4.8 and 9.7 years of age (Pearson's $r = 0.090$, $n = 28$, $p = 0.650$). Indeed, one of the three youngest children (a 4.8-year-old girl) reached the passing criterion, whereas the oldest child (a 9.7-year-old boy) did not. Moreover, the same proportion of younger children ($<$ 7 years of age: 9/14) and older children ($\geq$7 years of age: 9/14) reached the passing criterion for the cognitive mapping task.

3.4.2. Average distance from the target

There were differences between groups in the distance between the target object and the participant's end location in the novel path trials ($F_{(1,49)} = 17.019$, $p < 0.001$), no difference between paths ($F_{(3.592,175.990)} = 2.068$, $p = 0.094$; Greenhouse-Geisser correction) and no interaction between groups and paths ($F_{(3.592,175.990)} = 0.896$, $p = 0.459$). The distance between the end location and the target object was greater for children than for adults for all six paths, except for the path between the table and the chair for which the difference just failed to reach the predefined level of statistical significance. We also compared the adults' performance with that of the 18 children who passed the cognitive mapping task. There were no differences between the adult group and the group of children who passed the cognitive mapping task, except for the first path: Bench to Chair (adults: 105 ± 21 cm; vs all children: 264 ± 36 cm, $t_{(42.729)} = 3.841$, $p < 0.001$; adults vs passing children: 203 ± 35 cm, $t_{(28.842)} = 2.431$, $p = 0.022$); Chair to Table (adults: 95 ± 15 cm; vs all children: 212 ± 37 cm, $t_{(35.675)} = 2.933$, $p = 0.006$; adults vs passing children: 98 ± 17 cm, $t_{(37.079)} = 0.149$, $p = 0.882$); Table to Shelf (adults: 81 ± 13 cm; vs all children: 175 ± 30 cm, $t_{(36.805)} = 2.878$, $p = 0.007$; adults vs passing children: 131 ± 27 cm, $t_{(24.854)} = 1.648$, $p = 0.112$); Shelf to Table (adults: 78 ± 12 cm; vs all children: 169 ± 27 cm, $t_{(37.465)} = 3.105$, $p = 0.004$; adults vs passing children: 146 ± 34 cm, $t_{(21.273)} = 1.877$, $p = 0.074$); Table to Chair (adults: 78 ± 16 cm; vs all children: 163 ± 41 cm, $t_{(35.224)} = 1.904$, $p = 0.065$; adults vs passing children: 59 ± 12 cm, $t_{(37.800)} = 0.926$, $p = 0.360$); Chair to Bench (adults: 103 ± 17 cm; vs all children: 172 ± 27 cm, $t_{(43.868)} = 2.188$, $p = 0.034$; adults vs passing children: 120 ± 26 cm, $t_{(29.741)} = 0.564$, $p = 0.577$). Importantly, the average distance between the end location and the target object did not correlate with children's age across the six novel paths (Pearson's $r = -0.243$, $n = 28$, $p = 0.212$). The only path for which there was a negative correlation between the distance to target and children's age was the path from the shelf to the table (Pearson's $r = -0.506$, $n = 28$, $p = 0.006$). For all the other paths, the correlations were not statistically significant (all Pearson's

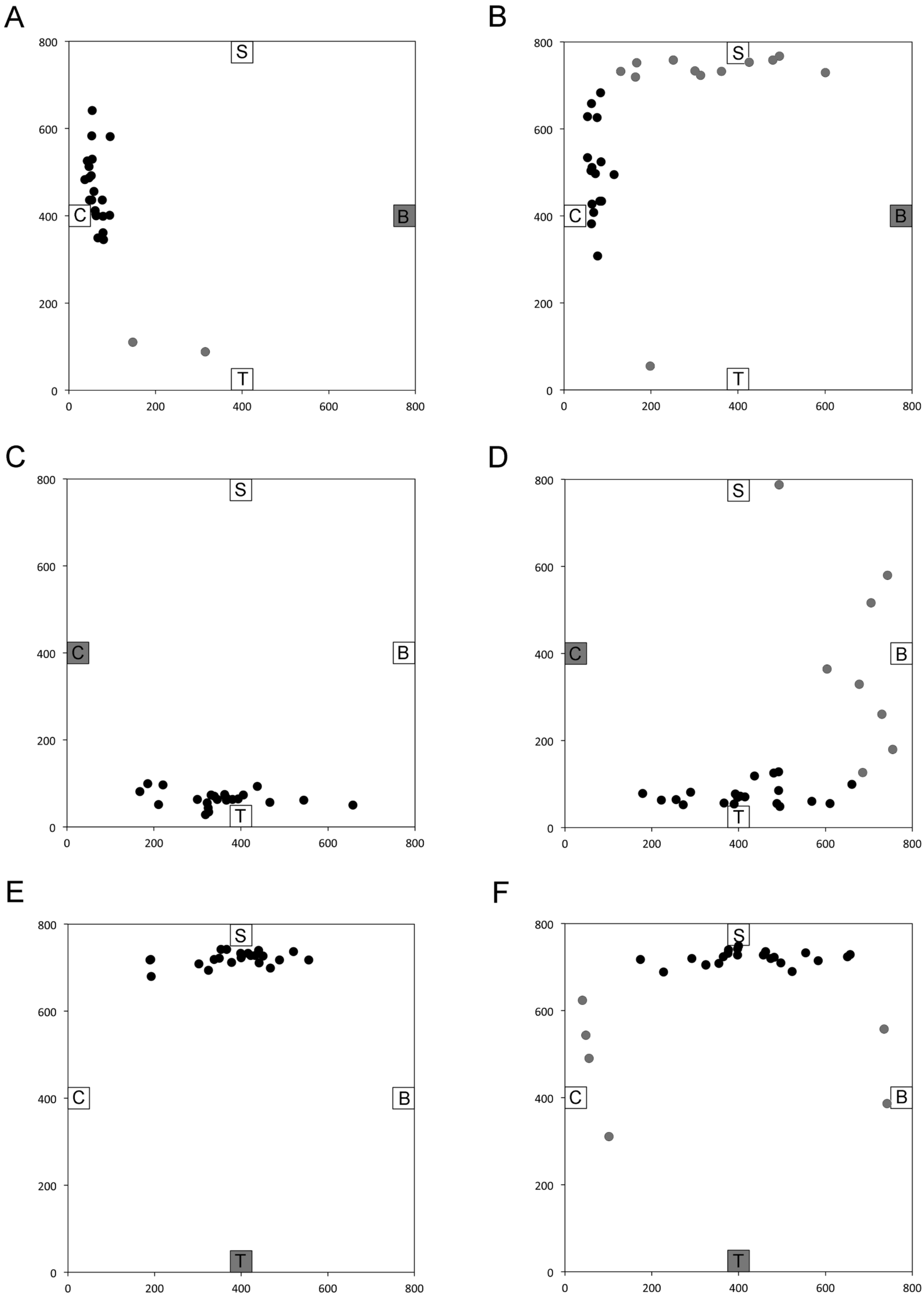

Fig. 4. End location of participants in the novel path trials of the cognitive mapping task. The shaded grey boxes represent the starting location. (A) Bench to Chair, adults: 21/23 ended in the quadrant of the room where the target object was located (black dot: in the correct quadrant; grey dot: in an incorrect quadrant). (B) Bench to Chair, children: 16/28 in the correct quadrant. (C) Chair to Table, adults: 23/23 in the correct quadrant. (D) Chair to Table, children: 20/28 in the correct quadrant. (E) Table to Shelf, adults: 23/23 adults in the correct quadrant. (F) Table to Shelf, children: 22/28 children in the correct quadrant. Room size: 800 cm × 800 cm.

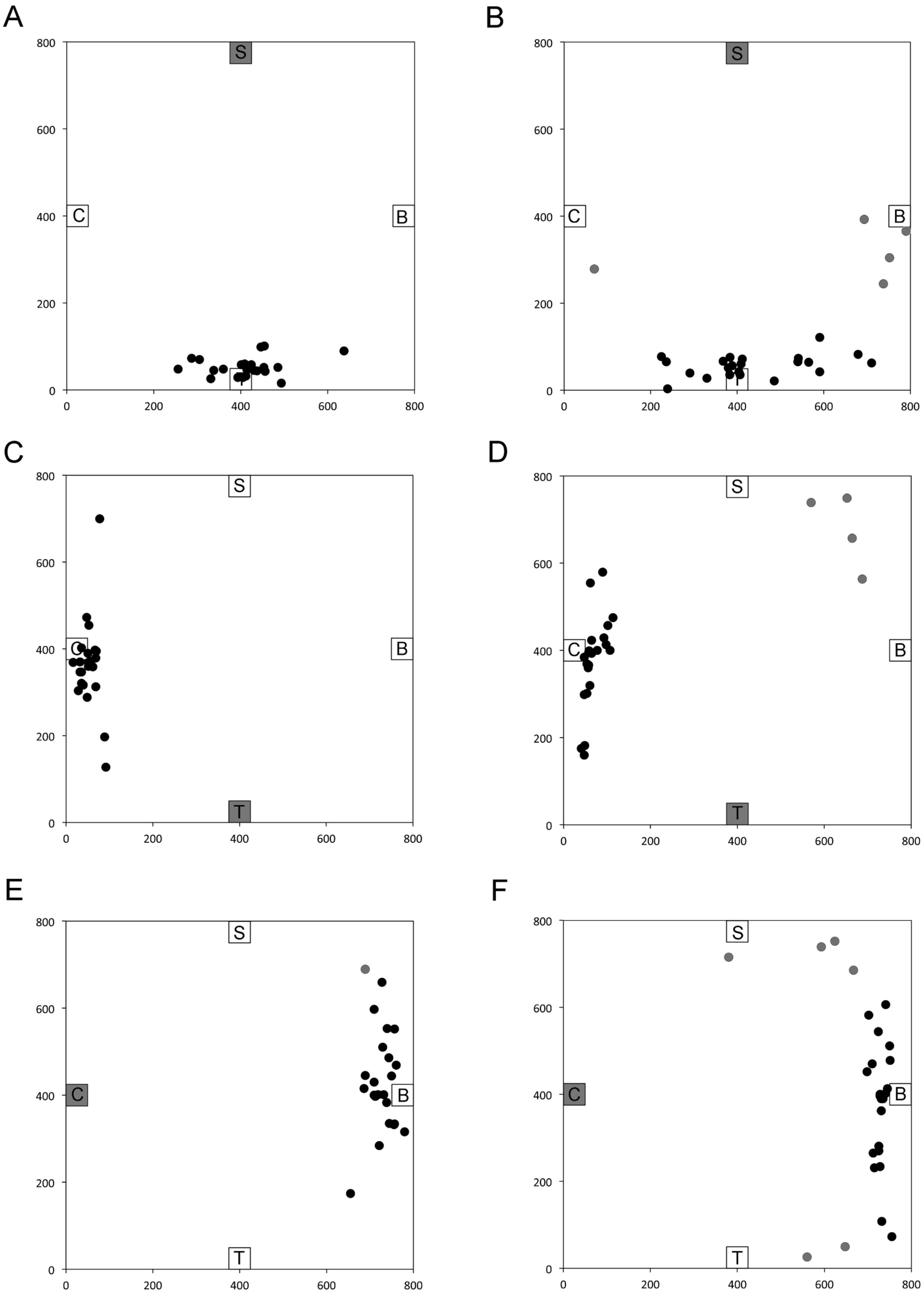

Fig. 5. End location of participants in the novel reverse path trials of the cognitive mapping task. The shaded grey boxes represent the starting location. (A) Shelf to Table, adults: 23/23 ended in the quadrant of the room where the target object was located (black dot: in the correct quadrant; grey dot: in an incorrect quadrant). (B) Shelf to Table, children: 23/28 in the correct quadrant. (C) Table to Chair, adults: 23/23 in the correct quadrant. (D) Table to Chair, children: 24/28 children in the correct quadrant. (E) Chair to Bench, adults: 22/23 in the correct quadrant. (F) Chair to Bench, children: 22/28 in the correct quadrant. Room size: 800 cm × 800 cm.

Table 1
Children's individual performance for the never traveled trajectories of the cognitive mapping task.

Subject	Gender	Age	Criterion	B-C	**C-T**	T-S	S-T	**T-C**	C-B
C39^{*a2}	F	4.83	Pass	1	**1**	1	0	**1**	1
C160	M	4.83	Fail	0	**0**	1	1	**0**	1
C167^{*s1}	M	4.83	Fail	0	**1**	1	1	**0**	0
C187	F	5.00	Pass	1	**1**	1	1	**1**	1
C50^{*a2}	M	5.50	Pass	1	**1**	1	0	**1**	1
C53^{*a1}	F	5.50	Pass	0	**1**	1	1	**1**	1
C186	F	5.67	Fail	0	**0**	0	0	**1**	0
C27	M	5.83	Fail	1	**1**	0	0	**1**	0
C36^{*s1a2}	M	5.92	Pass	1	**1**	1	1	**1**	1
C34	F	6.67	Pass	1	**1**	1	1	**1**	1
C35	M	6.67	Fail	1	**0**	0	1	**1**	1
C48	F	6.67	Pass	0	**1**	1	0	**1**	1
C141	F	6.67	Pass	0	**1**	1	1	**1**	0
C42	M	6.92	Pass	0	**1**	1	1	**1**	1
C49	F	7.08	Fail	1	**0**	1	1	**1**	0
C143	F	7.08	Fail	0	**0**	0	1	**0**	0
C31	F	7.17	Pass	1	**1**	1	1	**1**	1
C25	M	7.25	Fail	0	**0**	0	1	**0**	1
C191	M	7.50	Pass	1	**1**	1	1	**1**	1
C26	F	7.92	Pass	0	**1**	1	1	**1**	1
C29	F	7.92	Pass	1	**1**	0	1	**1**	1
C52^{*a1}	M	8.08	Pass	1	**1**	1	1	**1**	1
C37	M	8.25	Pass	1	**1**	1	1	**1**	1
C138	F	8.42	Pass	1	**1**	1	1	**1**	1
C28	F	8.58	Pass	0	**1**	1	1	**1**	1
C30	F	8.92	Fail	1	**0**	1	1	**1**	1
C142	M	9.17	Pass	1	**1**	1	1	**1**	1
C43	M	9.67	Fail	0	**0**	1	1	**1**	1

Abbreviations: B-C: Bench to Chair. C-T: Chair to Table. T-S: Table to Shelf. S-T: Shelf to Table. T-C: Table to Chair. C-B: Chair to Bench. The * indicates the subjects who were considered to have failed one session of the homing task: s1, straight session 1; s2, straight session 2; a1, angled session 1; a2, angled session 2.

$r > -0.237$, $n = 28$, all $p > 0.225$).

3.4.3. *Initial heading*

In order to determine why some children were less accurate than adults at navigating to the target objects using novel paths, we first analyzed the initial heading of participants after they had walked one meter from the starting object (Supplementary Material 6). Adults' group average initial heading after one meter did not differ from the ideal heading except for the path from the table to the shelf. Children's group average initial heading after one meter did not differ from the ideal heading, or from the adults' initial heading for the paths that required a straight path, but it deviated from the ideal heading and from the adults' initial heading for the two paths requiring a 45° angle path. In addition, the angular deviation of the children's group was greater than the adults' for all of the paths except for the path from the table to the shelf. Children's unsigned angle of initial heading did not correlate with age for any of the paths (Bench to Chair: Pearson's $r = 0.047$, $p = 0.813$; Chair to Table: r: -0.120, $p = 0.543$, Table to Shelf: r: 0.112, $p = 0.569$; Shelf to Table: r: -0.316, $p = 0.101$; Table to Chair: r: -0.309, $p = 0.110$; Chair to Bench: r: -0.251, $p = 0.197$).

Children's less precise and overall less accurate initial headings, as compared to the adults' and to the ideal heading, are consistent with our findings from the homing task showing that children's integration of turns is overall less accurate and less precise than the adults'. However, the fact that the children's initial headings differed only for the two paths requiring a 45° turn may be better explained by the fact that whereas all adults had created a cognitive map of their environment during the learning phase, some children had not. Thus, as a group, the children's initial heading differed from the ideal initial heading, as well as from that of adults for the two paths that required a 45° turn.

3.4.4. *Final heading*

The average heading of the adults at the end of their path did not differ from the ideal heading for any of the trajectories (Supplementary Material 7). The average heading of the children at the end of their path only differed from the ideal heading for the first route (Bench to Chair), and from that of the adults for the first two routes (Bench to Chair and Chair to Table). In contrast, the angular deviation was greater for the children's group than for the adults for all of the paths except for the path from the table to the chair. The unsigned angle of children's final heading did not correlate with age, except for the path from the shelf to the table (Bench to Chair: $r = 0.094$, $p = 0.634$; Chair to Table: $r = -0.062$, $p = 0.753$, Table to Shelf: $r = -0.116$, $p = 0.558$; Shelf to Table: $r = -0.551$, $p = 0.002$; Table to Chair: $r = -0.235$, $p = 0.230$; Chair to Bench: $r = -0.245$, $p = 0.209$).

3.4.5. Headings correlations

There are two important differences between the children's initial and final headings to note. First, children's initial headings differed from the ideal headings for the two angled paths, between the chair and the table and between the table and the chair. However, at the end of their trajectory, children's headings no longer differed from the ideal heading. Nevertheless, children's initial heading and final heading correlated for all paths (Bench to Chair: $r = 0.781$, $p < 0.001$; Chair to Table: $r = 0.788$, $p < 0.001$, Table to Shelf: $r = 0.746$, $p < 0.001$; Shelf to Table: $r = 0.629$, $p < 0.001$; Table to Chair: $r = 0.709$, $p < 0.001$; Chair to Bench: $r = 0.823$, $p < 0.001$).

3.5. Cognitive mapping task: Results summary

Altogether, these findings indicate that 5–9-year-old children are capable of using path integration to build an allocentric spatial representation to take shortcuts, the hallmark of cognitive mapping abilities. Interestingly, children may have solved the 45° angle paths by starting to walk somewhat straight, and then by angling toward the target object at some point after one meter. By comparison, adults turned first, and then walked to the target object. Moreover, whereas children's final heading from the bench to the chair (the first novel path) differed from the ideal heading (indeed, this was the path on which the fewest children succeeded, and the distance from the participants' end location to the chair differed between adults and children who passed the cognitive mapping task), their initial heading did not differ from the ideal heading. This suggests that either (1) some children thought the chair was not positioned directly in front of the bench (they had the correct topological relation, but they miscalculated its precise angular relations with the bench) or (2) the children could not walk straight. The results from the homing task, and the fact that children's final heading for the reverse path from the chair to the bench did not differ from that of adults or the ideal trajectory, indicated that 5–9-year-old children are capable of walking sufficiently straight for seven meters in absence of visual information. It is thus most likely that some of the children's initial estimation of the location of the chair was somewhat distorted or imprecise, and may have to do with an inaccurate estimation or integration of the two 45° angles experienced during the learning phase between the bench and the shelf, and between the shelf and the chair.

4. Discussion

The aim of this study was to characterize the capacity of 5–9-year-old children to use path integration to build egocentric and allocentric spatial representations to navigate in their environment. We found that children from five years of age can use path integration in absence of visual information to (1) return to a home base and (2) build a cognitive map. Ninety percent of the children between 4.8 and 9.7 years of age could reliably return to the home area in the homing task, and sixty-four percent of the children were judged to have successfully built a cognitive map enabling them to take novel routes or shortcuts between different object locations. Importantly, age did not predict children's ability to construct a cognitive map, as the proportion of children younger than seven years of age who succeeded was the same as the proportion of children older than seven years of age. In fact, the youngest child in our study (4.8 years old) succeeded, whereas the oldest child (9.7 years old) did not.

4.1. Comparison with previous studies

Our results are consistent with previous reports that very young children can gain knowledge of the spatial relationships between objects, and that vision is not essential in the development of this knowledge (Landau et al., 1981, 1984). Using the same paradigm, Morrongiello et al. (1995) presented data showing that young children were less precise than older children at navigating to objects via novel routes without vision. However, they made no claim as to whether 5–9-year-old children could use path integration to build a cognitive map. Given the individual variation that Morrongiello et al. (1995) observed, they urged "*caution in ascribing well developed Euclidean coding skills to very young children*", as was proposed by Landau and colleagues. Our results complement these two series of studies, by affirming that 5–9-year-old children can use path integration to build a cognitive map in absence of visual information, yet demonstrating that their performance in both the homing and cognitive mapping tasks is less accurate and more variable than that of young adults. Our results suggest that the capacity to build a cognitive map without vision is developed and accessible to children by at least 5 years of age. Moreover, due to substantial individual variability, as was shown previously in allocentric spatial learning tasks performed in the presence of visual information (Ribordy Lambert et al., 2016), chronological age is not a reliable predictor of task performance for children in this age range.

With respect to the cognitive mapping abilities of children between 2.5 and 5 years of age, the study of Landau et al. (1984) included Kelli, a congenitally blind 2.6-year-old child, and five normally sighted but blindfolded children between 2.8 and 3.8 years of age. In contrast, Morrongiello et al. (1995) limited their study to children between 4.5 and 9 years of age because the 12 children who they tested between 3 and 4 years of age refused to keep the obscuring goggles on, and/or refused to perform the task and walk alone without vision. Similarly, three participants between 4 and 5 years of age that we attempted to test refused to wear the sleeping mask and/or walk alone without vision. Thus, although we could not confirm the findings of Landau and colleagues with normally sighted participants younger than 4.8 years of age, we have no reason to doubt them either. Indeed, it was previously shown by independent laboratories that from around two years of age children can build and use an allocentric representation of their environment to locate a hidden reward in presence of visual information (Newcombe et al., 1998; Ribordy et al., 2013; Ribordy Lambert et al., 2015), and that 3-year-old children benefit from external "room" landmarks to identify a toy's location in an array of cups (Nardini et al., 2006). Altogether, these findings indicate that children as young as 2.5 years of age are capable of building cognitive maps of the spatial relationships between environmental objects. Importantly, although children's spatial representations of the environment, both in the absence and presence of visual information, are less precise than those of adults, our data reveal that adults' representations are also not perfectly accurate. Thus, although it is often argued that precise metric information, including angles and distances, must be accurately encoded in order to represent the Euclidean properties of space in cognitive maps (Gallistel, 1990; O'Keefe & Nadel, 1978; Warren, 2019), this does not appear to be the case, even in adults.

4.2. Path integration and a noisy cognitive mapping system

If a cognitive mapping system as proposed by O'Keefe and Nadel (1978) must necessarily encode precise metric information in order to build an exact Euclidean representation of space, then one must question the existence of cognitive maps in any organism, including adult humans. Nevertheless, behavioral and neurophysiological evidence suggest that both angular and distance information are represented in the brain, but that these representations are not exact replicates of the external world. In agreement with the concept of cognitive map as proposed by Tolman (1948), such representations encode the relationships between environmental objects and between the individual and other locations (Dabaghian, Brandt, & Frank, 2014; Poucet et al., 2015), and support flexible behavior (Behrens et al., 2018). Indeed, the representation of spatial information in the brain via individual head direction cells, place cells and grid cells is fundamentally noisy and thus imprecise in absolute terms (McNaughton et al., 1996; Taube, 2007). Yet, an animal's location can be decoded reliably from ensembles of place cells (Wilson & McNaughton, 1993) and grid cells (Fyhn, Molden, Witter, Moser, & Moser, 2004), and with increasing precision as the animal spends more time exploring the environment (Wilson & McNaughton, 1993). Accordingly, such spatial representations are sufficiently precise in order to enable successful navigation with or without visual information, as long as stable environmental visual, olfactory or somatosensory landmarks are occasionally available to update the representation of the animal's position (Etienne & Jeffery, 2004; McNaughton et al., 1996). In our study, both adults and children demonstrated the ability to take shortcuts to navigate between different objects, thus exhibiting their ability to use path integration to build a cognitive map of the relations between environmental objects in absence of visual information. However, all of our participants exhibited some degree of imprecision in their behavioral performance.

Our analyses of children's initial heading at one-meter in the homing task showed that they tended to under-rotate after being guided through the two-legged path (requiring an ideal left or right rotation of 135°), but they did not under-rotate following the straight path (requiring an ideal left or right rotation of 180°). Our results are consistent with those of Smith et al. (2013) who showed that 7–9-year-old blindfolded children under-rotated during a triangle completion task with a 90° guided turn, which also required an ideal 135° rotation before walking between 1.4 and 2.8 m to return home. Together, these results suggest that 5–9-year-old children are capable of producing turns of a specific desired angle, since they were capable of making a relatively precise 180° turn following the straight path journey in our experiment, but that their ability to integrate experienced rotations during the outward path is less precise than adults'. Indeed, previous authors have proposed that errors in path integration arise primarily from encoding errors of the experienced angles to be integrated (Fujita et al., 1993). However, across both the homing and the cognitive mapping tasks, even though children's initial heading was different from the ideal heading in four of ten paths (both angled paths in the homing task, and the two paths requiring a 45° turn in the cognitive mapping task), their final heading was only different from the ideal heading in one of these ten paths (the first path from the bench to the chair in the cognitive mapping task). Thus, children appeared to make less than ideal turns but continued to angle towards the goal while walking, whereas adults appear to have made more accurate turns first, and then walked straight to the goal. This difference in strategy between children and adults may be due to the fact that in our homing task participants repeated each of the four paths five times, and thus had the opportunity to correct their errors and compensate for their homing inaccuracies. Whereas adults had quite accurate initial and final headings and did not need to compensate, it is possible that some children recognized that they ended up to the left or the right of home (depending on the outward path) on the first trial or two, and then attempted to compensate while walking by veering more to the right or to the left, respectively.

In sum, when considering our data and the data from Smith et al. (2013), we believe that the most parsimonious explanation is that children are less precise than adults in integrating experienced rotations in the dark, leading them to systematically under-rotate when calculating the ideal return trajectory. Interestingly, however, Wiener, Berthoz, and Wolbers (2011) reported that when given specific instructions, adult individuals can either continuously update their position with respect to the start location (a.k.a. a continuous strategy) or remember the shape of the outbound path and calculate a homing vector based on this representation (a.k.a. a configural strategy). In their study, overall homing accuracy was better when subjects used the configural strategy, although experimental evidence indicated that these subjects also computed a homing vector continuously. Thus, an alternative explanation to our results may be that children relied more on a continuous computation to calculate their homing direction, whereas adults may have benefited from the added precision provided by a configural (cognitive) strategy in order to reconstruct the return path. Nevertheless, in our cognitive mapping task, there was a long temporal delay between when participants were guided to the first two objects and when they had to navigate the novel routes (usually more than 10 min for children), making the idea of a continuous computation strategy difficult to support theoretically.

If, however, children did systematically under-rotate when calculating a return trajectory, then this suggests that they overestimated the magnitude of the rotation experienced during the outward trajectory. This assumption is indeed consistent with the observed performance of some children in the cognitive mapping task. During the learning phase of this task, if these children similarly overestimated the experienced angles between the bench and the shelf ($> 45°$), and between the shelf and the chair ($> 45°$), their estimation of the position of the chair relative to the bench should place the chair to the right of the bench and not straight in front of it. Indeed, children's average final heading from the bench to the chair of 20.57° was outside of the 99% confidence interval (11.57°), and both their final heading and their angular deviation differed from that of adults. Moreover, 11 of the 12 children who failed this route ended their path to the right of the chair, a distribution that is clearly not random. However, this was the only novel route for which children's final heading was outside the 99% confidence interval, suggesting that after they were guided to the chair from their end location they were able to quickly update their cognitive map, allowing them to more accurately navigate from the chair to the table (with 20/28 passing), and from the table to the shelf (with 22/28 passing), with final headings that were in the 99% confidence interval for both of these paths.

Altogether, the findings from the homing and cognitive mapping tasks suggest that from at least five years of age children are capable of turning sufficiently accurately and walking a straight line in order to perform low-resolution cognitive mapping without vision. Nonetheless, as compared to adults, 5–9-year-old children may integrate experienced angular rotations less well and be less precise in their path integration computations.

4.3. Why did some children fail to build a cognitive map?

Whereas the imprecise integration of angular displacements may have resulted in some children not passing by our subjective criteria, we can nonetheless identify a number of children who clearly had not built a cognitive map during the learning phase. These children can be seen going straight or in the opposite direction of the target in the chair to table and the table to chair paths. Our observations while these children were performing the task suggested that they were either inattentive, bored or dismissive of the experiment during the learning phase. However, a number of other children who succeeded in building a cognitive map in our study could also be described in this same manner.

We are thus left to conclude that all children from five years of age, or indeed even from 2.5 years of age if we consider other previous results (Landau et al., 1984; Newcombe et al., 1998; Ribordy et al., 2013; Ribordy Lambert et al., 2015), should be capable of building a cognitive map using path integration, but that some children simply fail to construct a cognitive map when the specific goals of the experiment have not been explicitly explained. Interestingly, in our experience using a number of tasks in which participants are given very few explicit verbal instructions concerning the aim of the experiment, we have found that about 15% of participants, be they children or adults, and with typical or atypical development, do not implicitly infer the aim of the experiment (Bostelmann et al., 2017, 2018; Ribordy et al., 2013). In the current study, we believe that all children between five and nine years of age would have exhibited the capacity to build a cognitive map had we explained that: "We are going to lead you on some paths between different pieces of furniture. At the end of the experiment, it will be your job to go to all of the different objects, so make sure that you think about and remember where all of the objects are."

However, implying that some children did not implicitly make cognitive maps because they were not paying attention implies that cognitive mapping is necessarily effortful or requires explicit attention (Newcombe, 2019). Instead, cognitive mapping has been assumed to be a continuous and automatic process (O'Keefe & Nadel, 1978; Tolman, 1948). Nevertheless, as we can all attest, from time to time we become lost in new or unfamiliar environments. Our capacity to build a cognitive map can be diminished when we are distracted or not paying attention when navigating, or when we are "blindly" following someone else who is doing the navigating. In our study, participants were never told that they should keep track of the locations of the objects in the room so that they could later navigate between them autonomously. Whereas all of our adult participants were able to construct a cognitive map (some or all of whom may have implicitly inferred the goal of the experiment), one third of the children did not. Interestingly, however, four of the eight children who failed the first 45° angle trajectory between the chair and the table were able to perform the second 45° angle trajectory and navigate appropriately from the table back to the chair, suggesting that once they understood the goal of the task they were able to quickly construct or improve an imprecise or incomplete cognitive map during the testing phase of the task. Indeed, if we use a more liberal criterion for determining whether children constructed a cognitive map, by considering only the trajectory from the table to the chair, we could conclude that 86% (24 of 28) of the 5–9-year-old children succeeded. In contrast to previous assertions that successful cognitive mapping is not exhibited by children until early adolescence (Newcombe, 2019), the current findings, as well as data from previous studies (Landau et al., 1981, 1984; Morrongiello et al., 1995), demonstrate that from at least 5 years of age children are capable of constructing and using a cognitive map, a representation of the relationships between objects' locations, in order to behave flexibly and navigate between these locations using novel routes (Behrens et al., 2018; Tolman, 1948). In contrast to the cognitive map concept proposed by O'Keefe and Nadel (1978), although the precision of these representations improves between childhood and adulthood, humans do not appear to encode the precise metric information necessary to build an exact Euclidean representation of space even in adulthood (Banta Lavenex, Colombo, Ribordy Lambert, & Lavenex, 2014). However, an exact Euclidean representation is likely not necessary since the perception of external landmarks from a distance can often be used to pinpoint the goal location and guide the final approach.

4.4. Path integration is less precise in children than in adults

Although a majority of 5–9-year-old children were able to build a cognitive map representing the spatial relationships between environmental objects, their variability in task performance was greater than that of adults. However, we did not find consistently reliable correlations between children's age and task performance in the homing or cognitive mapping tasks. This suggests that although the integration of directional and distance information may become more precise with age between childhood and adulthood, such integration remains highly variable both within and between individual children until at least nine years of age. Moreover, as previously described, path integration accrues error with every turn and every step. Obviously, children and adults had to integrate the same number of turns of the same magnitude. In contrast, due to their smaller size children had to take many more steps than adults in order to travel along the guided and non-guided paths. The fact that neither the task nor the environment was scaled to the participants' size or step length may have contributed to the overall more variable performance of children as compared to adults. Note also that since children's size continues to evolve until young adulthood, the integration of sensory information derived from different sensory modalities must be constantly updated (Newcombe, 2019). This is another factor potentially contributing to the larger variability of behavioral performance observed in children, as compared to adults (Nardini et al., 2008; Ribordy et al., 2013; Ribordy Lambert et al., 2015, 2016). Interestingly, the calibration of path integration has been shown to change with experience (Jayakumar et al., 2019), and this plasticity may underlie developmental changes over the lifespan.

4.5. *Distance estimation and cognitive maps*

Whereas our experimental paradigm was very reliable for measuring the angular displacements (i.e., initial and final headings) of participants, it was less informative with respect to the linear displacements or distances traveled. First, in the homing task, participants repeated the same return path a total of 24 times, thus offering older children and adult participants the possibility of explicitly counting the number of steps required to return home, and adjusting this number based on trial and error (i.e., using a secondary cognitive strategy). Second, our experimental room was only 8 m × 8 m, thus limiting the maximal distance that participants could walk. Indeed, we found that children often had to be stopped before running into walls on their return paths, making the comparison of the distance traveled between adults and children invalid. However, it is impossible to know whether children were worse at estimating distance, or whether they had difficulties in understanding that they could consciously "estimate" distance and then explicitly use this knowledge to stop at a given point even though they had not reached a detectable goal location. Both explanations may have played a role in children's poor estimation of distance.

However, how important is distance estimation to the formation of cognitive maps? Whereas the critical role that precise angular estimation plays in cognitive map formation and navigation is obvious, the importance that distance estimation plays has long been disputed in the literature (Etienne & Jeffery, 2004; Etienne et al., 1996; M. L. Mittelstaedt & Mittelstaedt, 1980, 2001; O'Keefe & Nadel, 1978; Seguinot et al., 1993; Wehner & Wehner, 1986). Given that the distance travelled must be calculated via a combination of vestibular, proprioceptive and visual cues that integrate linear displacement, stride length and regularity, and visual flow (Campos, Butler, & Bulthoff, 2014; Souman, Freeman, Eikmeier, & Ernst, 2010), distance estimation must be highly sensitive to the age, size and health of the individual (Adamo, Briceno, Sindone, Alexander, & Moffat, 2012). Such integration must necessarily change across an individual's lifespan (Bullens et al., 2010), potentially making precise distance estimation difficult in long-lived and slowly-growing humans (Newcombe, 2019), even though the calibration of path integration changes with experience (Jayakumar et al., 2019). In contrast, a path integration system that has a relatively precise coding of angular displacement, combined with a gross and relative coding of linear displacement, may be accurate enough to support navigation over relatively short distances. Indeed, if one's angular estimation is correct, then navigating with a gross estimation of distance (a few meters away versus tens of meters away) will allow the individual to anticipate the location of the goal, and to recognize the goal or a familiar landmark that will help to localize the goal or the direction to the goal, when it is eventually approached (Etienne & Jeffery, 2004). In our cognitive mapping task, the target objects provided the necessary information to recalibrate the path integration system when building a cognitive map of the spatial relationships between these objects.

4.6. *Early emergence of cognitive mapping abilities*

In a recent review, Newcombe (2019) suggested that cognitive maps might not become widely evident in children until around 12 years of age. Evidence for such protracted development comes primarily from studies carried out in virtual environments (Broadbent et al., 2014; Buckley et al., 2015; Bullens et al., 2010), or from studies that dissociated different types of information in order to assess their role relative to, or in isolation from, other cues (e.g., Bullens et al., 2011; Nardini et al., 2008). However, as we and others have previously argued (Banta Lavenex et al., 2014; Cullen & Taube, 2017; Taube, Valerio, & Yoder, 2013), evidence from virtual reality paradigms, or from paradigms in which normally coherent cues are rendered incoherent, or from paradigms which require other higher order cognitive capacities (such as advanced linguistic, mental rotation, or theory of mind capacities) cannot be used to infer the absence of cognitive mapping capacities in the real world, in particular in developing individuals or in individuals with neurodevelopmental syndromes or acquired pathologies (i.e., the absence of evidence in an experimental setting cannot be considered as evidence of absence in the real world). Indeed, as described above, cognitive maps are constructed via the integration of coherent vestibular, proprioceptive, motor efference and visual information. In contrast, experiments carried out in virtual reality, for example, rely solely on visual information, and in fact oppose visual information with incoherent or absent vestibular and proprioceptive information (Adamo et al., 2012; Ravassard et al., 2013; Souman et al., 2010; Taube et al., 2013). This is especially problematic since experiments in rodents have shown that hippocampal place cell activity is abnormal without vestibular input (Ravassard et al., 2013; Stackman, Clark, & Taube, 2002), and since hippocampal place cells are at the core of cognitive maps (McNaughton et al., 2006; O'Keefe & Nadel, 1978). Similarly, although tasks that dissociate or render incoherent different cues may be informative about how the system performs under those specific conditions, they cannot inform about how the system works when all cues are present and coherent. Indeed, some experimental specificities may influence participants to use particular strategies, or to ignore other strategies, but this cannot be taken as evidence to conclude that the unused strategy is not available. In order to make such claims, paradigms that preclude the use of alternative strategies, yet afford participants the use of all normally coherent sensory information, and exclude the necessity of using other higher-order cognitive processes to understand or accomplish the task must be used (Nadel & Hardt, 2004). Our critique of these paradigms should not be taken to mean that we deny the interest and importance of using virtual reality and cue dissociation paradigms to study certain spatial processes. These paradigms can indeed be useful to tease apart some basic cognitive processes and to understand how other implicit and explicit cognitive processes might interact with and impact these basic spatial processes. However, there is a serious logical confound in using the results from virtual reality experiments or cue dissociation tasks to infer that children or individuals with neurodevelopmental disorders or acquired pathologies are incapable of constructing allocentric spatial representations in the real world where the individuals have access to coherent information from all of the sensory modalities normally available to be integrated in a multimodal spatial representation.

4.7. Conclusion

The current findings, together with those of Landau et al. (1981, 1984) and Morrongiello et al. (1995), provide consistent evidence that by at least five years of age children can use path integration in absence of visual information to build a cognitive map representing the spatial relationships between environmental objects. Based on earlier findings in the presence of visual information (Newcombe et al., 1998; Ribordy et al., 2013; Ribordy Lambert et al., 2015, 2016), as well as Landau's initial reports, we may hypothesize that a cognitive mapping system integrating all types of sensory information may already be functional by two years of age. The present evidence also suggests that children's cognitive mapping capacities may improve with age, due to decreased intra-individual variability and increased encoding precision, but these improvements should be considered quantitative changes rather than qualitative changes.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cogpsych.2020.101307.

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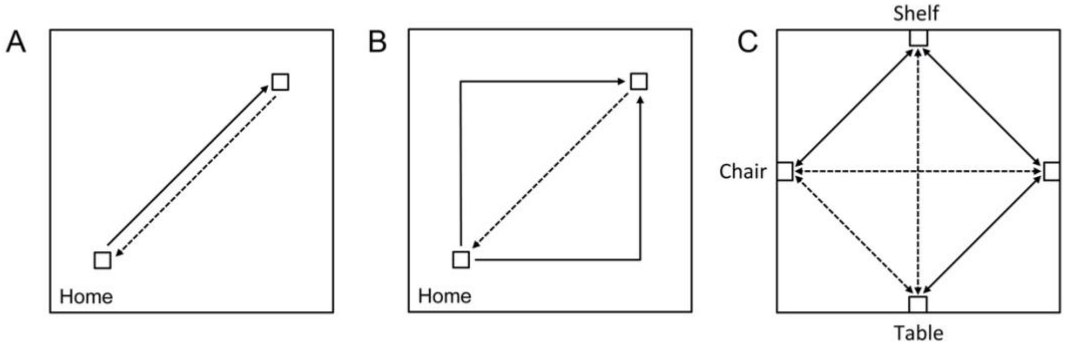
Supplementary Material 1: Schematic representation of the experimental design and sequence of trajectories performed by participants in the homing and cognitive mapping tasks.

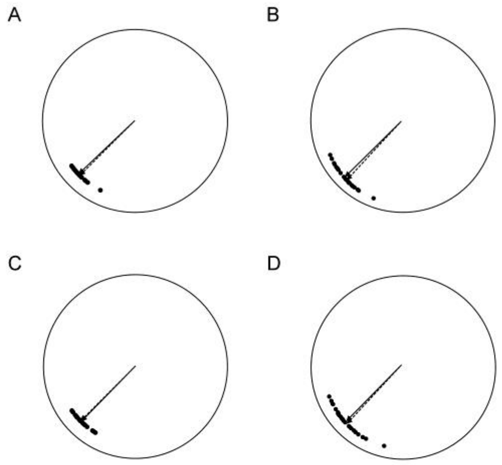


1.1 Schematic representation of the experimental design carried out in an 8 m x 8 m testing room. Solid lines indicate guided trajectories; dashed lines indicate direct paths that participants were verbally requested to make. A. Homing task, straight paths: 7 m straight line guided trajectory, 7 m return path. B. Homing task, angled paths: 10 m angular guided trajectory with a right or left turn (5 m + 5 m), and 7 m return path. C. Cognitive mapping task: Guided routes (solid) and novel routes (dashed) between four objects, in absence of vision. The paths between the bench and the chair, and between the table and the shelf were 7 m long; the other paths were 5 m long.

1.2 Sequence of trajectories performed by participants in the cognitive mapping task.

	Children	**Adults**
Learning Phase	Bench to shelf round-trip guided 2 x	Bench to shelf round-trip guided 2 x
	Bench to shelf round-trip alone 1 x	Bench to shelf round-trip alone 2 x
	Bench to shelf round-trip guided 2 x	Bench to shelf 1-way alone 1 x
	Bench to shelf round-trip alone 2 x	Shelf to chair round-trip guided 2 x
	Bench to shelf 1-way alone 1 x	Shelf to chair round-trip alone 2 x
	Shelf to chair round-trip guided 2 x	Shelf to bench 1-way alone 1 x
	Shelf to chair round-trip alone 1 x	Bench to table round-trip guided 2 x
	Shelf to chair round-trip guided 2 x	Bench to table round-trip alone 2 x
	Shelf to chair round-trip alone 2 x	
	Shelf to bench 1-way alone 1 x	
	Bench to table round-trip guided 2 x	
	Bench to table round-trip alone 1 x	
	Bench to table round-trip guided 2 x	
	Bench to table round-trip alone 2 x	
Testing Phase	Bench to chair alone 1 x	Bench to chair alone 1 x
	Chair to table alone 1 x	Chair to table alone 1 x
	Table to shelf alone 1 x	Table to shelf alone 1 x
	Shelf to table alone 1 x	Shelf to table alone 1 x
	Table to chair alone 1 x	Table to chair alone 1 x
	Chair to bench alone 1 x	Chair to bench alone 1 x

Supplementary Material 2. Initial heading - Homing task - Straight outward paths

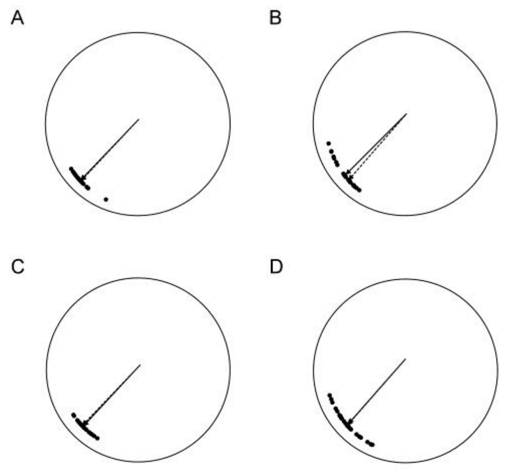


2.1 Average (solid-line arrow) and individual (dots) walking directions of participants after one meter along the return path, following a straight 7 m outward journey in the homing task. A. Adults, Session 1. B. Children, Session 1. C. Adults, Session 2. D. Children, Session 2. Dashed-line arrow: perfect home direction.

2.2 Statistical results: Initial heading - Homing task - Straight outward paths

	Adults				Children				Adults vs Children	
Path	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.	Initial Heading	Angular Deviation
Session 1	1.48°	<	3.62°	6.23°	2.31°	<	5.41°	10.32°	$F_{(1,49)}$ = 0.1104 p = 0.7411	$t_{(49)}$ = 2.2629 p = 0.0281
Session 2	0.65°	<	3.54°	6.10°	1.47°	<	6.25°	11.87°	$F_{(1,49)}$ = 0.5793 p = 0.4502	$t_{(49)}$ = 2.8377 p = 0.0066

Supplementary Material 3. Final heading - Homing task - Straight outward paths

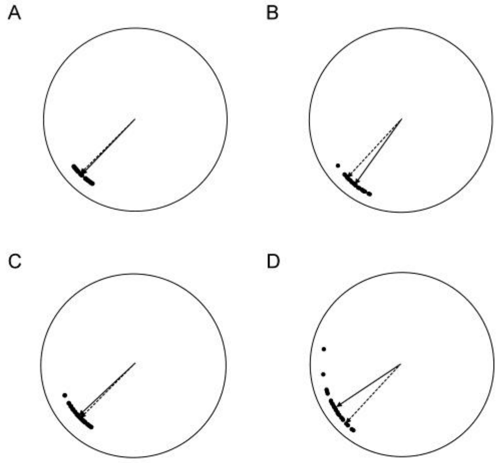


3.1 Average (solid-line arrow) and individual (dots) final heading direction at the end of the return path, following a straight 7 m outward journey in the homing task. A. Adults, Session 1. B. Children, Session 1. C. Adults, Session 2. D. Children, Session 2. Dashed-line arrow: perfect home direction.

3.2 Statistical results: Final heading - Homing task - Straight outward paths

	Adults				Children				Adults vs Children	
Path	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.	Final Heading	Angular Deviation
Session 1	0.61°	<	3.68°	6.33°	3.73°	<	5.17°	9.87°	$F_{(1,49)}$ = 1.6477 p = 0.2053	$t_{(49)}$ = 2.1482 p = 0.0367
Session 2	0.89°	<	3.32°	5.72°	0.05°	<	6.09°	11.57°	$F_{(1,49)}$ = 0.1197 p = 0.7308	$t_{(49)}$ = 2.5582 p = 0.0137

Supplementary Material 4. Initial heading - Homing task - Angled outward paths

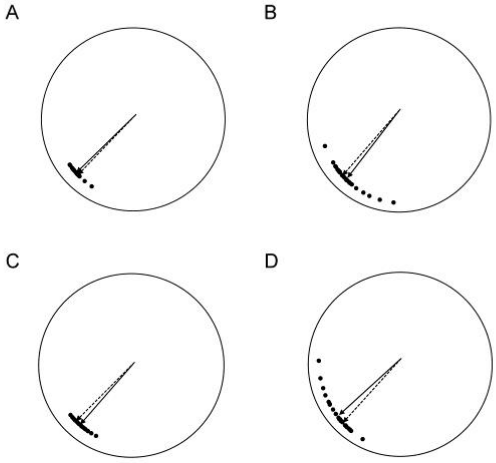


4.1 Average (solid-line arrow) and individual (dots) walking directions of participants after one meter along the return path, following a two-legged 10 m angled outward journey in the homing task. A. Adults, Session 1. B. Children, Session 1. C. Adults, Session 2. D. Children, Session 2. Dashed-line arrow: perfect home direction.

4.2 Statistical results: Initial heading - Homing task - Angled outward paths

	Adults				Children				Adults vs Children	
Path	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.	Initial Heading	Angular Deviation
Session 1 R Turn	1.34°	<	3.32°	5.72°	7.52°	>	3.84°	7.37°	$F_{(1,49)}$ = 10.4021 p = 0.0022	$t_{(49)}$ = 2.5015 p = 0.0158
Session 2 L Turn	2.18°	<	4.37°	7.51°	13.51°	>	6.79°	12.85°	$F_{(1,49)}$ = 13.4018 p <=0.0006	$t_{(49)}$ = 3.3516 p = 0.0016

Supplementary Material 5. Final heading - Homing task - Angled outward paths

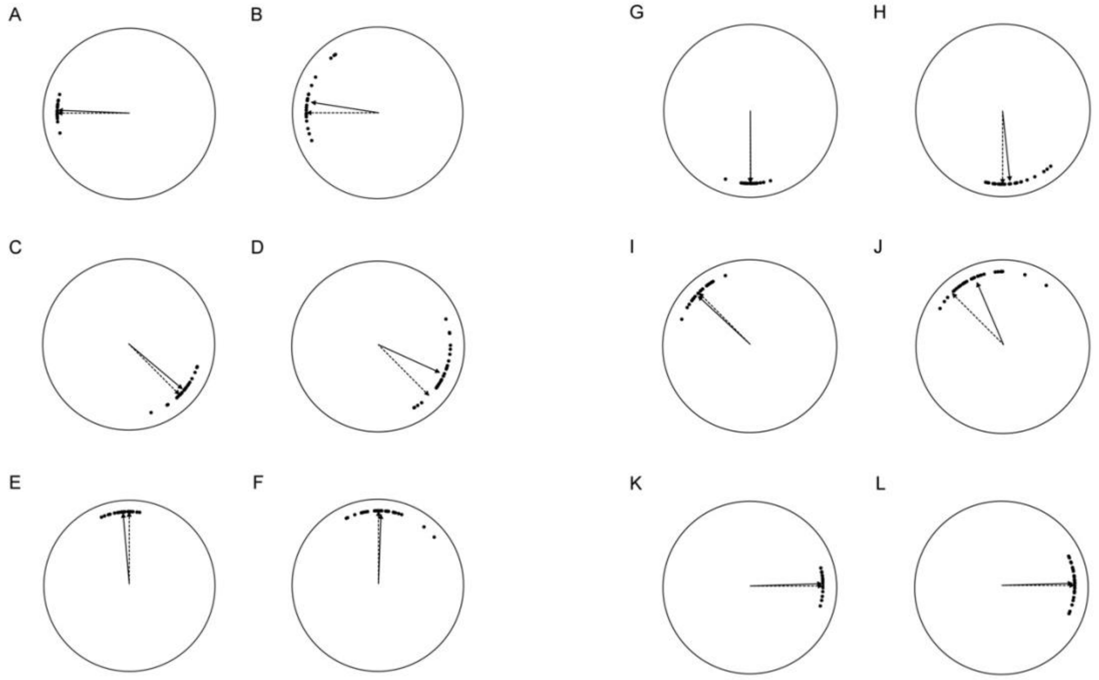


5.1 Average (solid-line arrow) and individual (dots) final heading direction at the end of the return path, following a two-legged 10 m outward journey in the homing task. A. Adults, Session 1. B. Children, Session 1. C. Adults, Session 2. D. Children, Session 2. Dashed-line arrow: perfect home direction.

5.2 Statistical results: Final heading - Homing task - Angled outward paths

	Adults				Children				Adults vs Children	
Path	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.	Final Heading	Angular Deviation
Session 1 R Turn	1.91°	<	2.68°	4.62°	3.66°	<	6.56°	12.44°	$F_{(1,49)}$ = 3.9721 p = 0.0518	$t_{(49)}$ = 2.5112 p = 0.0154
Session 2 L Turn	3.73°	>	3.45°	5.94°	5.24°	<	6.89°	13.03°	$F_{(1,49)}$ = 8.9929 p = 0.0043	$t_{(49)}$ = 1.8389 p = 0.0720

Supplementary Material 6. Initial heading – Cognitive mapping task - Novel paths

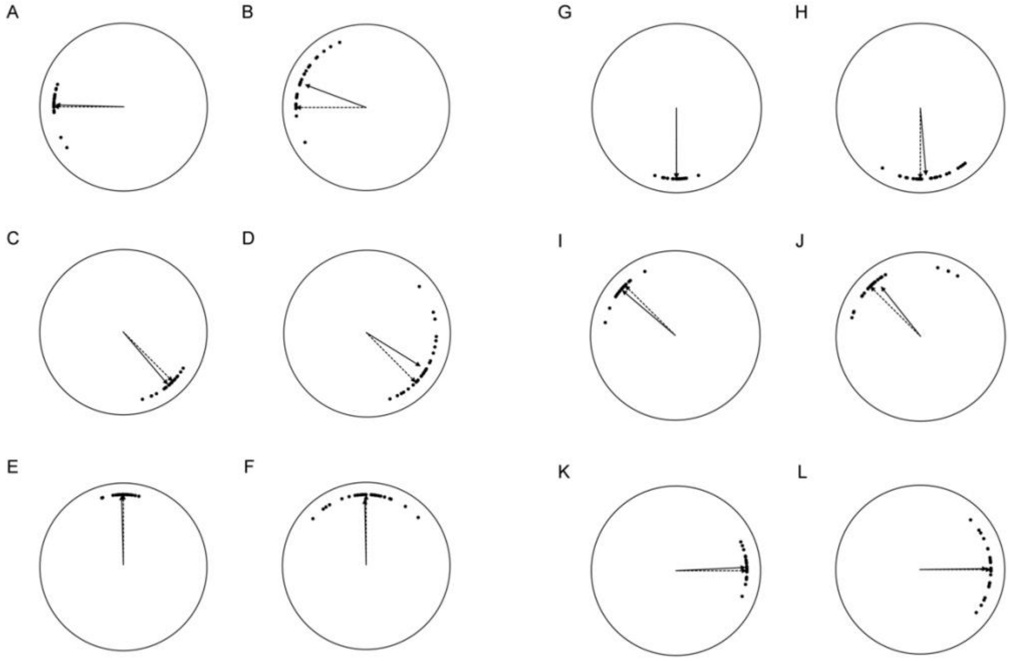


6.1 Average (solid-line arrow) and individual (dots) initial heading of participants after walking one meter along the path from the starting object in the cognitive mapping task. A. Adults, Bench to Chair. B: Children, Bench to Chair. C. Adults, Chair to Table. D. Children, Chair to Table. E. Adults, Table to Shelf. F: Children, Table to Shelf. G. Adults, Shelf to Table. H. Children, Shelf to Table. I. Adults, Table to Chair. J. Children, Table to Chair. K. Adults, Chair to Bench. L. Children, Chair to Bench. Dashed-line arrow: perfect direction.

6.2 Statistical results: Initial heading – Cognitive mapping task - Novel paths

Path	Adults				Children				Adults vs Children	
	Initial Head.	< >	99% C.I.	Ang. Dev.	Initial Head.	< >	99% C.I.	Ang. Dev.	Initial Heading	Angular Deviation
B to C	2.24°	<	3.61°	6.22°	8.92°	<	9.60°	17.81°	$F_{(1,49)}$ = 2.8157 p = 0.0997	$t_{(49)}$ = 2.7944 p = 0.0074
C to T	4.97°	<	6.96	11.81°	20.69°	>	10.68°	19.61°	$F_{(1,49)}$ = 10.8819 p = 0.0018	$t_{(49)}$ = 4.0430 p = 0.0002
T to S	4.91°	>	4.56°	7.83°	2.02°	<	8.69°	16.23°	$F_{(1,49)}$ = 3.3787 p = 0.0721	$t_{(49)}$ = 1.8109 p = 0.0763
S to T	0.26°	<	4.13°	7.09°	5.93°	<	7.64°	14.39°	$F_{(1,49)}$ = 2.8552 p = 0.0974	$t_{(49)}$ = 2.4322 p = 0.0187
T to C	2.37°	<	6.59°	11.20°	21.95°	>	11.39°	20.78°	$F_{(1,49)}$ = 15.8164, p = 0.0002	$t_{(49)}$ = 3.5816 p = 0.0008
C to B	1.86°	<	4.11	7.06°	1.67°	<	6.56°	12.43°	$F_{(1,49)}$ = 0.0044 p = 0.9473	$t_{(49)}$ = 2.5362 p = 0.0144

Supplementary Material 7. Final heading – Cognitive mapping task - Novel paths



7.1 Average (solid-line arrow) and individual (dots) final heading (at the end of the path) in the cognitive mapping task. A. Adults, Bench to Chair. B: Children, Bench to Chair. C. Adults, Chair to Table. D. Children, Chair to Table. E. Adults, Table to Shelf. F: Children, Table to Shelf. G. Adults, Shelf to Table. H. Children, Shelf to Table. I. Adults, Table to Chair. J. Children, Table to Chair. K. Adults, Chair to Bench. L. Children, Chair to Bench. Dashed-line arrow: perfect direction.

7.2 Statistical results: Final heading – Cognitive mapping task - Novel paths

Path	Adults				Children				Adults vs Children	
	Final head.	< >	99% C.I.	Ang. dev.	Final head.	< >	99% C.I.	Ang. dev.	Final heading	Angular deviation
B to C	1.69°	<	6.83°	11.61°	20.57°	>	11.57°	21.08°	$F_{(1,49)} =$ 14.1477 p = 0.0004	$t_{(49)} =$ 3.6105 p = 0.0007
C to T	4.67°	<	5.77°	9.86°	13.35°	<	13.41°	23.97°	$F_{(1,49)} =$ 10.8190 p = 0.0018	$t_{(49)} =$ 2.6778 p = 0.0101
T to S	1.43°	<	4.63°	7.94°	1.11°	<	10.92°	20.01°	$F_{(1,49)} =$ 0.0050 p = 0.9439	$t_{(49)} =$ 2.7299 p = 0.0088
S to T	0.02°	<	4.20°	7.21°	4.77°	<	9.35°	17.37°	$F_{(1,49)} =$ 1.4452 p = 0.2350	$t_{(49)} =$ 3.0506 p = 0.0037
T to C	4.52°	<	5.78°	9.87°	6.74°	<	14.19°	25.59°	$F_{(1,49)} =$ 3.7972 p = 0.0570	$t_{(49)} =$ 1.8103 p = 0.0764
C to B	2.67°	<	5.86°	10.00°	0.80°	<	10.04°	18.55°	$F_{(1,49)} =$ 0.1810 p = 0.6723	$t_{(49)} =$ 2.1092 p = 0.0401

2.4. Article 4: Path integration and cognitive mapping capacities in Down and Williams syndromes

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Path Integration and Cognitive Mapping Capacities in Down and Williams Syndromes

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Williams (WS) and Down (DS) syndromes are neurodevelopmental disorders with distinct genetic origins and different spatial memory profiles. In real-world spatial memory tasks, where spatial information derived from all sensory modalities is available, individuals with DS demonstrate low-resolution spatial learning capacities consistent with their mental age, whereas individuals with WS are severely impaired. However, because WS is associated with severe visuo-constructive processing deficits, it is unclear whether their impairment is due to abnormal visual processing or whether it reflects an inability to build a cognitive map. Here, we tested whether blindfolded individuals with WS or DS, and typically developing (TD) children with similar mental ages, could use path integration to perform an egocentric homing task and return to a starting point. We then evaluated whether they could take shortcuts and navigate along never-traveled trajectories between four objects while blindfolded, thus demonstrating the ability to build a cognitive map. In the homing task, 96% of TD children, 84% of participants with DS and 44% of participants with WS were able to use path integration to return to their starting point consistently. In the cognitive mapping task, 64% of TD children and 74% of participants with DS were able to take shortcuts and use never-traveled trajectories, the hallmark of cognitive mapping ability. In contrast, only one of eighteen participants with WS demonstrated the ability to build a cognitive map. These findings are consistent with the view that hippocampus-dependent spatial learning is severely impacted in WS, whereas it is relatively preserved in DS.

Keywords: egocentric, homing behavior, allocentric, cognitive map, spatial memory, navigation, neurodevelopmental disorders

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INTRODUCTION

Williams syndrome (WS) and Down syndrome (DS, Trisomy 21) are neurodevelopmental disorders of genetic origin, and individuals with these syndromes are generally described as having moderate to severe intellectual disabilities (Ewart et al., 1993; Vicari et al., 2005, 2006; Bittles et al., 2007; Martens et al., 2008). Nevertheless, despite the fact that individuals with these two syndromes have relatively similar IQs [DS: mean 50, range 30-70 (Megarbane et al., 2013); WS: mean 55, range 40-70 (Martens et al., 2008)], these syndromes are characterized by different cognitive profiles. Specific capacities considered to be relatively preserved or a strong point in one syndrome are often more impacted and considered to be a point of weakness in the other (Jarrold et al., 1999; Vicari, 2001; Karmiloff-Smith et al., 2012). The observation of opposite cognitive profiles in individuals with WS and DS has been especially true for spatial capacities. Spatial capacities are a crucial cognitive competence, and impairments in spatial capacities have significant negative impacts on the daily life and autonomy of individuals with intellectual disability. Characterizing the spatial profile of individuals with intellectual disability can thus not only help to identify particular deficits, but also preserved functions that can be targeted to develop syndrome-specific compensatory strategies in order to improve independent navigation (e.g., to go to work, grocery shopping or gather socially), thus increasing self-efficacy, self-confidence and social inclusion.

Small-Scale Spatial Capacities

Historically, clinical assessments of spatial memory capacities have employed small-scale visuospatial tasks administered using paper-and-pencil [e.g., the Benton line dissection task (Benton et al., 1975)], small apparatuses [e.g., the Corsi block tapping task (Corsi, 1972)] or computers (e.g., Claessen et al., 2015) placed on a desktop directly in front of the individual. Individuals with DS outperform individuals with WS in spatial working memory tasks such as the Corsi block tapping task (Wang and Bellugi, 1993; Jarrold and Baddeley, 1997; Jarrold et al., 1999), or when copying geometric figures (Bellugi et al., 1999). Individuals with DS also outperform individuals with WS on an item-in-location task that requires recalling in which quadrant on a piece of paper an item was previously seen (Vicari et al., 2005).

It has been proposed that global and local attentional capacities (Porter and Coltheart, 2006) or visuo-constructive capacities (the ability to draw or recreate observed visual patterns consistent with their global or local features) are differentially impaired in individuals with WS and DS (Bihrle et al., 1989; Bellugi et al., 1999; Farran et al., 2003); but see D'Souza et al. (2016) for an alternative interpretation. Individuals with DS exhibit relatively better global processing capacities, as compared to their own local processing capacities and the global processing capacities of individuals with WS. In contrast, individuals with WS exhibit relatively better local processing capacities, as compared to their own global processing capacities and the local processing capacities of individuals with DS. However, it is now well-accepted that space is represented in different frames of reference and subserved by distinct yet interconnected brain structures and circuits (White and Mcdonald, 2002; Hartley et al., 2003; Iaria et al., 2003; Burgess, 2006; Banta Lavenex and Lavenex, 2009; Lavenex and Banta Lavenex, 2013; Banta Lavenex et al., 2014; Epstein et al., 2017; Rolls, 2020). Thus, small-scale visuospatial capacities cannot be considered as representative of all spatial capacities for either individuals with typical or atypical development. Indeed, performance on small-scale visuospatial tasks does not necessarily correlate with or predict performance on large-scale spatial tasks in which participants must move around (Quaiser-Pohl et al., 2004; Hegarty et al., 2006; Farran et al., 2010), such as in everyday life.

Large-Scale Spatial Capacities

Given that the brain represents space in multiple manners, it is not surprising that when navigating in large-scale environments such as in the real world, humans and other animals use a variety of different spatial strategies (White and Mcdonald, 2002; Hartley et al., 2003; Burgess, 2006; Spiers and Maguire, 2007; Bostelmann et al., 2017). Thus, for example, objects and spatial locations can be represented in an egocentric reference frame which codes locations with respect to one's own body, in a viewpoint-dependent manner (Banta Lavenex and Lavenex, 2009). Egocentric representations enable route learning, or the ability to go from point A to point B via a rather inflexible stimulus-response type of navigation that entails using landmarks and/or a sequence of left or right turns in a fixed manner to reproduce a previously traveled or communicated route (Hartley et al., 2003; Wolbers and Wiener, 2014). Furthermore, landmarks can be used as beacons (i.e., move towards the church, at the church look for the city hall, move towards the city hall, etc.) or associative cues (i.e., at the church turn left, at city hall turn right, etc.) (Waller and Lippa, 2007). In contrast, objects and spatial locations can also be represented in an allocentric reference frame which codes locations in relation to other objects and locations in the environment, in a viewpoint-independent manner (Banta Lavenex and Lavenex, 2009). When using allocentric memory representations, individuals can navigate between objects in their environment in a flexible manner, and are able to take novel, never-before experienced routes or shortcuts to arrive at a desired destination (Tolman, 1948; O'Keefe and Nadel, 1978; Banta Lavenex et al., 2014; Howard et al., 2014; Behrens et al., 2018). As such, the ability to take shortcuts to successfully navigate has come to be regarded as hallmark evidence for the existence of cognitive maps (Epstein et al., 2017; Bostelmann et al., 2020).

Numerous studies have investigated the route learning capacities of individuals with WS or DS in virtual reality environments with local and distal landmarks (Pennington et al., 2003; Farran et al., 2012a,b, 2015, 2016; Courbois et al., 2013; Broadbent et al., 2014, 2015; Davis et al., 2014; Purser et al., 2015; Toffalini et al., 2018). Overall, participants with WS or DS were able to learn the routes, although they sometimes required more trials, or more time, than typically developing (TD) children of the same mental age. Nonetheless, these findings demonstrated that individuals with DS or WS are capable of using an egocentric strategy to solve a route learning task in a virtual environment. In contrast, when required to take a novel most direct route between two locations (i.e., shortcuts), which would provide evidence for flexible cognitive mapping abilities, Courbois et al. (2013) found that only 2 out of 7 participants with DS were able to find the most direct route within ten trials of unguided exploration. It is important to note, however, that since participants were given more than one trial to find the shortcut, it is not even clear whether those who succeeded had built a configural representation of the environment during initial learning or whether they had learned the new path during the several unguided test trials. Similarly, Farran et al. (2015) found that only 10% of participants with DS could successfully find a shortcut between two locations, despite the use of repeated trials which gave participants multiple opportunities to learn the shorter route on their own. For individuals with WS, Farran et al. (2015) found that 35% of their participants with WS were able to find the shorter route during the five unguided trials. Similarly, using a cross-maze design, Broadbent et al. (2014) reported that only 20% of participants with WS were considered to navigate the maze using an allocentric strategy. Overall, whereas participants with WS or DS exhibited some preserved route learning ability in virtual environments, the majority of participants with DS or WS were unable to learn and use the relationships between landmarks encountered in these environments to navigate successfully; in other words, they were unable to build a cognitive map.

Real-World Spatial Capacities

A number of studies have used a variety of real-world (i.e., not virtual reality) paradigms designed to assess the spatial capacities of individuals with WS or DS. These studies have reported impairments in the ability of individuals with WS to learn a large outdoor route (Farran et al., 2010), to efficiently find rewards in radial arm mazes (Mandolesi et al., 2009; Foti et al., 2015), to use egocentric search strategies efficiently (Smith et al., 2009; Foti et al., 2011), to use geometric cues to reorient in a rectangular room (Lakusta et al., 2010), or to locate an object hidden on an array disconnected from the external environment (Nardini et al., 2008). Surprisingly, these studies revealed that in contrast to what was reported in virtual reality experiments, participants with WS are substantially impaired on real-world spatial tasks. In contrast, fewer studies have investigated the real-world spatial capacities of individuals with DS. In one study that assessed route learning, participants with DS performed as well as TD children, thus exhibiting similar or better performance than in virtual tasks (Meneghetti et al., 2020). In another study that assessed real-world allocentric spatial capacities, although participants with DS were impaired as compared to TD children at locating three reward locations in a paradigm that precluded the use of visual scene matching and egocentric spatial strategies, they were nonetheless capable of orienting in the arena using allocentric cues (Banta Lavenex et al., 2015), thus contradicting findings from virtual reality experiments.

A careful examination of the paradigms previously used to asses spatial capacities reveals that they did not always meet the requirements to unequivocally conclude whether individuals with DS or WS are incapable of creating and using an allocentric spatial representation. First, the failure to take shortcuts in virtual environments cannot be used to infer performance in the real world, where coherent visual, vestibular and proprioceptive information is available. Second, in both virtual and real-world paradigms, care must be taken to eliminate the need to rely on other cognitive processes that may impact task performance (e.g., working memory, linguistic competence, mental rotation or imagined visualization, etc.). Accordingly, none of the above-mentioned studies has provided unequivocal evidence as to whether individuals with WS or DS are capable of integrating the various sources of spatial information normally available in the real world in order to create a cognitive map to navigate in their environment.

In that context, Bostelmann et al. (2017, 2018) assessed the allocentric spatial capacities of individuals with WS and DS in a real-world laboratory paradigm: an open-field arena in which participants had to learn the location of one reward among four visually identical reward locations arranged at the cardinal positions in a 4 m × 4 m enclosure surrounded on three sides by opaque curtains. The reward was always hidden in the same location in the arena, but participants entered and exited the arena by different doors on every single trial. Thus, in order to identify the reward location, participants must employ an allocentric representation of the environment to learn and remember that location in relation to distal objects, and to define their own location relative to the reward location. Individuals with WS were severely impaired on this task: only 17% of the participants with WS tested (mean mental age 5.9 years) could solve the task, whereas 95% of TD children can solve the task from 3 years of age (Ribordy et al., 2013; Ribordy Lambert et al., 2015; Bostelmann et al., 2017). In contrast, 78% of the participants with DS (mean mental age 5.6 years) could solve the task (Bostelmann et al., 2018), thus exhibiting markedly better allocentric spatial capacities than participants with WS. These results provide the clearest evidence to date of the most basic cognitive mapping capacities of individuals with WS and DS, in a real-world laboratory setting enabling the integration of all sources of sensory information normally available when moving freely in the environment. However, because WS is associated with severe visuo-constructive processing deficits, it is unclear whether their impairment is due to abnormal visual processing or whether it reflects an inability to build a cognitive map. What is not known, therefore, is whether individuals with DS or WS are able to rely on self-generated movement information, i.e., in absence of visual information, in order to navigate successfully in a real-world environment.

Building Spatial Representations Without Vision

Path integration is the ability to use information generated by one's own body movement, also known as idiothetic cues, to keep track of one's position in space (Etienne et al., 1996; Mittelstaedt, 1999). Although path integration is often thought of as a mechanism that is used only when visual information is minimized or absent, this is not the case. Path integration is a continuous and automatic process that animals use to determine their position that includes both distance from and direction to their previous position and to other objects and locations in the environment (McNaughton et al., 1996). When visual information is present, path integration is achieved by simultaneously integrating visual, optic flow, vestibular and proprioceptive information. In absence of visual input, angular displacement information (rotation) is provided primarily by vestibular input, and linear displacement information (translation) is provided primarily by proprioceptive input (Etienne et al., 1996; Etienne and Jeffery, 2004; Taube, 2007). Path integration is also often thought of as a mechanism that only allows an individual to return to an original starting point (i.e., home), but this is also not the case. Although path integration can be used to construct an egocentric spatial representation which allows an individual to home, path integration can be used to construct an allocentric spatial representation of the environment (McNaughton et al., 1996; Etienne et al., 1998). However, it is important to note that in absence of external landmarks, path integration is an imprecise process that accrues error with every step (translation) and every turn (rotation). Thus, when using path integration, occasional sensory information from the external environment, such as visual, tactile or olfactory stimuli, must provide a confirmation of the individual's position, thus eliminating cumulated error and (re)calibrating the path integration system (Klatzky et al., 1990; Fujita et al., 1993; Loomis et al., 1993; McNaughton et al., 1996, 2006; Allen, 2004; Etienne and Jeffery, 2004; Savelli and Knierim, 2019).

Egocentric representations constructed from path integration do not need to incorporate the contextual information from the environment that allows an individual to place themselves in a particular location relative to other objects or locations. As the individual moves along a trajectory, idiothetic information is constantly and automatically encoded. When the individual is ready to return to home, a direct path is calculated, even though the individual may have no knowledge of its location with respect to the surrounding environment other than its starting position. Adults and children from at least 5 years of age are capable of using path integration in absence of visual information to return to a starting point via a direct path, after being led or locomoting along a path that includes one or more turns in what are known as triangle-completion tasks (Corlett et al., 1985; Klatzky et al., 1990; Loomis et al., 1993; Giovannini et al., 2009; Smith et al., 2013; Bostelmann et al., 2020).

In contrast, allocentric representations incorporate the contextual spatial information from the surrounding environment that allows the individual to place themselves in a particular location relative to other objects and locations, as well as to define the position of objects and locations in the environment relative to one another and independently of the observer's position (McNaughton et al., 1996; Etienne and Jeffery, 2004; Jayakumar et al., 2019; Savelli and Knierim, 2019). Adults have been shown to be capable of using path integration in the absence of vision to create allocentric representations (Passini and Proulx, 1988; Giudice, 2018). And, germane to the present study, Bostelmann et al. (2020) recently showed that TD children between 5 and 9 years of age are also capable of using path integration in absence of visual information to create both egocentric and allocentric representations. In a large 8 m × 8 m empty room, children were first assessed on their ability to return along a 7 m path to a starting location after being led on a straight 7 m outward path, or on a 10 m outward path with a 90° right or left turn in the middle (**Figures 1A,B**). This experiment thus gave an indication of the children's ability to integrate their movements to create an egocentric representation, and to orient and walk straight while blindfolded. Ninety-six percent of the TD children tested were able to consistently return to the starting quadrant. In a second experiment, children were blindfolded before entering the same large room that now contained 4 pieces of furniture placed at the midpoint along the walls within the room (**Figure 1C**). Children were led along direct paths, and asked to navigate independently, between the bench and the shelf, the shelf and the chair, and the bench and the table, respectively. Children were then asked to go directly from the bench to the chair, from the chair to the table, and from the table to the shelf, which required them to take direct, novel shortcuts; and then to retrace the three novel routes in the opposite direction. Sixty-four percent of the 5-9-year-old children tested were capable of using path integration to build a cognitive map enabling them to take shortcuts. Importantly, task performance was not dependent on age, and as many of the younger participants (5-7 years) passed the test as older participants (7-9 years). The authors thus concluded that children from at least 5 years of age are able to use path integration to create a cognitive map of their environment.

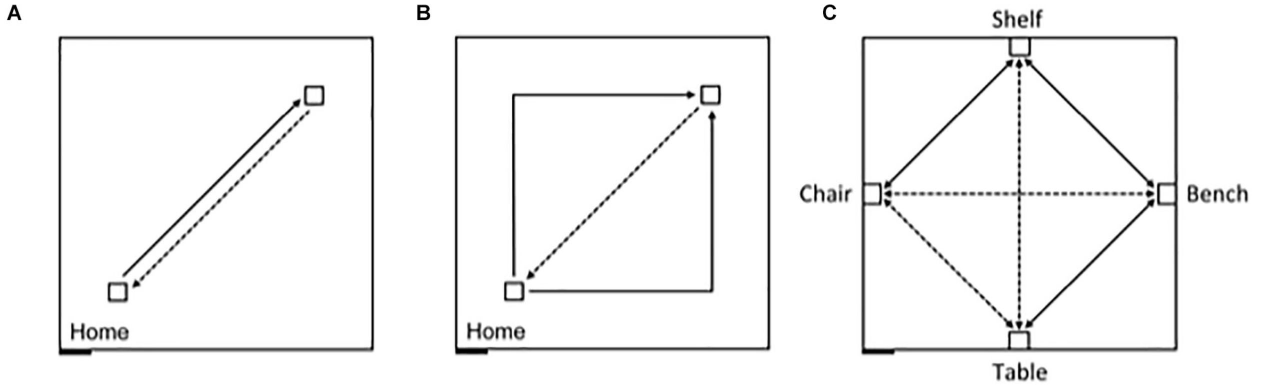

FIGURE 1 | Schematic representation of the experimental design, carried out in an 8 m × 8 m testing room. The black rectangle at the bottom left represents the entry door to the room. Solid lines indicate guided trajectories; dashed lines indicate direct paths that participants were verbally requested to make. **(A)** Egocentric task, straight paths: 7 m straight line guided trajectory, 7 m return path. **(B)** Egocentric task, angled paths: 10 m angular guided trajectory with a right or left turn (5 m + 5 m), and 7 m return path. **(C)** Allocentric task: guided routes (solid) and novel routes (dashed) between four objects, in absence of vision. The paths between the bench and the chair, and between the table and the shelf were 7 m long; the other paths were 5 m long.

Aim of This Study

The aim of this study was to characterize the ability of individuals with WS and individuals with DS to use path integration in the absence of visual information to build egocentric and allocentric spatial representations enabling them to navigate in their environment. We used the same paradigm previously used with TD children (Bostelmann et al., 2020), and compared the performance of participants with WS or DS to that of TD children with similar mental ages. Performance on the homing task informed us about the ability of participants to walk straight and return to their starting point when blindfolded, as well as to the levels of accuracy and precision that we could expect in the cognitive mapping task.

With vision, most individuals with DS are able to form low-resolution allocentric spatial representations (Bostelmann et al., 2018), whereas a minority of individuals with WS are able to do so (Bostelmann et al., 2017). If cognitive mapping is subserved by the same spatial representational system that underlies performance in the open-field allocentric spatial memory task with vision, then we can predict that a similar proportion of participants with DS will be capable of using path integration to build a cognitive map without vision (about two thirds), whereas very few individuals with WS should be able to do so. However, because WS is associated with severe visuo-constructive processing deficits, it is unclear whether their impairment is due to abnormal visual processing or whether it reflects an inability to build a cognitive map. Thus, precluding access to visual information might reveal the preservation of underlying allocentric spatial capacities in individuals with WS, in which case more individuals with WS may be capable of building a cognitive map using path integration without vision than solving the allocentric spatial memory task with vision.

METHODS

Participants

We tested eighteen participants with WS (8 females), nineteen participants with DS (9 females) and twenty-eight TD children (15 females) with a chronological age similar to the mental ages of the participants with WS and DS (**Table 1**). *NB*: The results of the TD children have been published previously (Bostelmann et al., 2020). Participants with WS and DS were recruited in Switzerland (WS: *n* =8; DS: *n* =5) and Italy (WS: *n* =10; DS: *n* =14). According to parents and/or caregivers, none of the participants exhibited signs of age-related dementia. All TD children were recruited in Switzerland. They were reported by their parents to have been typically developing, and were neither born prematurely, nor had any suspected or diagnosed neurological conditions or learning disabilities.

Participants were tested on the two tasks on separate days, which were anywhere from one day to several weeks apart. Participants were always assessed on the homing task first and on the cognitive mapping task second. Performance in the cognitive mapping task did not correlate with the interval between the two testing sessions (data not shown). Each experiment lasted approximately 45 min. Testing took place Mondays through Saturdays, between 8:00 A.M. and 6:30 P.M. Human subjects research was approved by the Cantonal Ethics Commission for Human Research (Vaud, Switzerland; protocol no. 60/14), and was in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving human subjects in research. All participants and/or their parents gave informed written consent.

Testing Facilities

Testing took place within an 8 m × 8 m room at the University of Lausanne for Swiss participants (**Figure 1**), and in similar-sized rooms in Nardò for Italian participants with DS and in Fano for Italian participants with WS. During the homing task, the room was devoid of objects. Construction tape was placed on the floor, 1.5 m from each of the walls that constituted the four corners of the room. At the corner closest to the entry door, the tape was arranged to represent a house, which was designated as "home," i.e., the position to which participants were instructed to always return to on each trial ("go home"). In the other three corners of the room, the tape was arranged in the form of a small "x" surrounded by a square that served as a visual landmark for the experimenter when guiding the blindfolded participants. During the homing task, participants were filmed with a camera on a tripod placed in the far corner of the room opposite the corner containing the home. During the cognitive mapping task, the testing room contained four real-size pieces of furniture. Each object was placed against the center of a wall: a bench (0°), a shelf (90°), a chair (180°), and a table (270°). Participants were filmed with a camera on a tripod placed in the corner of the room between the bench and the table.

Visual information was eliminated with a "sleeping mask" blindfold that was individually adjusted to the participant's head and face at the start of each trial for the homing task, and before entering the room for the cognitive mapping task. A black scarf was tied around the mask and the participant's head to ensure that they could not see any light. Two experimenters tested participants. Experimenter 1 (E1) would guide the participant,

TABLE 1 | Demographics of participants at the beginning of the study.

		Chronological age (years)				Mental age (years)			
		Mean	***SD***	**Min**	**Max**	**Mean**	***SD***	**Min**	**Max**
TD	*n* =28	6.91	1.41	4.83	9.67	-	-	-	-
DS	*n* =19	22.71	6.83	15.33	39.44	5.57	0.75	4.67	6.96
WS	*n* =18	24.28	11.22	9.00	44.92	5.89	0.94	4.42	7.50

and Experimenter 2 (E2) recorded the data. E1 walked next to or behind the participant, close enough to provide non-specific verbal encouragement (e.g., "You're doing great!," regardless of performance) and to assure their security when they were walking independently (e.g., to prevent them from walking into walls or objects), but far enough so as not to interfere with the participant's movements. In both tasks, participants with DS or WS were rewarded with coins of small denomination, and children were rewarded with small food rewards (e.g., Smarties®, Goldfish® crackers, gummy bears, pieces of breakfast cereal or pretzels, etc.). One reward was given for each completed trial and was not based on performance. Children's parents were queried with respect to alimentary allergies, and children were asked whether there were any treats that they did not like.

Specific Testing Procedures

Homing Task

Participants were tested on their ability to return to a starting point after being led along a predetermined route. Before beginning, participants were told that they would be guided along some paths while blindfolded, and that it was their job to try to return to the starting point as precisely as possible at the end of each guided route. Participants were instructed that once they thought that they were at the home location they were to stop walking and remain stationary. Each participant performed 4 sets of 5 trials without vision. Half of the trials consisted of a linear route of 7 m (**Figure 1A**), and the other half of the trials consisted of a 10 m route with a 90° left or right turn in the middle (**Figure 1B**). The trials were given in the following order: Straight path session 1: 5 × 7 m linear route, guided by the left arm; Two-legged path session 1: 5 × 10 m route with a 90° right turn at the halfway point, guided by the left arm; Straight path session 2: 5 × 7 m linear route, guided by the right arm; Two-legged path session 2: 5 × 10 m route with a 90° left turn at the halfway point, guided by the right arm. At the end of each guided route, and while still facing in the direction of the outbound travel, E1 released the participant's arm and instructed them to "go home" (to the starting point). Although participants had been instructed to stop walking once they estimated that they had arrived at home, if participants were approaching a wall and did not show signs of stopping, E1 gently placed a hand on the participant to stop them. Once participants were stationary, they could take off the blindfold, look where they were positioned in the room, and then return to the starting position in order to prepare for the next trial. To ensure that all participants understood the task, prior to the beginning of each session they experienced a practice trial during which they were led through the guided part of the path without the blindfold, their arm released at the end of the guided path, and then asked to "go home." A trial was terminated when a participant stopped alone or when the experimenter stopped the participant just before a wall.

Cognitive Mapping Task

Participants were tested on their ability to take novel paths (shortcuts) to navigate to previously visited locations marked by large stable objects. In this task, four objects were placed in the 8 m × 8 m room (**Figure 1C**). Prior to entering the room, participants were told that they were going to be blindfolded, and that they would then explore our laboratory's living room. Participants were never told the goal of the experiment, or that they would have to remember the positions of the objects in the room or navigate to those objects using novel routes. Although all participants were familiar with the room from having participated in the homing task, they were blindfolded prior to entering the room for the cognitive mapping task, and thus never saw the objects or their positions in the room. Once blindfolded, participants were led into the room and were guided to the bench where they were asked to sit down. Importantly, although the bench was located on the far right-hand wall relative to the entry door, some participants may not have had explicit knowledge of its absolute location in the room; it could just as easily be perceived as being on the far wall opposite the door.

Learning Phase

Participants were taught the routes between (1) the bench and the shelf, (2) the shelf and the chair, and (3) the bench and the table, always in the same order for each participant (**Supplementary Material 1**). Accordingly, at the beginning of each trial, participants were positioned so that they were either sitting straight on the bench or chair, or so that their back was touching the shelf or the table, and their feet pointing straight forward. For each route to be learned, participants were guided by the arm round-trip between the two objects twice by E1, then asked to make the round-trip alone one time, then guided through two more round-trips, and finally asked to make two more round-trips alone (for a total of four guided and three non-guided round-trips per route). Each time participants reached an object by themselves or when guided by E1, E1 named the object and participants were asked to touch the object or sit on it, for the chair and the bench.

In non-guided trials, if a participant came within 30 cm of the target object, E1 would gently take their arm and guide them into contact with the object, so that the participants would not startle or injure themselves colliding with the object, thus terminating the trial. If the participant was in the correct quadrant of the room (within an arc of 45° extending from the starting object and centered around the target object; tape markings on the floor outlined this zone), but not within 30 cm of the target object, the participant was allowed to continue walking until they came within 30 cm of a wall, at which point E1 gently stopped the participant and guided them to the target object. If a participant began walking in the wrong direction and after traveling 4 m was not in the correct quadrant, E1 would gently stop them and guide them back to the starting object, and then begin escorting the participant through the next two guided trials.

Testing Phase

Participants ended the learning phase sitting on the bench, and immediately began the testing phase from there. Participants were asked to walk alone and directly to objects, which would require them to take novel paths or shortcuts to these objects. First, E1 asked participants to walk directly from the bench to the chair ("now, go alone directly to the chair"). Once sitting in the chair, they were asked to walk directly to the table. Once their back was to the table, they were asked to walk directly to the shelf. Then, participants were asked to perform the three reverse routes: from the shelf to the table ("now, go alone directly to the table"), from the table to the chair, and from the chair to the bench. In the testing phase, each trial and data collection terminated when a participant either: (1) came within 30 cm of the target, at which point E1 gently guided the participant to the object, or (2) came within 30 cm of a wall, at which point E1 gently stopped the participant and guided them to the target object.

Data Collection

Participants' movements and trajectories were recorded with the Noldus TrackLab system (Wageningen, Netherlands). Participants wore a vest on which a radio frequency-emitting Ultra-Wide Band tag was affixed to each shoulder. The system collected the X and Y coordinates of each tag at a frequency of 4.75 Hz. The smoothed averaged X and Y coordinates of the two tags were computed to plot the location of the participant's head on a 2D representation of the room. Each trajectory was then transferred to the ImageJ program (NIH, United States), and retraced to measure the distance and angle information for the different parts of each individual trajectory.

We used several measures to quantify participants' performance on each trial: (1) The initial heading, defined as the angular difference between the ideal path and the participant's path one meter after starting their journey. (2) The final heading, defined as the angular difference between the ideal path and the participant's path after the participant either stopped alone (homing task), reached the target object (cognitive mapping task), or was stopped by E1 (homing and cognitive mapping tasks). (3) The distance to target, defined as the shortest distance between the participant's final position and home, or the target object. For the homing task, the five trials of each session without vision were averaged to obtain one single value for each of these measures (1-3) for each participant. For the cognitive mapping task, the six novel paths were analyzed separately.

We also provided an overall measure of task performance: (4) "Pass" or "Fail." For the homing task, we estimated whether participants passed or failed by determining whether their average end location was within the quadrant of the room that included the outbound journey's starting point, as defined by the two perpendicular bisectors of the room's walls. In the cognitive mapping task, we estimated whether participants passed or failed each of the three novel paths and the three reverse paths. To be considered as passing, the end point of the participant's trajectory had to be within the same quadrant as the target object, as defined by the two diagonals bisecting the room. This defined the area of the room in which participants were closer to the target object than any other object. We did not use a more restrictive criterion (within an arbitrary distance to the target), because even young adults do not exhibit perfect performance and do not always come within contact-distance of the object at the end of their trajectory (Bostelmann et al., 2020).

Data Analysis

For angular measures of direction, we used circular statistics computed in Excel following the formulas described by Zar (1999). To quantify the variability of individual participants within each session of the homing task, we computed the length of the mean vector (i.e., of the average angle) for each participant ($l_j = \sqrt{X^2 + Y^2}$, where $X = \sum_{i=1}^{n} \cos \alpha_i / n$ and $Y = \sum_{i=1}^{n} \sin \alpha_i / n$). Since the average value of l across all participants was 0.97 ± 0.04, and to give the same weight to the results of each individual participant, we considered this value to be 1 for the computation of second-order group analyses.

We performed one-sample tests for the mean angle to determine whether each group's average initial or final heading followed a mean heading that deviated from the perfect angle. We considered a 99% confidence interval to define a significant departure from the ideal direction. Group comparisons were performed with the Watson-Williams test for angular measures. We reported the groups' angular deviation, $s = \frac{180}{\pi}\sqrt{2\,(1-r)}$, in order to provide a measure of inter-individual variability within each group (Zar, 1999; pp. 602-605). We further compared the groups' angular deviation based on the absolute differences of the rectangular coordinates between individual average angles and an ideal heading angle of zero: $abs_j = \sqrt{\left(\sin \alpha_j - 0\right)^2 + \left(\cos \alpha_j - 1\right)^2}$.

Statistical analyses were performed with IBM SPSS Statistics for Macintosh, version 25.0 (IBM Corp. Armonk, NY, United States). We used General Linear Model analyses with groups as a between-subject factor and test sessions or trials as repeated measures to analyze the distance to target, and the variability of initial and final headings. We used independent samples t-tests to compare performance between two groups. We used Chi^2 tests to compare the number of participants in different groups that passed the tasks. The level of statistical significance was set at $p < 0.05$ for all analyses.

RESULTS

Homing Task: Straight Outbound Paths

"Pass" or "Fail"

Figure 2 shows the average end locations of TD children, participants with DS, and participants with WS who were asked to return to their starting point after being led blindfolded on a straight 7 m path, thus ideally requiring a 180° turn and a 7 m straight walk to return to the starting point. For Session 1 (**Figures 2A-C**), 93% of TD children, 74% of participants with DS and 39% of participants with WS had an average end location in the quadrant of the room where the home was located (**Tables 2-4**). Thus, in Session 1, fewer participants with WS were considered to have passed the homing task than both TD children (X^2 = 15.740, $p < 0.001$) and participants with DS (X^2 = 4.560, p = 0.033). The difference between participants with DS and TD children failed to reach the predefined level of statistical significance (X^2 = 3.283, p = 0.070). For Session 2 (**Figures 2D-F**), 100% of TD children, 95% of participants with DS and 78% of participants with WS had an average end location in the quadrant of the room where the home was located (**Tables 2-4**). Thus, in Session 2, fewer participants with WS were considered to have passed the homing task than TD children (X^2 = 6.815,

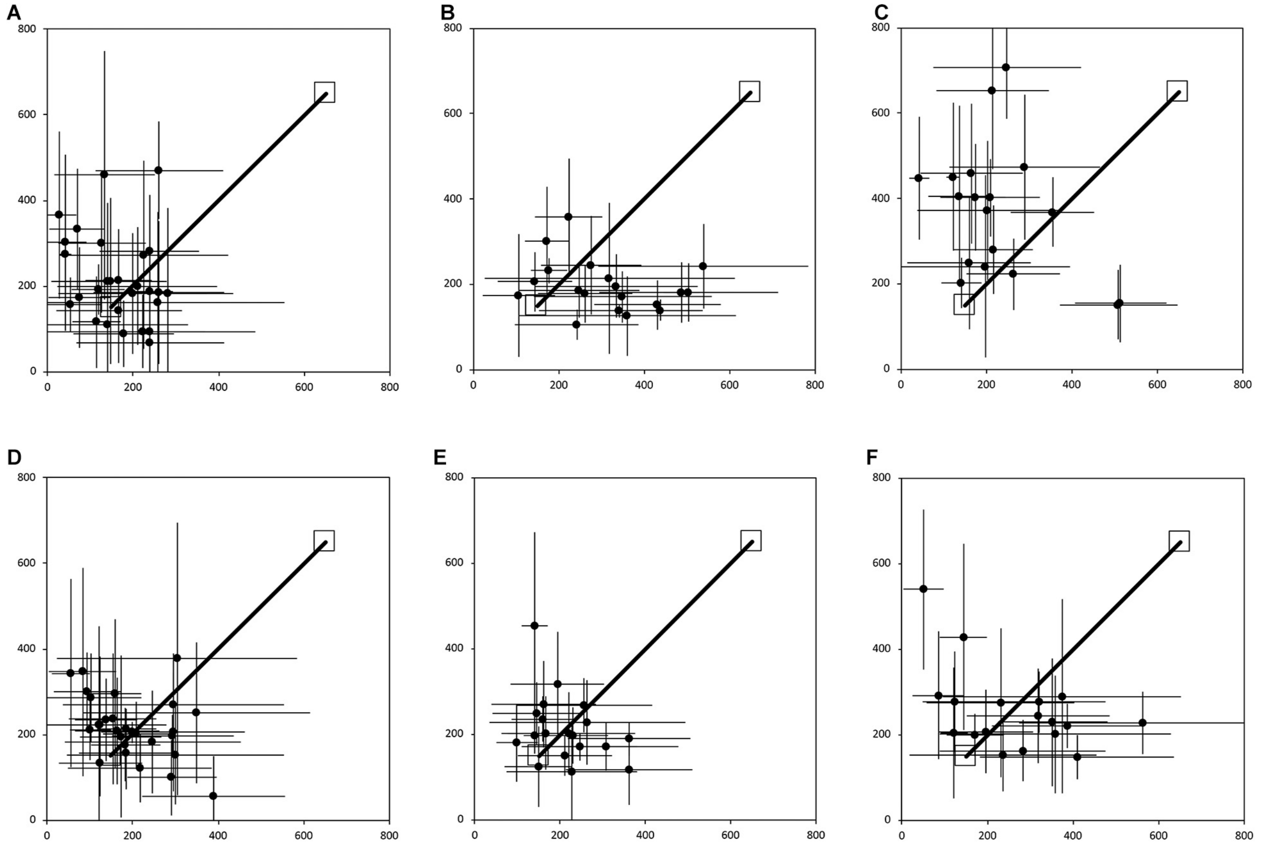

FIGURE 2 | Average end location of individual participants' return paths, following a straight 7 m outward path in the egocentric homing task. The horizontal and vertical error bars represent the standard deviation for each individual across one session. The solid line indicates the outward straight path. The top right square indicates the starting point of the return path. The bottom left square indicates "home." In Session 1, participants were guided by the left arm, and in Session 2 they were guided by the right arm. **(A)** TD, Session 1. **(B)** DS, Session 1. **(C)** WS, Session 1. **(D)** TD, Session 2. **(E)** DS, Session 2. **(F)** WS, Session 2. Room size: 800 cm × 800 cm.

$p = 0.009$), whereas there were no differences between the number of participants with DS and the number of participants with WS ($X^2 = 2.275$, $p = 0.131$) or TD children ($X^2 = 1.506$, $p = 0.219$).

Average Distance From Home

They were differences between the groups of TD children, participants with DS and participants with WS ($F_{(2,62)} = 7.933$, $p = 0.001$) and between sessions ($F_{(2,62)} = 18.411$, $p < 0.001$), but no interaction between groups and sessions ($F_{(2,62)} = 2.088$, $p = 0.133$; **Table 5**). In both sessions, the distance between the end location and home was greater for participants with WS than for participants with DS and TD children. In contrast, the distance between the end location and home did not differ between participants with DS and TD children. The distance from home was shorter in Session 2 than in Session 1 when all groups were considered together ($t_{(64)} = 3.912$, $p < 0.001$), for the group of participants with WS ($t_{(17)} = 2.387$, $p = 0.029$) and the group of participants with DS ($t_{(18)} = 3.063$, $p = 0.007$), but not for the group of TD children ($t_{(27)} = 1.359$, $p = 0.185$). It is important to note, also, that they were differences between groups in the number of times participants were stopped by the experimenter because they were approaching a wall ($F_{(2,62)} = 4.427$, $p = 0.016$; out of 10 trials; TD: 3.96 ± 2.62 (average ± standard deviation), DS: 6.53 ± 2.46, WS: 5.22 ± 3.69). Participants with DS were stopped more often than TD children ($t_{(45)} = 3.374$, $p = 0.002$), whereas there were no differences between participants with WS and TD children ($t_{(44)} = 1.354$, $p = 0.183$) or between participants with WS and participants with DS ($t_{(35)} = 1.272$, $p = 0.212$).

Initial Heading

The average initial heading of participants with WS, participants with DS and TD children did not differ from the ideal heading (**Supplementary Material 2**). Nevertheless, there were group differences in initial heading. In both sessions, the average initial heading of participants with WS deviated slightly to the right from the ideal heading, whereas the average initial heading of participants with DS deviated slightly to the left. In Session 1, the average initial heading of participants with DS differed from that of TD children. In both sessions, the average initial heading of participants with DS differed from that of participants with WS. Angular deviation (a measure of variability between participants within a group) did not differ between groups in either session (**Supplementary Material 2**). Accordingly, within-subject variability in initial heading (the length of the mean

TABLE 2 | Individual performance of TD children in the homing task.

Participant	Gender	Age (years)		Criterion	S-1	S-2	A-1	A-2
TD39	F	4.83		Pass	Pass	Pass	Pass	Fail
TD160	M	4.83		Pass	Pass	Pass	Pass	Pass
TD167	M	4.83		Pass	Fail	Pass	Pass	Pass
TD187	F	5.00		Pass	Pass	Pass	Pass	Pass
TD50	M	5.50		Pass	Pass	Pass	Pass	Fail
TD53	F	5.50		Pass	Pass	Pass	Fail	Pass
TD186	F	5.67		Pass	Pass	Pass	Pass	Pass
TD27	M	5.83		Pass	Pass	Pass	Pass	Pass
TD36	M	5.92		Fail	Fail	Pass	Pass	Fail
TD34	F	6.67		Pass	Pass	Pass	Pass	Pass
TD35	M	6.67		Pass	Pass	Pass	Pass	Pass
TD48	F	6.67		Pass	Pass	Pass	Pass	Pass
TD141	F	6.67		Pass	Pass	Pass	Pass	Pass
TD42	M	6.92		Pass	Pass	Pass	Pass	Pass
TD49	F	7.08		Pass	Pass	Pass	Pass	Pass
TD143	F	7.08		Pass	Pass	Pass	Pass	Pass
TD31	F	7.17		Pass	Pass	Pass	Pass	Pass
TD25	M	7.25		Pass	Pass	Pass	Pass	Pass
TD191	M	7.50		Pass	Pass	Pass	Pass	Pass
TD26	F	7.92		Pass	Pass	Pass	Pass	Pass
TD29	F	7.92		Pass	Pass	Pass	Pass	Pass
TD52	M	8.08		Pass	Pass	Pass	Fail	Pass
TD37	M	8.25		Pass	Pass	Pass	Pass	Pass
TD138	F	8.42		Pass	Pass	Pass	Pass	Pass
TD28	F	8.58		Pass	Pass	Pass	Pass	Pass
TD30	F	8.92		Pass	Pass	Pass	Pass	Pass
TD142	M	9.17		Pass	Pass	Pass	Pass	Pass
TD43	M	9.67		Pass	Pass	Pass	Pass	Pass
			Pass	27	26	28	26	25
			Fail	1	2	0	2	3
			% Pass	96%	93%	100%	93%	89%

S-1, First session with straight outbound paths; S-2, Second session with straight outbound paths; A-1, First session with angled outbound paths; A-2, Second session with angled outbound paths; Pass, average final location within the target quadrant; Fail, average final location not within the target quadrant. Criterion, Passing on 3 of 4 sessions.

TABLE 3 | Individual performance of participants with DS in the homing task.

Participant	Gender	M. A.	C. A.		Criterion	S-1	S-2	A-1	A-2
DS19	M	4.67	16.42		Fail	Fail	Pass	Pass	Fail
DS6	M	4.75	21.17		Pass	Fail	Pass	Pass	Pass
DS8	F	4.75	21.92		Fail	Fail	Pass	Pass	Fail
DS1	M	4.83	28.58		Pass	Pass	Pass	Pass	Fail
DS5	F	5.00	15.33		Pass	Fail	Pass	Pass	Pass
DS13	M	5.00	19.67		Pass	Pass	Pass	Pass	Fail
DS12	M	5.08	22.25		Pass	Pass	Pass	Pass	Pass
DS30	M	5.25	36.17		Pass	Pass	Pass	Pass	Pass
DS24	M	5.29	15.50		Pass	Pass	Pass	Pass	Pass
DS7	M	5.33	18.25		Pass	Pass	Pass	Pass	Pass
DS15	F	5.33	17.75		Pass	Pass	Pass	Pass	Pass
DS23	M	5.58	23.92		Pass	Pass	Pass	Fail	Pass
DS25	F	5.88	20.75		Pass	Pass	Pass	Fail	Pass
DS27	F	6.00	21.17		Pass	Pass	Pass	Fail	Pass
DS26	F	6.21	39.42		Fail	Fail	Fail	Pass	Pass
DS2	F	6.67	18.17		Pass	Pass	Pass	Pass	Pass
DS4	F	6.67	27.42		Pass	Pass	Pass	Pass	Pass
DS22	M	6.67	30.50		Pass	Pass	Pass	Pass	Pass
DS21	F	6.96	17.17		Pass	Pass	Pass	Fail	Pass
				Pass	16	14	18	15	15
				Fail	3	5	1	4	4
				% Pass	84%	74%	95%	74%	74%

S-1, First session with straight outbound paths; S-2, Second session with straight outbound paths; A-1, First session with angled outbound paths; A-2, Second session with angled outbound paths; Pass, average final location within the target quadrant; Fail, average final location not within the target quadrant. Criterion, Passing on 3 of 4 sessions.

vector) did not differ between groups ($F_{(2,62)} = 0.746$, $p = 0.479$) or between sessions ($F_{(2,62)} = 2.693$, $p = 0.106$); there was no interaction between groups and sessions ($F_{(2,62)} = 0.676$, $p = 0.513$).

Final Heading

The average final heading of participants with DS differed from the ideal heading in Session 1, but not in Session 2 (**Supplementary Material 3**). In contrast, the average final heading of participants with WS and TD children did not differ from the ideal heading in either session. The final heading differed between groups in Session 1, but not in Session 2. In Session 1, the average final heading of participants with WS deviated slightly to the right from the ideal heading, whereas the average final heading of participants with DS deviated slightly to the left. In Session 2, the average final heading did not differ between groups. Angular deviation (a measure of variability) differed between groups in both sessions (**Supplementary Material 3**). In Session 1, the angular deviation of TD children was smaller than the angular deviation of participants with DS and participants with WS; it did not differ between participants with DS and participants with WS. In Session 2, the angular deviation of participants with WS was greater than that of TD children, whereas it did not differ between participants with DS and the other groups. Within-subject variability in final heading (the length of the mean vector) did not differ between groups ($F_{(2,62)} = 1.019$, $p = 0.367$), or between sessions ($F_{(2,62)} = 0.403$, $p = 0.528$); there was no interaction between groups and sessions ($F_{(2,62)} = 1.662$, $p = 0.198$).

Homing Task: Two-Legged Angled Outbound Paths

"Pass" or "Fail"

Figure 3 shows the average end locations of TD children, participants with DS, and participants with WS who were asked to return "home" after being led blindfolded on a two-legged path of 10 m, with a 90° right turn after 5 m (Session 1) or a 90° left turn after 5 m (Session 2), thus ideally requiring a 135° right (Session 1) or 135° left (Session 2) turn at the end of the guided path, and a 7 m straight walk to return to home. For Session 1 (**Figures 3A-C**), 93% of TD children, 79% of participants with DS and 61% of participants with WS had an

TABLE 4 | Individual performance of participants with WS in the homing task.

Participant	Gender	M. A.	C. A.		Criterion	S-1	S-2	A-1	A-2
WS13	F	4.42	9.00		Pass	Fail	Pass	Pass	Pass
WS2	M	4.75	23.92		Pass	Pass	Pass	Pass	Pass
WS15	M	4.75	26.92		Pass	Fail	Pass	Pass	Pass
WS22	F	5.00	14.30		Fail	Pass	Pass	Fail	Fail
WS3	M	5.33	12.83		Pass	Pass	Pass	Pass	Pass
WS5	F	5.33	19.00		Fail	Fail	Pass	Pass	Fail
WS18	F	5.54	23.42		Pass	Fail	Pass	Pass	Pass
WS10	F	5.92	35.08		Fail	Fail	Fail	Pass	Fail
WS17	M	6.00	11.83		Fail	Fail	Pass	Fail	Pass
WS7	M	6.21	26.67		Fail	Fail	Pass	Fail	Fail
WS8	M	6.21	16.17		Fail	Fail	Pass	Fail	Pass
WS4	M	6.67	44.92		Fail	Fail	Pass	Fail	Fail
WS9	F	7.00	15.25		Pass	Pass	Pass	Pass	Fail
WS1	F	7.08	27.17		Fail	Pass	Fail	Pass	Fail
WS12	M	7.08	21.83		Pass	Pass	Pass	Pass	Pass
WS16	M	7.50	42.75		Pass	Pass	Fail	Pass	Pass
WS20	M	-	21.08		Fail	Fail	Fail	Fail	Pass
WS21	F	-	44.83		Fail	Fail	Pass	Fail	Pass
				Pass	8	7	14	11	11
				Fail	10	11	4	7	7
				% Pass	44%	39%	78%	61%	61%

S-1, First session with straight outbound paths; S-2, Second session with straight outbound paths; A-1, First session with angled outbound paths; A-2, Second session with angled outbound paths; Pass, average final location within the target quadrant; Fail, average final location not within the target quadrant. Criterion: Passing on 3 of 4 sessions.

TABLE 5 | Homing task.

	Homing Straight path S1	Homing Straight path S2	Homing Angled path S1	Homing Angled path S2
TD *n* =16	202 ± 71	184 ± 70	190 ± 73	203 ± 102
DS *n* =18	231 ± 94	164 ± 62	205 ± 85	225 ± 121
WS *n* =15	306 ± 122	244 ± 97	274 ± 83	266 ± 131
TD vs. DS	$t_{(45)} = 1.184$ $p = 0.243$	$t_{(45)} = 1.010$ $p = 0.318$	$t_{(45)} = 0.646$ $p = 0.522$	$t_{(45)} = 0.668$ $p = 0.508$
TD vs. WS	$t_{(44)} = 3.649$ $p = 0.001$	$t_{(44)} = 2.450$ $p = 0.018$	$t_{(44)} = 3.584$ $p = 0.001$	$t_{(44)} = 1.813$ $p = 0.077$
DS vs. WS	$t_{(35)} = 2.103$ $p = 0.043$	$t_{(35)} = 3.024$ $p = 0.005$	$t_{(35)} = 2.490$ $p = 0.018$	$t_{(35)} = 0.980$ $p = 0.334$

Distance from home, in centimeters. Groupe average ± standard deviation.

average end location in the quadrant of the room where the home was located (**Tables 2-4**). Thus, in Session 1, fewer participants with WS were considered to have passed the homing task than TD children ($X^2 = 7.017$, $p = 0.008$). There was no difference in the number of participants with DS and the number of participants with WS ($X^2 = 1.408$, $p = 0.235$) or TD children ($X^2 = 1.967$, $p = 0.161$). For Session 2 (**Figures 3D-F**), 89% of TD children, 79% of participants with DS and 61% of participants with WS had an average end location in the quadrant of the room where the home was located (**Tables 2-4**). Thus, in Session 2, fewer participants with WS were considered to have passed the homing task than TD children ($X^2 = 5.112$, $p = 0.024$). There was no difference in the number of participants with DS and the number of participants with WS ($X^2 = 1.408$, $p = 0.235$) or TD children ($X^2 = 1.967$, $p = 0.161$).

Average Distance From Home

There were differences between groups ($F_{(2,62)} = 5.297$, $p = 0.008$), but no difference between sessions ($F_{(2,62)} = 0.259$, $p = 0.613$) and no interaction between groups and sessions ($F_{(2,62)} = 0.239$, $p = 0.788$; **Table 5**). In Session 1, the distance between the end location and home was greater for participants with WS than for participants with DS or TD children. In Session 2, the distance between the end location and home did not differ between participants with WS and participants with DS or TD children. There were no differences between participants with DS and TD children in Session 1 or 2. It is important to note, also, that there were differences between groups in the number of times participants were stopped by the experimenter because they were approaching a wall ($F_{(2,64)} = 6.077$, $p = 0.004$; out of 10 trials; TD: 4.14 ± 2.68 (average ± standard deviation); DS: 7.21 ± 2.92; WS: 5.89 ± 3.55). Participants with DS were stopped more often than TD children ($t_{(45)} = 3.719$, $p = 0.001$). There was no difference between participants with WS and participants with DS ($t_{(35)} = 1.241$, $p = 0.223$), and the difference between participants with WS and TD children failed to reach the predefined level of statistical significance ($t_{(44)} = 1.900$, $p = 0.064$).

Initial Heading

The average heading after turning and walking one meter toward home did not differ from the ideal heading for participants with WS in either session (**Supplementary Material 4**). In contrast, the average initial heading of participants with DS and TD children differed from the ideal heading in both sessions. It deviated slightly to the left from the ideal heading for both groups in Session 1, whereas it deviated slightly to the right for both groups in Session 2. Accordingly, there were group differences in initial heading in both sessions. In addition, angular deviation (a measure of variability) was greater for the group of participants with DS than for the group of participants with WS in Session 2 (**Supplementary Material 4**). Within-subject variability in initial heading (the length of the mean vector) did not differ between groups ($F_{(2,62)} = 1.931$, $p = 0.154$) or between sessions ($F_{(1,62)} = 0.754$, $p = 0.389$); there was no interaction between groups and sessions ($F_{(2,62)} = 0.524$, $p = 0.595$).

Final Heading

The average final heading did not differ from the ideal heading for any of the groups, for either session (**Supplementary Material 5**). Nevertheless, there were group differences in final heading in both sessions. In Session 1, the average final heading of the group of participants with WS deviated slightly to the right, and thus differed from the final heading of participants with DS and TD children, which both deviated slightly to the left. In Session 2, the average final heading of participants with WS deviated slightly to the left, and thus differed from the final heading of participants with DS and TD children, which both deviated slightly to the right. Angular deviation (a measure of variability) differed between groups in Session 1 but not in Session 2. In

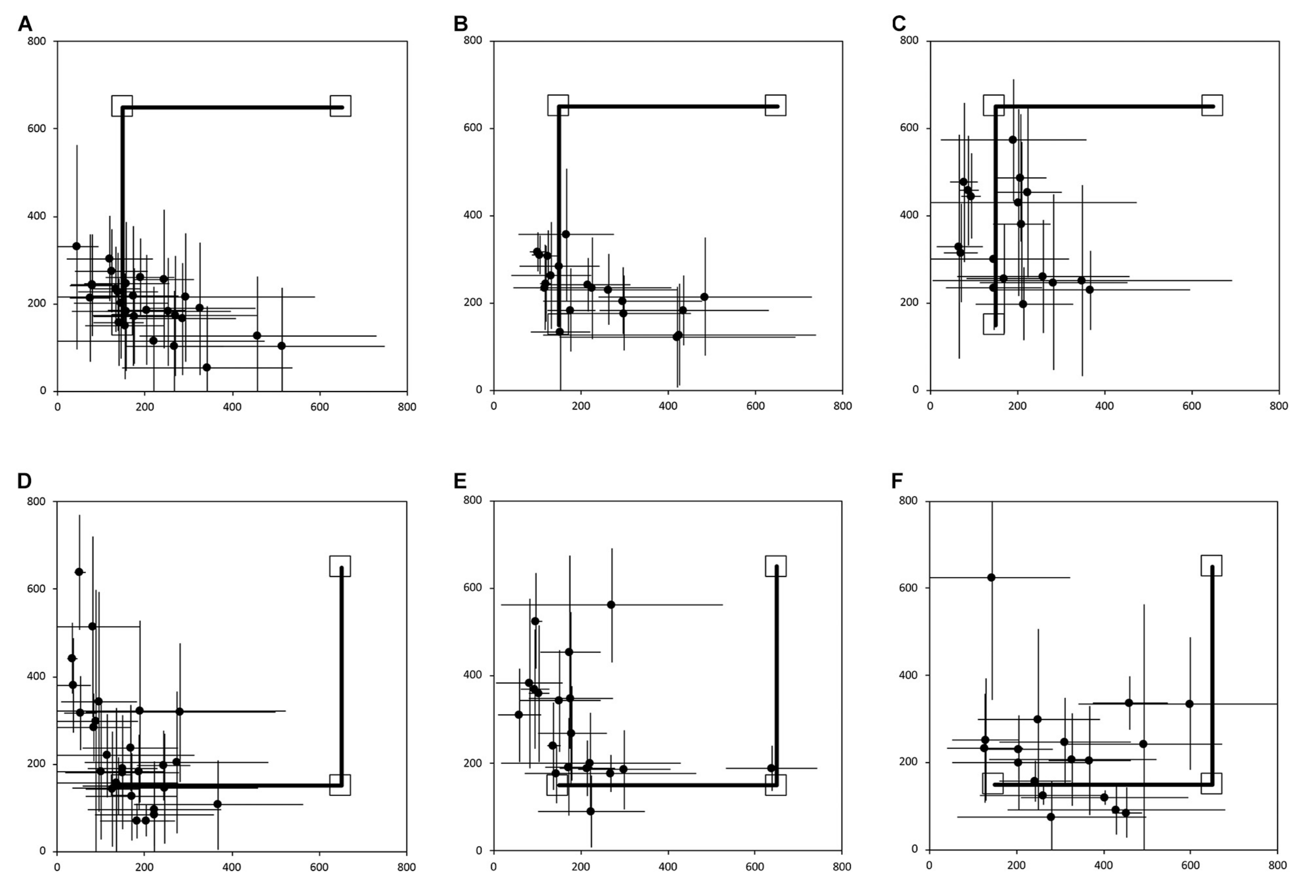

FIGURE 3 | Average end location of individual participants' return paths, following a two-legged 10 m angled outward journey in the egocentric homing task. The horizontal and vertical error bars represent the standard deviation for each individual across one session. The solid line indicates the outward angled path. The top right square indicates the starting point of the return path. The bottom left square indicates "home." In Session 1, participants were guided by the left arm, and in Session 2 they were guided by the right arm. **(A)** TD, Session 1. **(B)** DS, Session 1. **(C)** WS, Session 1. **(D)** TD, Session 2. **(E)** DS, Session 2. **(F)** WS, Session 2. Room size: 800 cm × 800 cm.

Session1, the angular deviation of participants with WS was greater than that of TD children; participants with DS did not differ from participants with WS or TD children. Accordingly, within-subject variability in final heading (the length of the mean vector) differed between groups ($F_{(2,62)} = 3.858$, $p = 0.026$); it did not differ between sessions ($F_{(1,62)} = 0.247$, $p = 0.621$) and there was no interaction between groups and sessions ($F_{(2,62)} = 0.139$, $p = 0.871$). The variability was greater for participants with WS, as compared to both TD children ($p = 0.011$) and participants with DS ($p = 0.028$). It did not differ between participants with DS and TD children ($p = 0.876$).

Homing Task: Results Summary

We considered that a reasonably stringent criterion to define overall successful performance would require participants' average final location to be in the home quadrant for at least 3 of the 4 sessions. A majority of TD children (96%) and participants with DS (84%), and a minority of participants with WS (44%) were capable of using path integration to build an egocentric spatial representation supporting homing behavior in absence of vision. Although the estimation that only 44% of the individuals with WS exhibited passing performance may not seem representative when considering that the percentage of individuals that passed on each of the four sessions ranged from 39 to 78%, it is critical to note that there was no consistency in the ability of individual participants to pass the different sessions. In other words, it was not always the same participants who succeeded in the different sessions, making an overall interpretation of greater success in individuals with WS misleading.

We next evaluated whether participants were capable of using path integration to build an allocentric spatial representation to take shortcuts, the hallmark of cognitive mapping abilities.

Cognitive Mapping Task

"Pass" or "Fail"

After having been blindfolded and guided along three selected paths between different objects, participants were asked to make six direct never-traveled trajectories between these objects, the first three being entirely novel paths and the last three being their reverse paths (**Figure 1** and **Supplementary Material 1**). **Figures 4**, **5** show the individual end location, for each

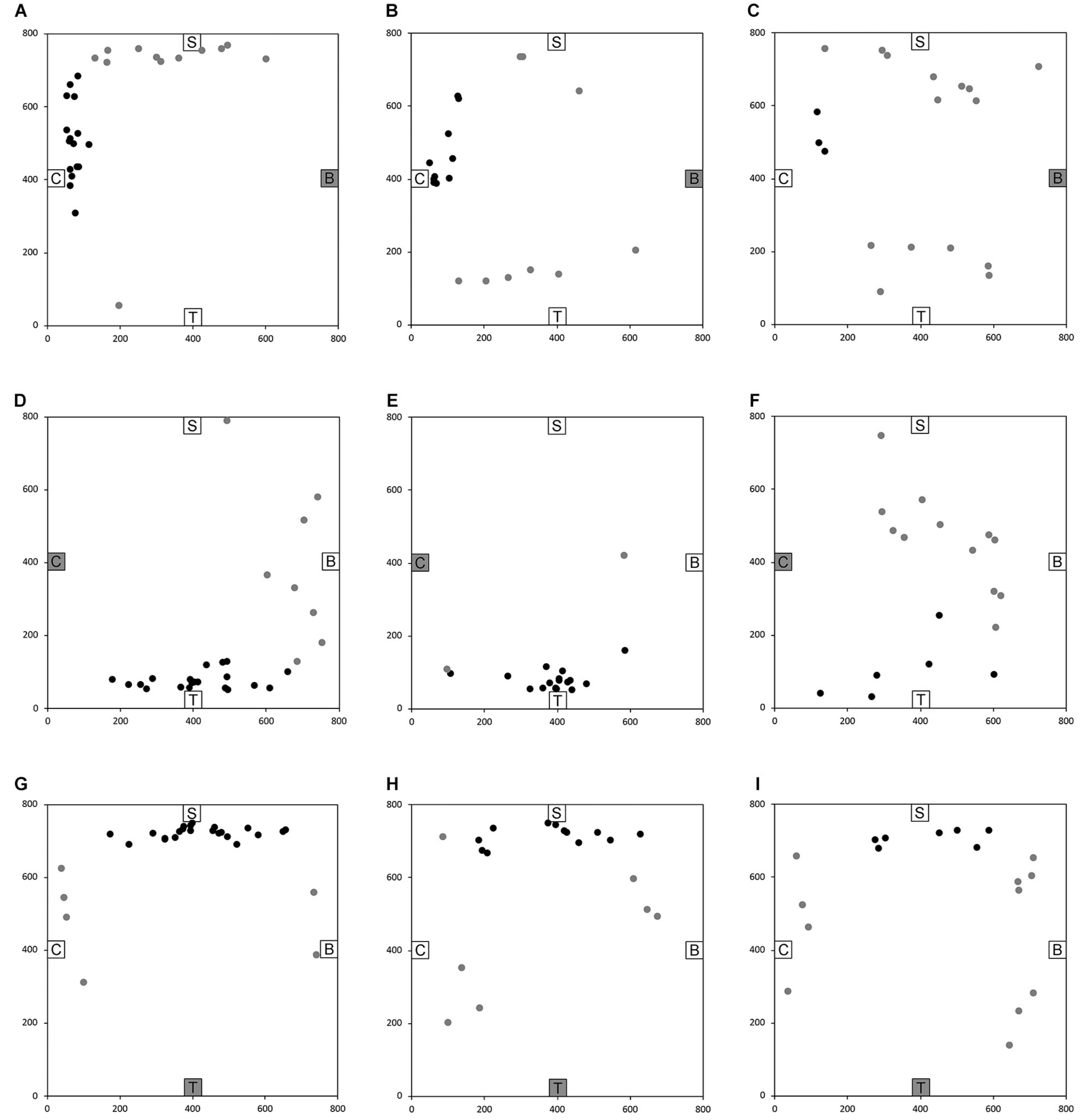

FIGURE 4 | End location of participants in the novel path trials of the allocentric cognitive mapping task. **(A)** Bench to Chair, TD: 16/28 individuals ended in the quadrant of the room where the target object was located (black dot: in the correct quadrant; gray dot: in an incorrect quadrant). **(B)** Bench to Chair, DS: 10/19 individuals in the correct quadrant. **(C)** Bench to Chair, WS: 3/18 individuals in the correct quadrant. **(D)** Chair to Table, TD: 20/28 individuals in the correct quadrant. **(E)** Chair to Table, DS: 17/19 individuals in the correct quadrant. **(F)** Chair to Table, WS: 6/18 individuals in the correct quadrant. **(G)** Table to Shelf, TD: 22/28 individuals in the correct quadrant. **(H)** Table to Shelf, DS: 12/19 individuals in the correct quadrant. **(I)** Table to Shelf, WS: 7/18 individuals in the correct quadrant. Room size: 800 cm × 800 cm.

participant, for each trajectory. Between 57 and 86% of TD children exhibited passing performance by ending in the quadrant that contained the target object on each trial (**Table 6**). Between 53 and 95% of participants with DS exhibited passing performance by ending in the quadrant that contained the target object on each trial (**Table 7**). Between 17 and 67% of participants with WS exhibited passing performance by ending in the quadrant that contained the target object on each trial (**Table 8**). We considered that a reasonably stringent criterion to define overall successful performance in the cognitive mapping

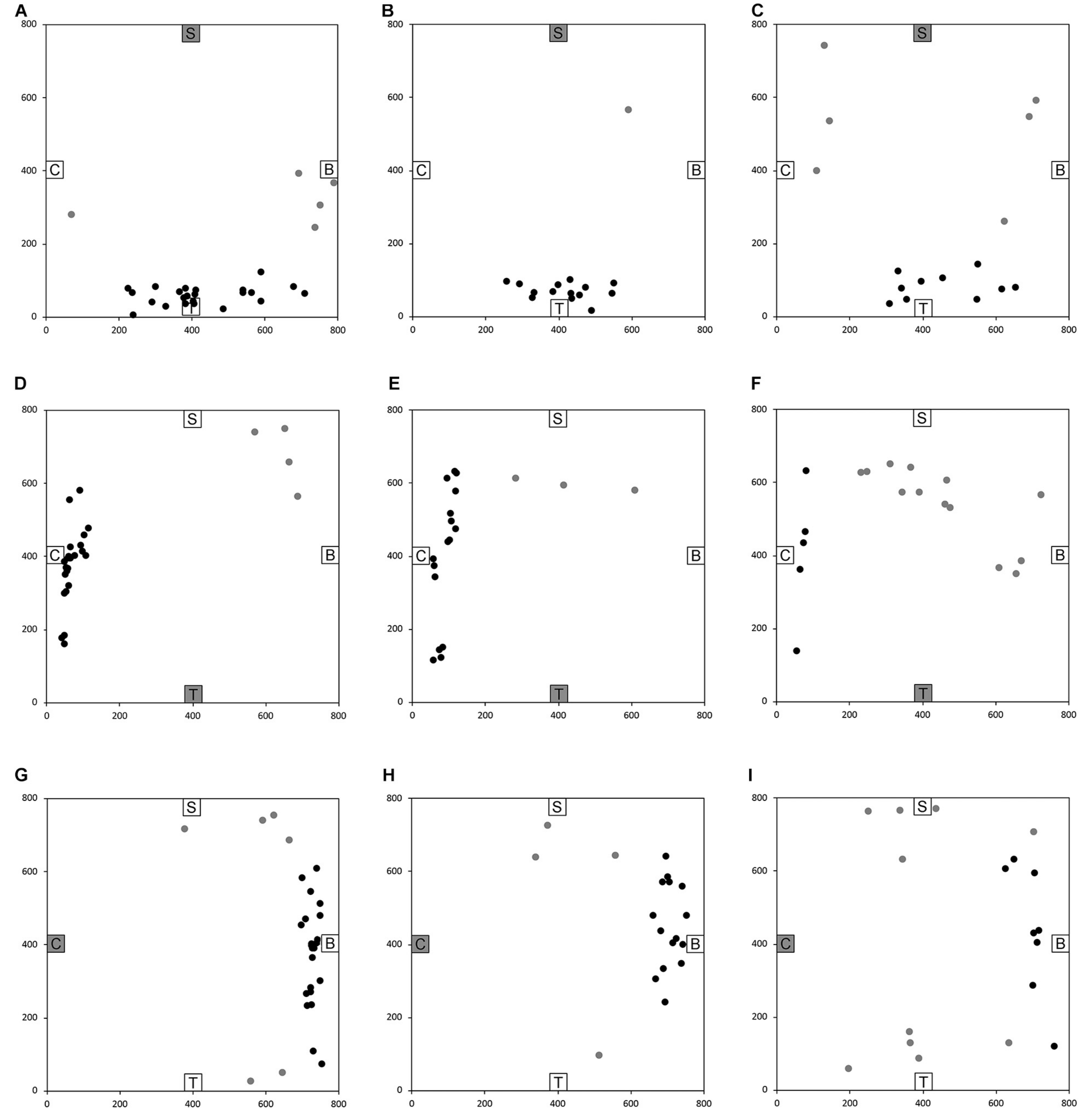

FIGURE 5 | End location of participants in the novel reverse path trials of the allocentric cognitive mapping task. **(A)** Shelf to Table, TD: 23/28 individuals ended in the quadrant of the room where the target object was located (black dot: in the correct quadrant; gray dot: in an incorrect quadrant). **(B)** Shelf to Table, DS: 18/19 individuals in the correct quadrant. **(C)** Shelf to Table, WS: 12/18 individuals in the correct quadrant. **(D)** Table to Chair, TD: 24/28 individuals in the correct quadrant. **(E)** Table to Chair, DS: 16/19 individuals in the correct quadrant. **(F)** Table to Chair, WS: 5/18 individuals in the correct quadrant. **(G)** Chair to Bench, TD: 22/28 individuals in the correct quadrant. **(H)** Chair to Bench, DS: 15/19 individuals in the correct quadrant. **(I)** Chair to Bench, WS: 8/18 in the correct quadrant. Room size: 800 cm × 800 cm.

task would require participants to succeed on at least four of the six novel paths, including the two paths with a 45° angle (Chair to Table, Table to Chair). We reasoned that successful performance on the two paths with a 45° angle was necessary in order to infer the existence of a cognitive map, since successful performance on the other novel routes could be achieved by simply walking straight from the object at the beginning of the path, and that such a strategy might be adopted by participants that had not constructed a cognitive map of the spatial relationships between the four objects' locations (Bostelmann et al., 2020). In contrast, however, failure to succeed on the straight paths should be considered as evidence against the ability to build a cognitive

TABLE 6 | Individual performance of TD children for the never traveled trajectories of the cognitive mapping task.

Participant	Gender	Age (years)	Homing task	Allo task	Criterion	B-C	C-T	T-S	S-T	T-C	C-B
TD39	F	4.83	a2	/	Pass	Pass	Pass	Pass	Fail	Pass	Pass
TD160	M	4.83		/	Fail	Fail	Fail	Pass	Pass	Fail	Pass
TD167	M	4.83	s1	/	Fail	Fail	Pass	Pass	Pass	Fail	Fail
TD187	F	5.00		/	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD50	M	5.50	a2	Pass	Pass	Pass	Pass	Pass	Fail	Pass	Pass
TD53	F	5.50	a1	/	Pass	Fail	Pass	Pass	Pass	Pass	Pass
TD186	F	5.67		/	Fail	Fail	Fail	Fail	Fail	Pass	Fail
TD27	M	5.83		Pass	Fail	Pass	Pass	Fail	Fail	Pass	Fail
TD36	M	5.92	s1a2	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD34	F	6.67		Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD35	M	6.67		Pass	Fail	Pass	Fail	Fail	Pass	Pass	Pass
TD48	F	6.67		Pass	Pass	Fail	Pass	Pass	Fail	Pass	Pass
TD141	F	6.67		/	Pass	Fail	Pass	Pass	Pass	Pass	Fail
TD42	M	6.92		Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
TD49	F	7.08		Pass	Fail	Pass	Fail	Pass	Pass	Pass	Fail
TD143	F	7.08		/	Fail	Fail	Fail	Fail	Pass	Fail	Fail
TD31	F	7.17		Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD25	M	7.25		Pass	Fail	Fail	Fail	Fail	Pass	Fail	Pass
TD191	M	7.50		/	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD26	F	7.92		Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
TD29	F	7.92		Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
TD52	M	8.08	a1	/	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD37	M	8.25		Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD138	F	8.42		/	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD28	F	8.58		Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
TD30	F	8.92		Pass	Fail	Pass	Fail	Pass	Pass	Pass	Pass
TD142	M	9.17		/	Pass	Pass	Pass	Pass	Pass	Pass	Pass
TD43	M	9.67		Pass	Fail	Fail	Fail	Pass	Pass	Pass	Pass
			Pass	16	18	16	20	22	23	24	22
			Fail	0	10	12	8	6	5	4	6
			% Pass	100%	64%	57%	71%	79%	82%	86%	79%

B-C, Bench to Chair; C-T, Chair to Table; T-S, Table to Shelf; S-T, Shelf to Table; T-C, Table to Chair; C-B, Chair to Bench; Homing task, the letter/number indicates sessions in which the participant was considered to have failed; s1, straight session 1; s2, straight session 2; a1, angled session 1; a2, angled session 2. Allo task, performance of participants who were also tested in the open-field allocentric spatial learning task (Bostelmann et al., 2017, 2018): Pass, succeeded at the task; Fail, failed the task; /, not tested. Pass, average final location within the target quadrant; Fail, average final location not within the target quadrant. Criterion: 4 paths passed, including the C-T and the T-C paths.

map. When applying this criterion, 64% of TD children, 74% of participants with DS, and 6% of participants with WS (**Tables 6-8**, respectively) demonstrated the ability to reliably travel to the target objects using novel paths, therefore demonstrating that they had built a cognitive map using path integration and could use this map to successfully navigate without vision.

Average Distance From the Target

There were differences between groups in the distance between the participant's end location and the target object ($F_{(2,62)} = 14.151$, $p < 0.001$), differences between paths ($F_{(5,310)} = 3.962$, $p = 0.002$), and no interaction between groups and paths ($F_{(10,310)} = 1.170$, $p = 0.310$; **Tables 9-10**). The distance from the target was greater for participants with WS than for participants with DS for all six paths, except for the path between the table and the shelf. The distance from the target was greater for participants with WS than for TD children for all six paths. There were no differences between participants with DS and TD children except for the path between the chair and the table, for which the distance from the target of participants with DS was actually shorter than that of TD children.

Initial Heading

For all three groups, the average initial heading did not differ from the ideal heading, except for the two paths requiring a 45° angle (**Supplementary Material 6**). Similarly, there were no differences between groups in initial heading, except for the two paths requiring a 45° angle. For these two paths, participants with WS deviated more from the ideal heading and tended to orient straight ahead, whereas participants with DS or TD children initiated their walk with an angle; there was no difference in the average initial heading between participants with DS and TD children. For these two paths, the angular deviation (a measure of variability) of participants with WS was greater than that of

TABLE 7 | Individual performance of participants with DS for the never traveled trajectories of the cognitive mapping task.

Participant	Gender	M. A. (years)	Homing task	Allo task	Criterion	B-C	C-T	T-S	S-T	T-C	C-B
DS19	M	4.67	s1a2	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
DS6	M	4.75	s1	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
DS8	F	4.75	s1a2	Pass	Fail	Fail	Fail	Fail	Pass	Pass	Fail
DS1	M	4.83	a2	Fail	Fail	Fail	Pass	Pass	Pass	Fail	Pass
DS5	F	5.00	s1	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
DS13	M	5.00	a2	Pass	Fail	Pass	Pass	Fail	Pass	Fail	Pass
DS12	M	5.08		Fail	Pass	Pass	Pass	Pass	Pass	Pass	Pass
DS30	M	5.25		Fail	Pass	Pass	Pass	Pass	Pass	Pass	Pass
DS24	M	5.29		Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
DS7	M	5.33		Fail	Pass	Pass	Pass	Pass	Pass	Pass	Pass
DS15	F	5.33		/	Pass	Pass	Pass	Pass	Pass	Pass	Pass
DS23	M	5.58	a1	Pass	Fail	Fail	Pass	Fail	Pass	Pass	Fail
DS25	F	5.88	a1	Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
DS27	F	6.00	a1	Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
DS26	F	6.21	s1s2	Pass	Fail	Fail	Fail	Fail	Fail	Fail	Fail
DS2	F	6.67		Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
DS4	F	6.67		Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
DS22	M	6.67		Pass	Pass	Fail	Pass	Pass	Pass	Pass	Pass
DS21	F	6.96	a1	Pass	Pass	Pass	Pass	Fail	Pass	Pass	Fail
			Pass	14	14	10	17	12	18	16	15
			Fail	4	5	9	2	7	1	3	4
			% Pass	78%	74%	53%	89%	63%	95%	84%	79%

B-C, Bench to Chair; C-T, Chair to Table; T-S, Table to Shelf; S-T, Shelf to Table; T-C, Table to Chair; C-B, Chair to Bench; Homing task, the letter/number indicates sessions in which the participant was considered to have failed; s1, straight session 1; s2, straight session 2; a1, angled session 1; a2, angled session 2. Allo task, performance of participants who were also tested in the open-field allocentric spatial learning task (Bostelmann et al., 2017, 2018): Pass, succeeded at the task; Fail, failed the task; /, not tested. Pass, average final location within the target quadrant; Fail, average final location not within the target quadrant. Criterion: 4 paths passed, including the C-T and the T-C paths.

participants with DS and TD children; there was no difference in angular deviation between participants with DS and TD children.

Final Heading

The average final heading differed from the ideal heading for TD children for the first novel path, and for participants with WS for the two paths requiring a 45° angle (**Supplementary Material 7**). The average final heading of participants with WS differed from those of participants with DS and TD children for the two paths with a 45° turn. Angular deviation (a measure of variability) was greater for participants with WS than for participants with DS and TD children for all paths, except for the path from the table to the shelf for which the difference between participants with WS and participants with DS was not statistically significant. There was no difference in angular deviation between participants with DS and TD children.

One important difference between initial and final headings must be noted. For all three groups the average initial heading differed from the ideal heading for the two paths requiring a 45° turn. However, at the end of their trajectory, only the average final heading of the group of participants with WS differed from the ideal heading. In contrast, the average final heading of participants with DS and that of TD children no longer differed from the ideal heading. These findings suggest that participants with DS and TD children may have solved the 45° angle paths by first walking somewhat straight (albeit less straight than participants with WS), and then by angling toward the target object at some point after one meter.

Cognitive Mapping Task: Results Summary

Altogether, our findings showed that the average initial and final headings of participants with WS differed from the ideal heading for the two 45° angle paths. Moreover, for these two critical paths participants with WS were overall less accurate and more variable than participants with DS and TD children. Altogether, individual data and group analyses indicate that a majority of participants with DS (74%), a proportion slightly higher than that of TD children (64%; the difference was not statistically significant), exhibited the ability to use path integration to build a cognitive map of the environment in absence of visual information. In contrast, only one participant with WS was able to use path integration to build a cognitive map, whereas the vast majority (94%) were not, even though almost half of the participants with WS (44%) were able to use path integration to support homing behavior.

DISCUSSION

This study aimed to characterize the capacity of individuals with DS and individuals with WS to use path integration to build

TABLE 8 | Individual performance of participants with WS for the never traveled trajectories of the cognitive mapping task.

Participant	Gender	M. A. (years)	Homing task	Allo task	Criterion	B-C	C-T	T-S	S-T	T-C	C-B
WS13	F	4.42	s1	Fail	Fail	Fail	Fail	Pass	Pass	Fail	Pass
WS2	M	4.75		Fail	Fail	Pass	Fail	Pass	Fail	Fail	Fail
WS15	M	4.75	s1	Pass	Fail	Pass	Fail	Fail	Pass	Fail	Pass
WS22	F	5.00	a1a2	/	Fail	Fail	Pass	Pass	Pass	Fail	Fail
WS3	M	5.33		Fail	Fail	Fail	Fail	Fail	Pass	Fail	Fail
WS5	F	5.33	s1a2	Fail	Fail	Fail	Fail	Fail	Pass	Pass	Fail
WS18	F	5.54	s1	Fail	Fail	Fail	Pass	Pass	Fail	Fail	Fail
WS10	F	5.92	s1s2a2	Fail	Fail	Fail	Fail	Pass	Pass	Fail	Pass
WS17	M	6.00	s1a1	Fail	Fail	Fail	Pass	Pass	Fail	Fail	Pass
WS7	M	6.21	s1a1a2	Fail	Fail	Fail	Fail	Fail	Fail	Pass	Fail
WS8	M	6.21	s1a1	Fail	Fail	Fail	Fail	Fail	Pass	Pass	Fail
WS4	M	6.67	s1a1a2	Fail	Fail	Fail	Pass	Fail	Pass	Pass	Fail
WS9	F	7.00	a2	Fail	Fail	Fail	Fail	Fail	Pass	Fail	Pass
WS1	F	7.08	s2a2	Fail	Fail	Fail	Fail	Fail	Fail	Fail	Fail
WS12	M	7.08		Pass	Pass	Pass	Pass	Fail	Pass	Pass	Pass
WS16	M	7.50	s2	Pass	Fail	Fail	Fail	Fail	Fail	Fail	Fail
WS20	M	-	s1s2a1	/	Fail	Fail	Pass	Fail	Pass	Fail	Pass
WS21	F	-	s1a1	/	Fail	Fail	Fail	Pass	Pass	Fail	Pass
			Pass	3	1	3	6	7	12	5	8
			Fail	12	17	15	12	11	6	13	10
			% Pass	20%	6%	17%	33%	39%	67%	28%	44%

B-C, Bench to Chair; C-T, Chair to Table; T-S, Table to Shelf; S-T, Shelf to Table; T-C, Table to Chair; C-B, Chair to Bench; Homing task, the letter/number indicates sessions in which the participant was considered to have failed; s1, straight session 1; s2, straight session 2; a1, angled session 1; a2, angled session 2. Allo task, performance of participants who were also tested in the open-field allocentric spatial learning task (Bostelmann et al., 2017, 2018): Pass, succeeded at the task; Fail, failed the task; /, not tested. Pass, average final location within the target quadrant; Fail, average final location not within the target quadrant. Criterion: 4 paths passed, including the C-T and the T-C paths.

egocentric and allocentric spatial representations to navigate in a real-world environment without vision. We found that 84% of participants with DS could use path integration to return to a home base and 74% of participants with DS could build a cognitive map. In contrast, only 44% of participants with WS could use path integration to return to a home base consistently, and only 6% of participants with WS could build a cognitive map. Our study thus revealed that in a real-world laboratory setting, individuals with DS exhibit cognitive mapping abilities that are similar to those of TD children within the same mental age range, whereas individuals with WS are comparatively impaired. These findings are consistent with previous findings suggesting a relative preservation of the ability to create and use low-resolution allocentric spatial representations in DS (Banta Lavenex et al., 2015; Bostelmann et al., 2018), and significant impairments in WS (Bostelmann et al., 2017).

Comparison With Previous Studies in Individuals With DS

Egocentric Tasks in the Real-World

Bostelmann et al. (2018) tested the ability of individuals with DS and TD children to solve a spatial response-learning task in a 4 m × 4 m open-field arena. In that task, the reward was hidden in one of four possible locations, which alternated between the left and right sides of the arena on each trial. It was therefore not

TABLE 9 | Cognitive mapping task. Distance from home, in centimeters.

	Bench to Chair	Chair to Table	Table to Shelf
TD *n* =16	264 ± 189	212 ± 195	175 ± 158
DS *n* =18	240 ± 188	101 ± 119	234 ± 179
WS *n* =15	425 ± 166	353 ± 164	320 ± 188
TD vs. DS	$t_{(45)} = 0.432$ $p = 0.668$	$t_{(45)} = 2.206$ $p = 0.033$	$t_{(45)} = 1.186$ $p = 0.242$
TD vs. WS	$t_{(44)} = 2.966$ $p = 0.005$	$t_{(44)} = 2.541$ $p = 0.015$	$t_{(44)} = 2.813$ $p = 0.007$
DS vs. WS	$t_{(35)} = 3.176$ $p = 0.003$	$t_{(35)} = 5.365$ $p < 0.001$	$t_{(35)} = 1.425$ $p = 0.163$

Groupe average ± standard deviation.

TABLE 10 | Cognitive mapping task.

	Shelf to Table	Table to Chair	Chair to Bench
TD *n* =16	169 ± 141	163 ± 218	172 ± 141
DS *n* =18	144 ± 120	203 ± 145	179 ± 145
WS *n* =15	285 ± 220	365 ± 192	334 ± 196
TD vs. DS	$t_{(45)} = 0.622$ $p = 0.537$	$t_{(45)} = 0.704$ $p = 0.485$	$t_{(45)} = 0.172$ $p = 0.864$
TD vs. WS	$t_{(44)} = 2.179$ $p = 0.035$	$t_{(44)} = 3.216$ $p = 0.002$	$t_{(44)} = 3.273$ $p = 0.002$
DS vs. WS	$t_{(35)} = 2.426$ $p = 0.021$	$t_{(35)} = 2.909$ $p = 0.006$	$t_{(35)} = 2.749$ $p = 0.009$

Distance from home, in centimeters. Groupe average ± standard deviation.

TABLE 11 | Number of participants who passed or failed the open-field allocentric spatial memory task with one location and with vision (Bostelmann et al., 2017, 2018) and the cognitive mapping task with four objects in the absence of vision (current study).

	Pass Allo & Pass CogMap	Pass Allo & Fail CogMap	Fail Allo & Pass CogMap	Fail Allo & Fail CogMap
TD *n* =16	10	6	0	0
DS *n* =18	10	4	3	1
WS *n* =15	1	2	0	12

in the same location with respect to the environment, but instead was always found opposite from where the participant entered the arena. Optimal performance in this response-learning task requires not only the ability to encode the reward location in a viewpoint-dependent manner and always walk across the arena to find the reward along the middle of the opposite wall, but also the ability to ignore contradictory allocentric strategies that would lead the participant to return to the location where the reward was found on the preceding trial. Interestingly, whereas 95% of TD children exhibited optimal performance on an allocentric spatial memory task in the same arena (see below), only 16% succeeded on the response-learning task. In fact, most TD children persisted in employing an allocentric strategy and returning to the location where the reward was found on the preceding trial. In contrast, 56% of participants with DS succeeded on the response-learning task, demonstrating that they were better at ignoring conflicting allocentric strategies. In the current study, homing behavior could be supported by an egocentric spatial representation of the individual's position with respect to their starting position on the outbound journey, which did not conflict with any other spatial representation or strategy to guide behavior. We found that 84% of participants with DS could return to home consistently, only slightly fewer than the number of TD children (96%; the difference was not statistically significant). These results demonstrating relatively preserved egocentric capacities in DS are also in agreement with findings from a recent study showing that individuals with DS performed as well as MA-matched TD children in reproducing an egocentric 1- to 7-step route (consisting of sequential moves forward, right or left) on a 4 × 4 floor matrix comprising 16 squares of 50 cm × 50 cm separated by 10 cm gaps, after either studying a map of the route or observing an experimenter take the same route (Meneghetti et al., 2020). Specifically, individuals with DS were able to reproduce an average of 3.00 steps after visualizing the trajectory on a map, while MA-matched TD children reproduced an average of 3.53 steps. After observing an experimenter walk along the same path, individuals with DS reproduced an average of 3.50 steps, while TD children reproduced an average of 4.23 steps. Interestingly, both individuals with DS and TD children performed better after observing the experimenter walking the route (real-world correspondence) than after studying the route on a map (transfer from a schematic representation to the real world).

Egocentric Tasks in Virtual Reality

Our results are partially consistent with studies investigating egocentric route learning in virtual environments, which have found that the majority of individuals with DS can learn the routes, yet their performance is not always comparable to that of MA-matched TD children, and the specific learning strategies used by the different groups of participants may differ (Purser et al., 2012; Courbois et al., 2013; Davis et al., 2014; Farran et al., 2015; N'Kaoua et al., 2019). Altogether, these findings suggested that participants with DS may pay less attention to environmental landmarks or have more difficulty in associating those landmarks with specific spatial locations or behaviors, and are thus more likely to rely on a sequence of directional changes to learn routes. In contrast, TD children may benefit from the congruence of the two strategies, relying both on the sequence of directional changes and their consistency with environmental landmarks at choice points or along the path (Purser et al., 2015). In the present study, since visual information could not be used to support navigational strategies and thus facilitate performance in TD children, we found similar performance for participants with DS and MA-matched TD children.

Allocentric Tasks in the Real-World

Our findings that 74% of participants with DS were capable of using path integration to build a cognitive map of the four objects' locations in absence of visual information are very similar to previous findings from an open-field allocentric spatial memory task showing that 78% of participants with DS were able to learn and remember the location of one reward amongst four identical locations in the presence of visual information (**Table 11**) (Bostelmann et al., 2018). Importantly, a majority of our participants in all three groups (DS, WS and TD children) were also tested previously in this open-field task, allowing us to compare the performance of these individuals across these two allocentric tasks theoretically subserved by the same neural substrates. For both tasks, in order to succeed participants had to create a cognitive map of the environment using path integration, but in one condition in the presence of vision (open-field arena), and in the other in the absence of vision (cognitive mapping task). Of the sixteen TD children who were tested on both tasks, all passed the open-field allocentric task, whereas 10 passed and 6 failed the cognitive mapping task (this proportion was similar to that of the TD children who participated only in the cognitive mapping study). Note that the only TD child who failed the open-field task with one location (a 3.5-year-old boy) refused to walk with the sleeping mask covering his eyes and was therefore not tested in the present study. Thus, fewer TD children passed the cognitive mapping task than the open-field task. However, performance was not correlated with age, suggesting that children who failed may have been dismissive or inattentive during the learning phase (Bostelmann et al., 2020). Of the 18 participants with DS who were tested on both tasks, 14 passed the open-field task, whereas 13 passed the cognitive mapping task. Surprisingly, of the 13 participants with DS who passed the cognitive mapping task, three failed the open-field task with one location, a finding which may highlight poor comprehension of the goals of the task or an inability to inhibit egocentric responding in the open-field task.

In sum, both theoretical and empirical evidence support the view that performance in both tasks depends on the ability to form and use a low-resolution allocentric spatial representation of the environment. Our data show that this ability is largely preserved in individuals with DS. It is important to note, however, that the ability to form and use high-resolution allocentric spatial representations of the environment has been shown to be impaired in a majority of individuals with DS (Banta Lavenex et al., 2015).

Allocentric Task in Virtual Reality

Although several studies reported an impaired ability of individuals with DS to demonstrate allocentric spatial capacities or configural knowledge of landmark locations using virtual reality paradigms, no study has provided unequivocal evidence of a specific impairment as compared to MA-matched TD children (Purser et al., 2012; Courbois et al., 2013; Farran et al., 2015; N'Kaoua et al., 2019). The main reason is the fact that none of these studies actually demonstrated that the TD children relied on an allocentric or configural spatial representation to solve these tasks, thus making comparisons with individuals with DS uninformative. In another example, Pennington et al. (2003) tested individuals with DS and MA-matched TD children on a virtual Morris water maze task. During a probe trial in absence of the platform, participants with DS spent on average less time searching in the quadrant of the platform than TD children. However, other factors such as motivation or the drive to explore other parts of the environment to look for the platform may also influence the time spent searching in the target quadrant. Indeed, in a subsequent study, Edgin et al. (2010) failed to reveal any difference between participants with DS and MA-matched TD children, thus raising doubts about a global impairment of allocentric spatial capacities in individuals with DS. Finally, Toffalini et al. (2018) evaluated the ability of individuals with DS and MA-matched TD children to learn the locations of five local landmarks distributed at the four corners and along one of the walls of a square area. Although some subtle differences were reported in the performance of the two groups in different learning conditions, statistical analyses suggested that participants with DS performed as well as TD children when asked to place the landmarks at their approximate locations on a layout of the environment.

In sum, previous studies carried out in virtual reality have not provided reliable evidence regarding the ability of individuals with DS to build an allocentric spatial representation of their environment. In contrast, the current study has shown unequivocally that 74% of participants with DS were able to build a cognitive map in absence of visual information. These findings are consistent with previous findings showing that 78% of participants with DS were able to learn and remember the location of one reward amongst four identical locations in presence of visual information (Bostelmann et al., 2018).

Comparison With Previous Studies in WS

Egocentric Tasks in the Real-World

Bostelmann et al. (2017) previously tested the ability of individuals with WS to solve the egocentric response-learning task and the allocentric place learning task as described above for individuals with DS and TD children (Bostelmann et al., 2018). Again, whereas 95% of TD children exhibited optimal performance on the allocentric spatial memory task, only 16% passed the response-learning task. In contrast, 72% of participants with WS succeeded on the response-learning task, thus exhibiting superior and even facilitated egocentric response-learning as compared to TD children. In the current study, however, only 44% of participants with WS were able to use an egocentric strategy to consistently return to the starting point of the outbound journey. It is possible that the differing performance of individuals with WS on these two different egocentric tasks can be explained by the presence of visual landmarks or beacons that can be used in combination with idiothetic information to confirm the target location. Indeed, in the egocentric response-learning task participants can see the potential reward locations that when combined with idiothetic cues allow them to encode the reward location in a viewpoint-dependent manner and thus always walk across the arena to choose the visible reward location along the middle of the opposite wall. These findings indicate that the performance of participants with WS is overall less accurate and more variable than that of MA-matched TD children and participants with DS when using egocentric representations constructed from self-generated motion information alone.

Accordingly, individuals with WS have been shown to be able to learn a new 1 km long route including 20 choice points (left, right, straight ahead) through an unfamiliar environment, although they performed less well than MA-matched TD children (Farran et al., 2010). However, the performance of participants with WS improved if they were given verbal instructions including directional information and information about features along the routes, including the highlighting of four major landmarks to remember for future use, and repeated experience walking the route. These findings suggest that individuals with WS benefit from verbal memory and the presence of visual landmarks along the path, and may therefore rely on sequential egocentric responses combined with viewpoint-matching of a series of landmarks in order to learn a route in a real-world environment.

Egocentric Tasks in Virtual Reality

Studies carried out in virtual reality also suggest that a majority of individuals with WS are capable of route learning using visual landmarks located along the path (Broadbent et al., 2014, 2015; Farran et al., 2015). In a study using a design similar to the one described above for individuals with DS (Courbois et al., 2013), Farran et al. (2015) reported that about two thirds of individuals with WS can learn at least one of two different routes requiring four changes of direction. Using a differently shaped virtual environment, Broadbent et al. (2015) showed that individuals with WS exhibited a reliance on visual landmarks for route-learning and failed to learn a route containing 6 changes in direction that did not contain landmarks. These findings are consistent with those reported by Broadbent et al. (2014) for the learning of a route comprising 4 directional changes in a cross-maze virtual environment. Thus, in contrast to what has been shown for individuals with DS, who do not benefit from the presence of environmental landmarks but can learn a sequence of directional changes, individuals with WS appear to rely more heavily on local environmental landmarks.

Allocentric Tasks in the Real-World

Our findings that only one of 18 participants with WS was capable of using path integration to build a cognitive map in the absence of visual information are consistent with previous findings in the open-field allocentric spatial memory task, which showed that only 17% of participants with WS were capable of using a low-resolution allocentric spatial representation to learn and remember the location of one reward amongst four possible locations in the presence of visual information (Bostelmann et al., 2017). Of the participants tested in the current study, sixteen TD children and 15 participants with WS were also tested in the open-field allocentric spatial memory task (**Table 11**). As described above, 100% of the TD children passed the open-field task, whereas 64% of these TD children passed the cognitive mapping task and 36% failed. In contrast, only 20% of participants with WS passed the open-field task (3 of 15), and only one of these individuals passed the cognitive mapping task, whereas the other two failed. Thus, as discussed above, theoretical and empirical evidence suggest that performance on both tasks depends on the ability to form and use a low-resolution allocentric spatial representation of the environment. Our findings show that the vast majority of participants with WS are unable to solve either task.

In agreement with our findings, Farran et al. (2010) showed that individuals with WS learned a route through a natural environment, and that their route knowledge was improved by verbal coding of the route, and by walking it more than once (Farran et al., 2010). However, in contrast to MA-matched TD children, individuals with WS did not appear to learn the spatial relationships between environmental landmarks, as shown by their inability to point accurately in the direction of several landmarks from different points along the route. As discussed previously (Bostelmann et al., 2017), although other studies employing real-world paradigms have suggested deficits in allocentric spatial processing in individuals with WS, because success in these paradigms was also dependent on other cognitive processes [i.e., the ability to understand complex verbal instructions, mental rotation and working memory (Nardini et al., 2008; Mandolesi et al., 2009; Foti et al., 2011)] or could be solved using egocentric coding of multiple visible locations (Smith et al., 2009; Foti et al., 2011), it was not clear whether allocentric spatial learning per se was impacted in WS. In contrast, our current and previous findings (Bostelmann et al., 2017) provide unequivocal evidence that allocentric spatial processes are severely impaired, if not abolished, in a large majority of individuals with WS.

Allocentric Tasks in Virtual Reality

As discussed above for individuals with DS, although a few studies have reported an impaired ability of individuals with WS to demonstrate allocentric spatial capacities or configural knowledge of landmark locations using virtual reality paradigms (Broadbent et al., 2015; Farran et al., 2015), they did not provide unequivocal evidence of a specific impairment as compared to MA-matched TD children. The main reason was that these paradigms did not conclusively demonstrate that TD children actually relied on an allocentric or configural spatial representation to solve these tasks either. Further confirmation of this conclusion is a study by Broadbent et al. (2014) which showed that less than 50% of 10-year-old TD children may have used an allocentric strategy to solve a cross-maze task, and only between 20 and 30% of TD children between 5 and 8 years of age, which corresponds to the mental age of individuals with WS, may have solved the task using an allocentric strategy. Such poor performance by TD children makes comparisons of the performance of individuals with WS relatively uninformative.

CONCLUSION

Our study revealed that in a real-world laboratory setting, individuals with DS exhibit homing and cognitive mapping abilities similar to those of TD children with similar mental ages. These results are consistent with previous findings suggesting a preservation of the neural circuits subserving the creation and use of low-resolution egocentric and allocentric spatial representations in DS. In contrast, individuals with WS are severely impaired in their ability to build cognitive maps, and although many are impaired in their ability to home without vision, more individuals may be capable of successful route finding in the presence of visual landmarks. These findings are consistent with previous findings suggesting abnormalities of the neural circuits subserving the creation of egocentric and allocentric spatial representations in WS.

Thus, although individuals with DS and WS have similar mental ages, they exhibit distinct spatial cognitive profiles that should be considered carefully when designing training paradigms to improve navigational capacities that can lead to greater autonomy, self-confidence and social inclusion. Specifically, preserved capacities should be targeted to develop syndrome-specific navigational strategies. Since individuals with WS are essentially unable to build cognitive maps of their environment, they should not be expected or trained to use cognitive mapping strategies, since these strategies are unlikely to be successful. In contrast, individuals with WS can be encouraged to memorize sequences of directional changes to learn an itinerary and may benefit from the presence of environmental landmarks to learn a route from point A to point B. For individuals with DS, due to an overall weakness in their working memory capacities, navigation training should not include strategies that rely heavily on the memorization of multiple sequences of directional changes or environmental landmarks. Because individuals with DS can build low-resolution cognitive maps they should be encouraged to have confidence in their overall sense of direction, and to use cognitive mapping strategies when navigating.

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 the Commission Cantonale d'Éthique de la Recherche sur l'Être Humain, Vaud, Switzerland. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

PBL and PL were responsible for the conception and design of the work, acquisition, analysis and interpretation of the data, and writing of the manuscript. MB was responsible for the design of the work, acquisition, analysis and interpretation of the data, and drafting of the manuscript. PR was responsible for data acquisition and drafting of the manuscript. AR, FC, and DM were responsible for data acquisition. SV was responsible for conception of the work and drafting of the manuscript. All authors approved the final version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2020.571394/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.

Supplementary Material 1: Schematic representation of the experimental design and sequence of trajectories performed by participants in the homing and cognitive mapping tasks.

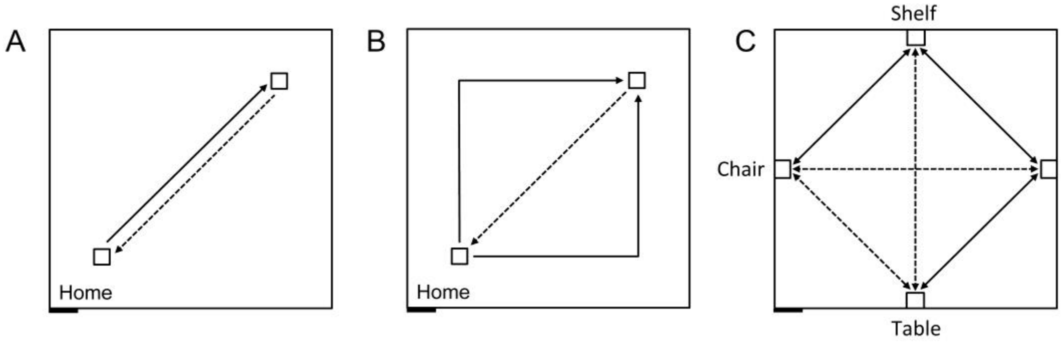

Figure 1.1 Schematic representation of the experimental design, carried out in an 8 m x 8 m testing room. The black rectangle at the bottom left represents the entry door to the room. Solid lines indicate guided trajectories; dashed lines indicate direct paths that participants were verbally requested to make. A. Homing task, straight paths: 7 m straight line guided trajectory, 7 m return path. B. Homing task, angled paths: 10 m angular guided trajectory with a right or left turn (5 m + 5 m), and 7 m return path. C. Cognitive mapping task: Guided routes (solid) and novel routes (dashed) between four objects, without vision. The paths between the bench and the chair, and between the table and the shelf were 7 m long; the other paths were 5 m long.

Table 1.1 Sequence of trajectories performed by participants in the cognitive mapping task.

	Route learning paradigm
Learning Phase	Bench to shelf round-trip guided 2 x
	Bench to shelf round-trip alone 1 x
	Bench to shelf round-trip guided 2 x
	Bench to shelf round-trip alone 2 x
	Bench to shelf 1-way alone 1 x
	Shelf to chair round-trip guided 2 x
	Shelf to chair round-trip alone 1 x
	Shelf to chair round-trip guided 2 x
	Shelf to chair round-trip alone 2 x
	Shelf to bench 1-way alone 1 x
	Bench to table round-trip guided 2 x
	Bench to table round-trip alone 1 x
	Bench to table round-trip guided 2 x
	Bench to table round-trip alone 2 x
Testing Phase	Bench to chair alone 1 x
	Chair to table alone 1 x
	Table to shelf alone 1 x
	Shelf to table alone 1 x
	Table to chair alone 1 x
	Chair to bench alone 1 x

Supplementary Material 2. Homing task - Straight outward paths –Initial heading

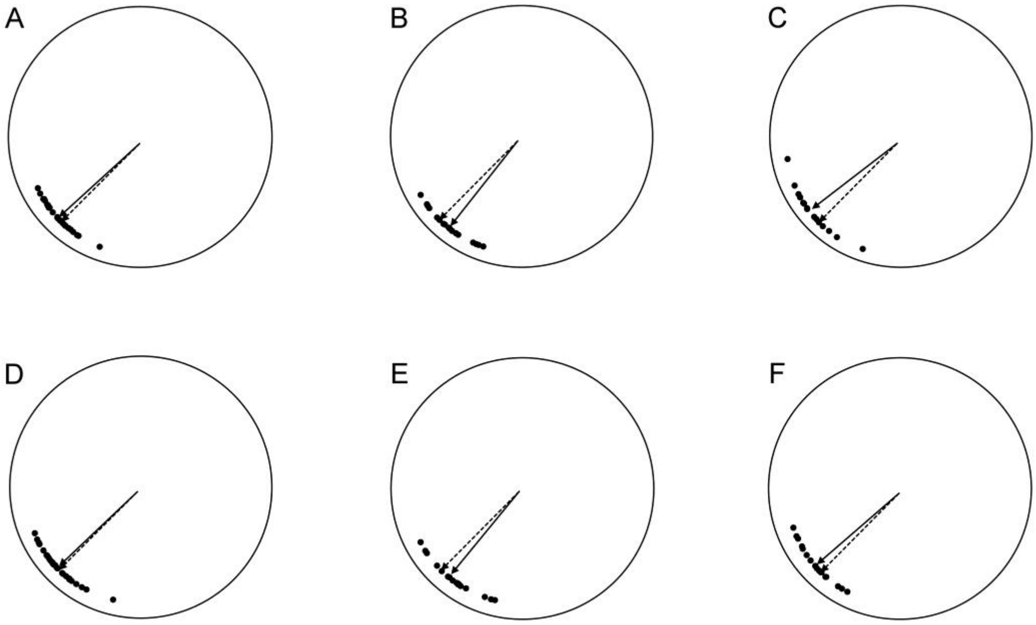

Figure 2.1 Average (solid-line arrow) and individual (dots) walking directions of participants after one meter along the return path, following a straight 7 m outward journey in the homing task. A. TD, Session 1. B. DS, Session 1. C. WS, Session 1. D. TD, Session 2. E. DS, Session 2. F. WS, Session 2. Dashed-line arrow: perfect home direction.

Table 2.1 Within-group results: Homing task - Straight outward paths - Initial heading

	TD				DS				WS			
Path	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.
Session 1	2.31°	<	5.41°	10.32°	6.32°	<	7.80°	11.83°	7.56°	<	9.44°	13.77°
Session 2	1.47°	<	6.25°	11.87°	5.55°	<	10.15°	15.21°	4.43°	<	8.25°	12.11°

Table 2.2 Between groups comparisons: Homing task - Straight outward paths - Initial heading

	TD vs DS vs WS		TD vs DS		TD vs WS		DS vs WS	
Path	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.
Session 1	$F_{(2,62)}$ = 12.5014 **p < 0.001**	$F_{(2,62)}$ = 1.893 p = 0.159	$F_{(1,45)}$ = 6.703 **p = 0.013**	$t_{(45)}$ = 1.188 p = 0.241	$F_{(1,44)}$ = 2.064 p = 0.239	$t_{(44)}$ = 1.935 p = 0.059	$F_{(1,35)}$ = 10.240 **p = 0.003**	$t_{(35)}$ = 0.695 p = 0.492
Session 2	$F_{(2,62)}$ = 5.5611 **p = 0.006**	$F_{(2,62)}$ = 1.818 p = 0.171	$F_{(1,45)}$ = 2.986 p = 0.091	$t_{(45)}$ = 1.855 p = 0.070	$F_{(1,44)}$ = 0.636 p = 0.429	$t_{(44)}$ = 0.249 p = 0.804	$F_{(1,35)}$ = 4.558 **p = 0.040**	$t_{(35)}$ = 1.361 p = 0.182

Supplementary Material 3. Homing task - Straight outward paths - Final heading

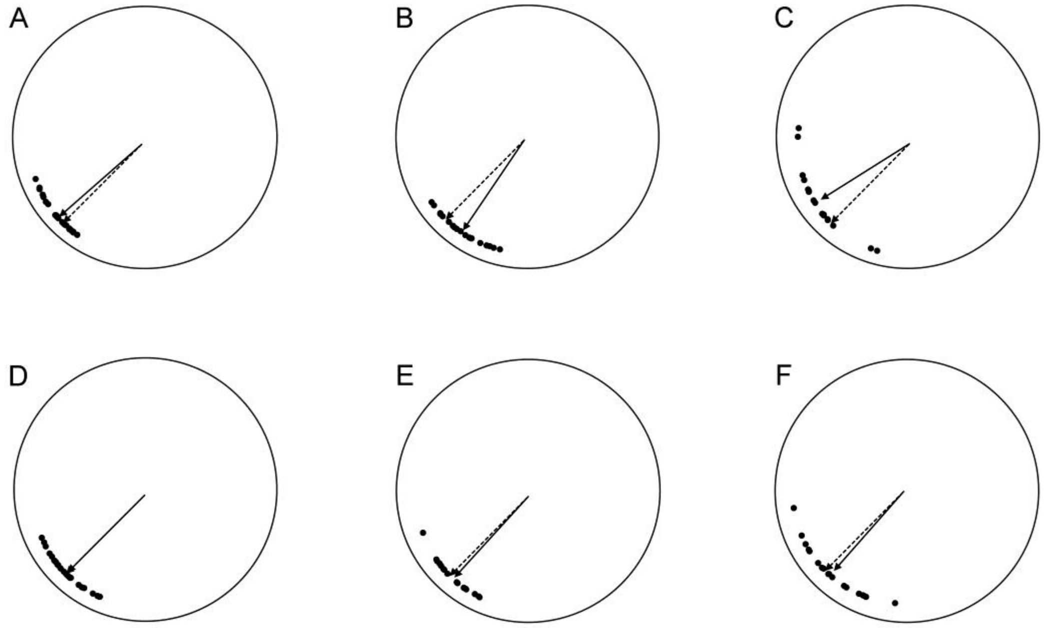

Figure 3.1 Average (solid-line arrow) and individual (dots) final heading direction at the end of the return path, following a straight 7 m outward journey in the homing task. A. TD, Session 1. B. DS, Session 1. C. WS, Session 1. D. TD, Session 2. E. DS, Session 2. F. WS, Session 2. Dashed-line arrow: perfect home direction.

Table 3.1 Within-group results: Homing task - Straight outward paths - Final heading

	TD				DS				WS			
Path	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.
Session 1	3.73°	<	5.17°	9.87°	**10.48°**	**>**	**8.42°**	12.73°	13.09°	<	14.03°	19.86°
Session 2	0.05°	<	6.09°	11.57°	2.44°	<	7.45°	11.32°	3.50°	<	13.20°	18.80°

Table 3.2 Between groups comparisons: Homing task - Straight outward paths - Final heading

	TD vs DS vs WS		TD vs DS		TD vs WS		DS vs WS	
Path	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.
Session 1	$F_{(2,62)}$ = 24.815 **p < 0.001**	$F_{(2,62)}$ = 6.293 **p = 0.003**	$F_{(1,45)}$ = 17.654 **p < 0.001**	$t_{(45)}$ = 2.304 **p = 0.026**	$F_{(1,44)}$ = 4.224 **p = 0.046**	$t_{(44)}$ = 3.423 **p = 0.001**	$F_{(1,35)}$ = 17.593 **p < 0.001**	$t_{(35)}$ = 1.338 p = 0.190
Session 2	$F_{(2,62)}$ = 0.753 p = 0.475	$F_{(2,62)}$ = 3.551 **p = 0.035**	$F_{(1,45)}$ = 0.510 p = 0.479	$t_{(45)}$ = 0.460 p = 0.648	$F_{(1,44)}$ = 0.590 p = 0.447	$t_{(44)}$ = 2.357 **p = 0.023**	$F_{(1,35)}$ = 0.040 p = 0.842	$t_{(35)}$ = 1.868 p = 0.070

Supplementary Material 4. Homing task - Angled outward paths - Initial heading

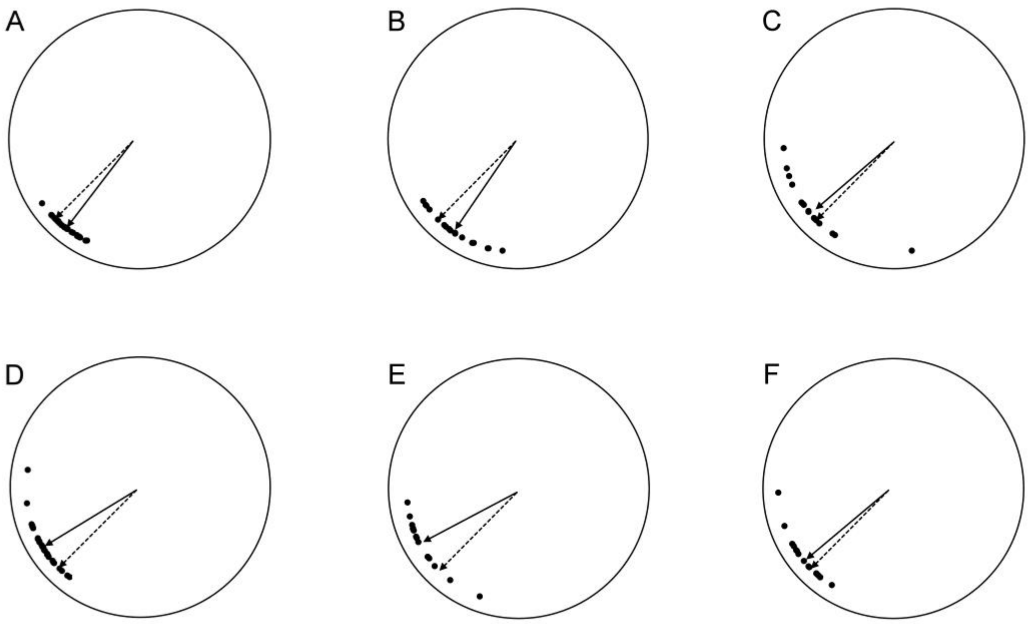

Figure 4.1 Average (solid-line arrow) and individual (dots) walking directions of participants after one meter along the return path, following a two-legged 10 m angled outward journey in the homing task. A. TD, Session 1. B. DS, Session 1. C. WS, Session 1. D. TD, Session 2. E. DS, Session 2. F. WS, Session 2. Dashed-line arrow: perfect home direction.

Table 4.1 Within-group results: Homing task - Angled outward paths - Initial heading

	TD				DS				WS			
Path	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.
Session 1	**7.52°**	>	**3.84°**	7.37°	**10.12°**	>	**9.13°**	13.76°	4.49°	<	14.01°	19.84°
Session 2	**13.51°**	>	**6.79°**	12.85°	**17.36°**	>	**9.68°**	14.54°	5.17°	<	9.17°	13.40°

Table 4.2 Between groups comparisons: Homing task - Angled outward paths - Initial heading

	TD vs DS vs WS		TD vs DS		TD vs WS		DS vs WS	
Path	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.
Session 1	$F_{(2,62)}$ = 11.353 **$p < 0.001$**	$F_{(2,62)}$ = 2.344 $p = 0.104$	$F_{(1,45)}$ = 0.669 $p = 0.418$	$t_{(45)}$ = 2.286 **$p = 0.027$**	$F_{(1,44)}$ = 7.939 **$p = 0.007$**	$t_{(44)}$ = 1.834 $p = 0.073$	$F_{(1,35)}$ = 6.340 **$p = 0.016$**	$t_{(35)}$ = 0.093 $p = 0.926$
Session 2	$F_{(2,62)}$ = 7.473 **$p = 0.001$**	$F_{(2,62)}$ = 4.356 **$p = 0.017$**	$F_{(1,45)}$ = 0.869 $p = 0.356$	$t_{(45)}$ = 1.821 $p = 0.075$	$F_{(1,44)}$ = 4.234 **$p = 0.046$**	$t_{(44)}$ = 1.330 $p = 0.190$	$F_{(1,35)}$ = 6.595 **$p = 0.015$**	$t_{(35)}$ = 3.159 **$p = 0.003$**

Description 4.3 When returning to home on the Angled path sessions, participants could also turn “the long way around” requiring an ideal turn of 225° to the left in the Angled path Session 1, or to the right in the Angled path Session 2. In Session 1, only three TD children turned left one time each (TD31, TD49, TD138), and in Session 2, only two TD children turned right one time (TD26, TD191), and one TD child turned right two times (TD167) for a total of only seven long way turns, out of 280 turns. In Session 1, only two participants with DS turned left one time (DS23, DS25), and in Session 2 only two participants with DS turned right one time each (DS19, DS25) for a total of only four long way turns, out of 190 turns. In Session 1, one participant with WS turned left five times (WS17), one participant with WS turned left four times (WS13), and two participants with WS turned left one time (WS5, WS7), and in Session 2, one participant with WS turned right three times (WS2), one participant with WS turned right two times (WS9), and two participants with WS turned right one time (WS7, WS20), for a total of 18 long way turns, out of 180 turns.

Supplementary Material 5. Homing task - Angled outward paths - Final heading

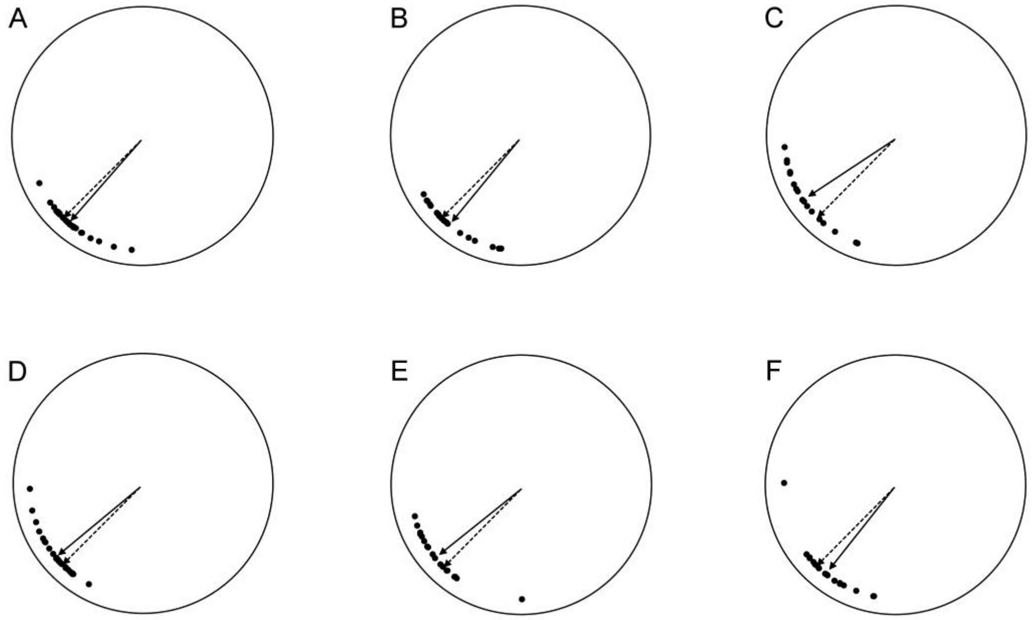

Figure 5.1 Average (solid-line arrow) and individual (dots) final heading direction at the end of the return path, following a two-legged 10 m outward journey in the homing task. A. TD, Session 1. B. DS, Session 1. C. WS, Session 1. D. TD, Session 2. E. DS, Session 2. F. WS, Session 2. Dashed-line arrow: perfect home direction.

Table 5.1 Within-group results: Homing task - Angled outward paths - Final heading

	TD				DS				WS			
Path	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.
Session 1	3.66°	<	6.56°	12.44°	5.32°	<	10.22°	15.30°	11.93°	<	13.12°	18.70°
Session 2	5.24°	<	6.89	13.03°	6.39°	<	11.09°	16.52°	6.35°	<	12.21°	17.51°

Table 5.2 Between groups comparisons: Homing task - Angled outward paths - Final heading

	TD vs DS vs WS		TD vs DS		TD vs WS		DS vs WS	
Path	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.
Session 1	$F_{(2,62)}$ = 14.003 **p < 0.001**	$F_{(2,62)}$ = 5.183 **p = 0.008**	$F_{(1,45)}$ = 0.158 p = 0.693	$t_{(45)}$ = 0.986 p = 0.330	$F_{(1,44)}$ = 10.888 **p = 0.002**	$t_{(44)}$ = 3.293 **p = 0.002**	$F_{(1,35)}$ = 8.884 **p = 0.005**	$t_{(35)}$ = 1.943 p = 0.060
Session 2	$F_{(2,62)}$ = 7.520 **p = 0.001**	$F_{(2,62)}$ = 1.021 p = 0.366	$F_{(1,45)}$ = 0.067 p = 0.797	$t_{(45)}$ = 1.342 p = 0.186	$F_{(1,44)}$ = 6.229 **p = 0.016**	$t_{(44)}$ = 1.114 p = 0.271	$F_{(1,35)}$ = 4.856 **p = 0.034**	$t_{(35)}$ = 0.098 p = 0.922

Supplementary Material 6. Cognitive mapping task - Novel paths - Initial heading

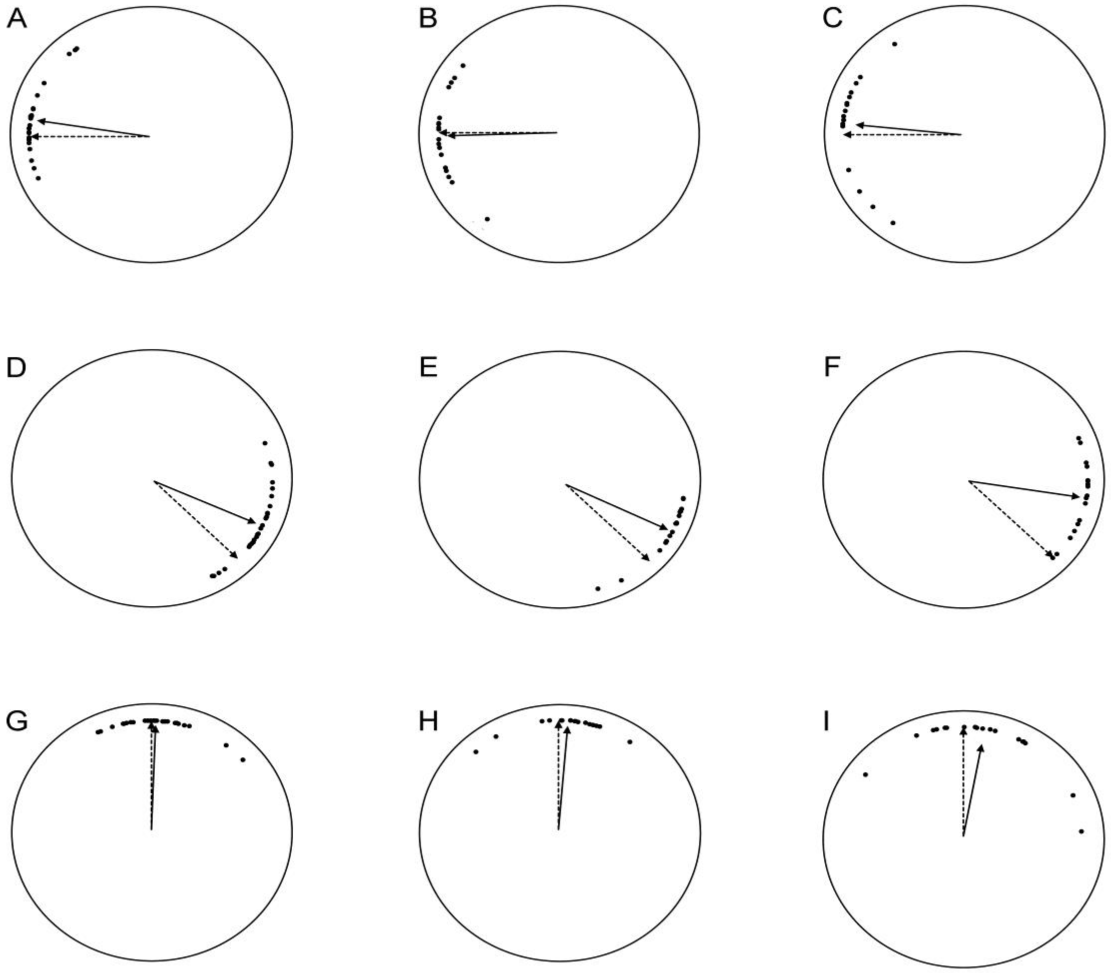

Figure 6.1.1 Average (solid-line arrow) and individual (dots) initial heading of participants after walking one meter along the path from the starting object in the cognitive mapping task. A. TD, Bench to Chair. B: DS, Bench to Chair. C: WS, Bench to Chair. D. TD, Chair to Table. E. DS, Chair to Table. F. WS, Chair to Table. G. TD, Table to Shelf. H. DS, Table to Shelf. I. WS, Table to Shelf.

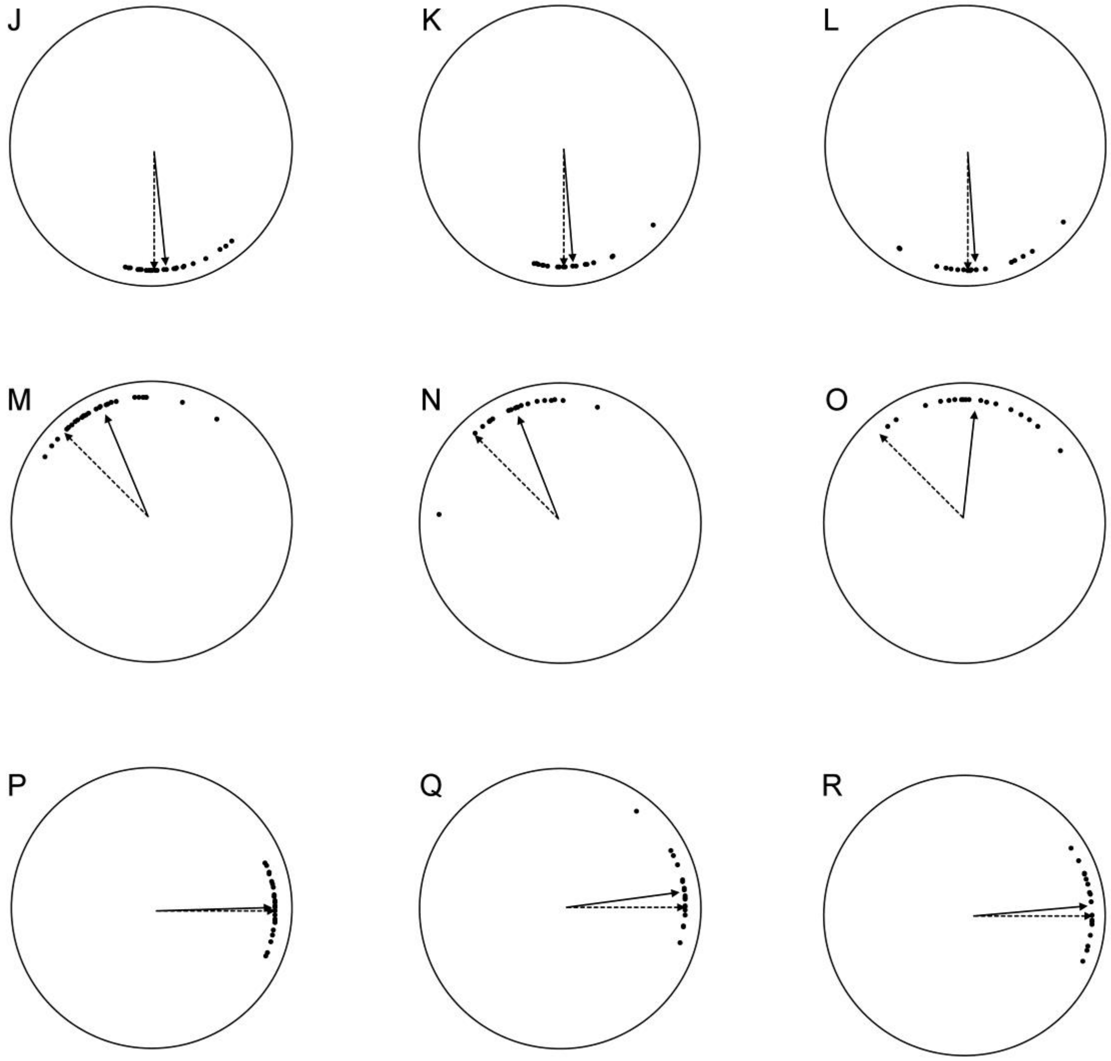

Figure 6.1.2 Average (solid-line arrow) and individual (dots) initial heading of participants after walking one meter along the path from the starting object in the cognitive mapping task. J. TD, Shelf to Table. K. DS, Shelf to Table. L. WS, Shelf to Table. M. TD, Table to Chair. N. DS, Table to Chair. O. WS, Table to Chair. P. TD, Chair to Bench. Q. DS, Chair to Bench. R. WS, Chair to Bench.

Table 6.1 Within-group results: Cognitive mapping task - Novel paths - Initial heading

	TD				DS				WS			
Path	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.	Initial Head.		99% C.I.	Ang. Dev.
B to C	8.92°	<	9.60°	17.81°	1.77°	<	14.87°	21.53°	5.90°	<	18.94°	25.71°
C to T	**20.69°**	**>**	**10.68°**	19.61°	**19.07°**	**>**	**11.01°**	16.41°	**35.88°**	**>**	**13.24°**	18.85°
T to S	2.02°	<	8.69°	16.23°	4.42°	<	11.66°	17.30°	10.49°	<	23.58°	30.56°
S to T	5.93°	<	7.64°	14.39°	4.63°	<	10.44°	15.60°	3.57°	<	15.17°	21.28°
T to C	**21.95°**	**>**	**11.39°**	20.78°	**23.92°**	**>**	**14.73°**	21.35°	**51.03°**	**>**	**17.02°**	23.51°
C to B	1.67°	<	6.56°	12.43°	7.65°	<	10.38°	15.53°	4.89°	<	10.69°	15.47°

Table 6.2 Between groups comparisons: Cognitive mapping task - Novel paths - Initial heading

	TD vs DS vs WS		TD vs DS		TD vs WS		DS vs WS	
Path	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.	Initial Head.	Ang. Dev.
B to C	$F_{(2,62)}$ = 2.714 p = 0.074	$F_{(2,62)}$ = 1.439 p = 0.245	$F_{(1,45)}$ = 3.223 p = 0.079	$t_{(45)}$ = 0.670 p = 0.507	$F_{(1,44)}$ = 0.203 p = 0.654	$t_{(44)}$ = 1.668 p = 0.102	$F_{(1,35)}$ = 0.893 p = 0.351	$t_{(35)}$ = 0.957 p = 0.345
C to T	$F_{(2,62)}$ = 9.043 **p < 0.001**	$F_{(2,62)}$ = 3.794 **p = 0.028**	$F_{(1,45)}$ = 0.083 p = 0.775	$t_{(45)}$ = 0.140 p = 0.890	$F_{(1,44)}$ = 6.396 **p = 0.015**	$t_{(44)}$ = 2.198 **p = 0.033**	$F_{(1,35)}$ = 7.866 **p = 0.008**	$t_{(35)}$ = 2.424 **p = 0.021**
T to S	$F_{(2,62)}$ = 1.549 p = 0.221	$F_{(2,62)}$ = 3.982 **p = 0.024**	$F_{(1,45)}$ = 0.220 p = 0.641	$t_{(45)}$ = 0.459 p = 0.648	$F_{(1,44)}$ = 1.355 p = 0.251	$t_{(44)}$ = 2.531 **p = 0.015**	$F_{(1,35)}$ = 0.511 p = 0.479	$t_{(35)}$ = 1.885 p = 0.068
S to T	$F_{(2,62)}$ = 0.206 p = 0.814	$F_{(2,62)}$ = 0.794 p = 0.456	$F_{(1,45)}$ = 0.082 p = 0.776	$t_{(45)}$ = 0.289 p = 0.774	$F_{(1,44)}$ = 0.189 p = 0.666	$t_{(44)}$ = 1.191 p = 0.240	$F_{(1,35)}$ = 0.028 p = 0.868	$t_{(35)}$ = 0.836 p = 0.409
T to C	$F_{(2,62)}$ = 20.568 **p < 0.001**	$F_{(2,62)}$ = 10.374 **p < 0.001**	$F_{(1,45)}$ = 0.093 p = 0.762	$t_{(45)}$ = 0.707 p = 0. 483	$F_{(1,44)}$ = 18.177 **p < 0.001**	$t_{(44)}$ = 4.161 **p < 0.001**	$F_{(1,35)}$ = 12.586 **p = 0.001**	$t_{(35)}$ = 3.377 **p = 0.002**
C to B	$F_{(2,62)}$ = 1.928 p = 0.154	$F_{(2,62)}$ = 0.606 p = 0.549	$F_{(1,45)}$ = 2.030 p = 0.161	$t_{(45)}$ = 0.643 p = 0.523	$F_{(1,44)}$ = 0.573 p = 0.453	$t_{(44)}$ = 1.265 p = 0.212	$F_{(1,35)}$ = 0.276 p = 0.603	$t_{(35)}$ = 0.346 p = 0.731

Supplementary Material 7. Cognitive mapping task - Novel paths - Final heading

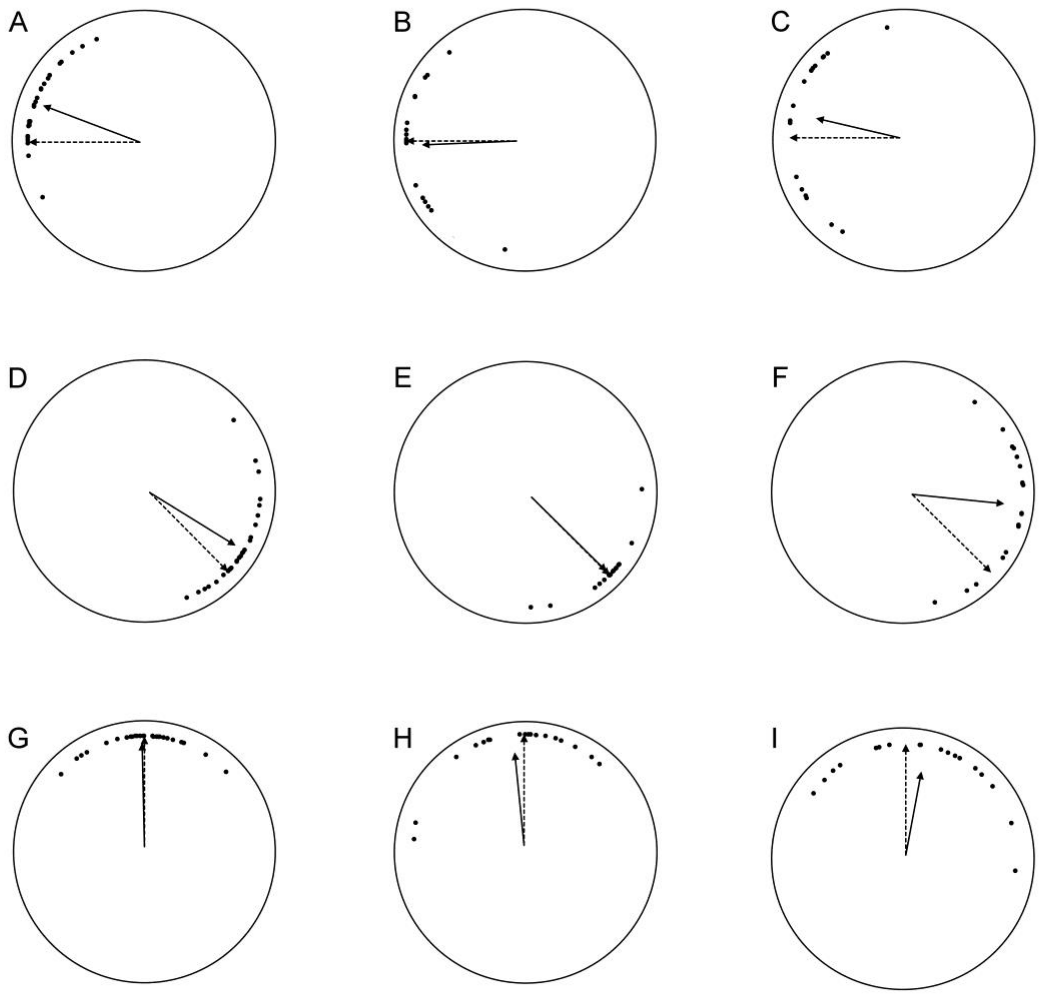

Figure 7.1.1 Average (solid-line arrow) and individual (dots) final heading (at the end of the path) in the cognitive mapping task. A. TD, Bench to Chair. B: DS, Bench to Chair. C: WS, Bench to Chair. D. TD, Chair to Table. E. DS, Chair to Table. F. WS, Chair to Table. G. TD, Table to Shelf. H. DS, Table to Shelf. I. WS, Table to Shelf.

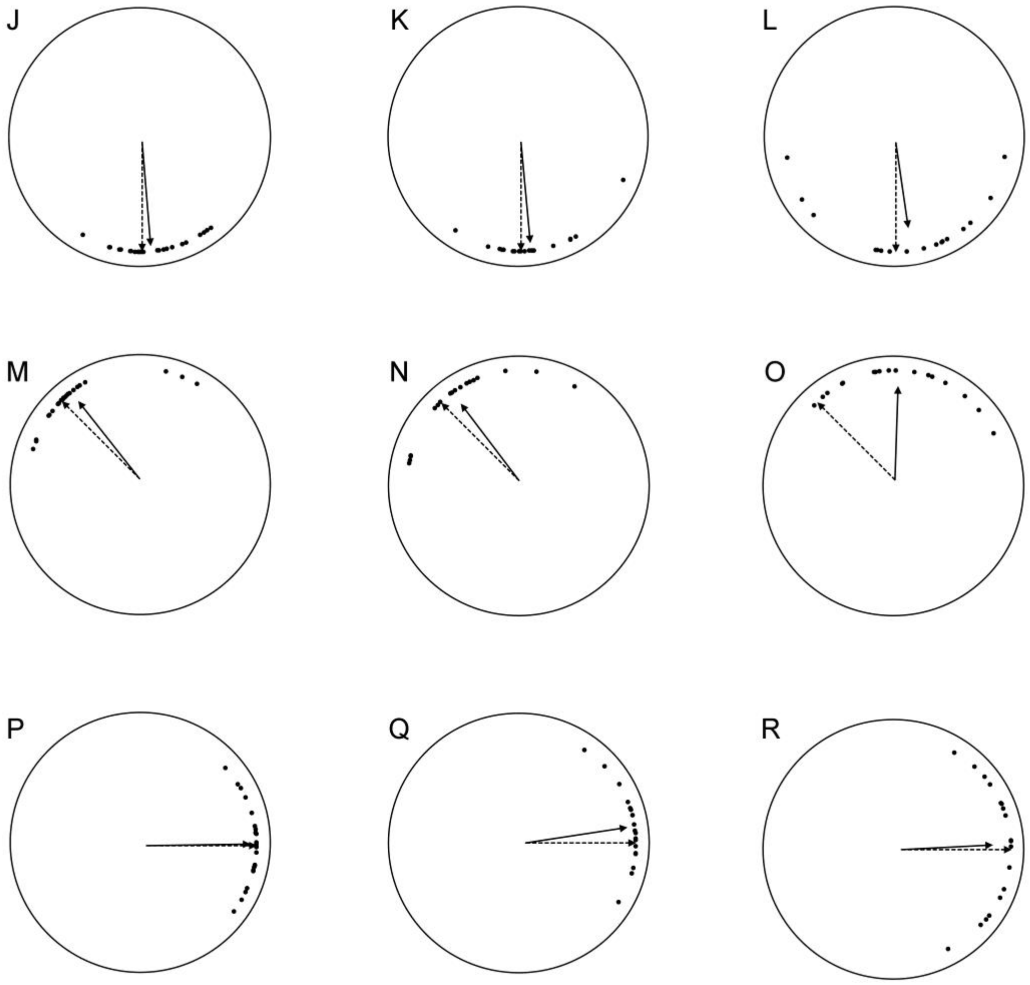

Figure 7.1.2 Average (solid-line arrow) and individual (dots) final heading (at the end of the path) in the cognitive mapping task. J. TD, Shelf to Table. K. DS, Shelf to Table. L. WS, Shelf to Table. M. TD, Table to Chair. N. DS, Table to Chair. O. WS, Table to Chair. P. TD, Chair to Bench. Q. DS, Chair to Bench. R. WS, Chair to Bench.

Table 7.1 Within-group results: Cognitive mapping task - Novel paths - Final heading

	TD				DS				WS			
Path	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.	Final Head.		99% C.I.	Ang. Dev.
B to C	**20.57°**	>	**11.57°**	21.08°	2.58°	<	22.53°	30.29°	13.28°	<	32.29°	37.94°
C to T	13.35°	<	13.41°	23.97°	0.29°	<	12.17°	17.98°	**38.85°**	>	**26.25°**	33.05°
T to S	1.11°	<	10.92°	20.01°	5.95°	<	24.09°	31.84°	10.40°	<	33.85°	39.04°
S to T	4.77°	<	9.35°	17.37°	5.14°	<	14.53°	21.09°	7.77°	<	31.64°	37.46°
T to C	6.74°	<	14.48°	25.59°	8.02°	<	20.24°	27.87°	**46.73°**	>	**23.38°**	30.36°
C to B	0.80°	<	10.04°	18.55°	8.70°	<	13.89°	20.26°	2.82°	<	26.56°	33.32°

Table 7.2 Between groups comparisons: Cognitive mapping task - Novel paths - Final heading

	TD vs DS vs WS		TD vs DS		TD vs WS		DS vs WS	
Path	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.	Final Head.	Ang. Dev.
B to C	$F_{(2,62)}$ = 6.579 **p = 0.003**	$F_{(2,62)}$ = 3.370 **p = 0.041**	$F_{(1,45)}$ = 8.726 **p = 0.005**	$t_{(45)}$ = 0.048 p = 0.962	$F_{(1,44)}$ = 0.605 p = 0.440	$t_{(44)}$ = 2.499 **p = 0.016**	$F_{(1,35)}$ = 1.722 p = 0.198	$t_{(35)}$ = 2.161 **p = 0.038**
C to T	$F_{(2,62)}$ = 19.865 **p < 0.001**	$F_{(2,62)}$ = 13.237 **p < 0.001**	$F_{(1,45)}$ = 3.849 p = 0.056	$t_{(45)}$ = 1.655 p = 0.105	$F_{(1,44)}$ = 8.249 **p = 0.006**	$t_{(44)}$ = 3.618 **p = 0.001**	$F_{(1,35)}$ = 18.099 **p < 0.001**	$t_{(35)}$ = 4.944 **p < 0.001**
T to S	$F_{(2,62)}$ = 2.448 p = 0.095	$F_{(2,62)}$ = 5.888 **p = 0.005**	$F_{(1,45)}$ = 0.370 p = 0.546	$t_{(45)}$ = 1.869 p = 0.068	$F_{(1,44)}$ = 1.488 p = 0.229	$t_{(44)}$ = 3.671 **p = 0.001**	$F_{(1,35)}$ = 1.680 p = 0.203	$t_{(35)}$ = 1.340 p = 0.189
S to T	$F_{(2,62)}$ = 0.140 p = 0.870	$F_{(2,62)}$ = 5.949 **p = 0.004**	$F_{(1,45)}$ = 0.004 p = 0.950	$t_{(45)}$ = 0.290 p = 0.773	$F_{(1,44)}$ = 0.117 p = 0.734	$t_{(44)}$ = 3.188 **p = 0.003**	$F_{(1,35)}$ = 0.062 p = 0.805	$t_{(35)}$ = 2.348 **p = 0.025**
T to C	$F_{(2,62)}$ = 23.945 **p < 0.001**	$F_{(2,62)}$ = 8.869 **p < 0.001**	$F_{(1,45)}$ = 0.024 p = 0.878	$t_{(45)}$ = 1.128 p = 0. 265	$F_{(1,44)}$ = 21.244 **p < 0.001**	$t_{(44)}$ = 3.889 **p < 0.001**	$F_{(1,35)}$ = 14.907 **p < 0.001**	$t_{(35)}$ = 2.794 **p = 0.008**
C to B	$F_{(2,62)}$ = 1.120 p = 0.308	$F_{(2,62)}$ = 5.689 **p = 0.005**	$F_{(1,45)}$ = 1.793 p = 0.187	$t_{(45)}$ = 0.670 p = 0.506	$F_{(1,44)}$ = 0.062 p = 0.804	$t_{(44)}$ = 3.284 **p = 0.002**	$F_{(1,35)}$ = 0.383 p = 0.540	$t_{(35)}$ = 2.236 **p = 0.032**

3. GENERAL DISCUSSION

3.1. Summary of my results

Spatial memory is a critical cognitive competence that is subserved by parallel learning and memory systems in the brain. My thesis research work has employed novel behavioral paradigms to investigate the basic spatial learning and memory capacities of individuals with WS and DS, and my findings have allowed me to provide unequivocal evidence concerning these state of these capacities. The first aim of my doctoral work was to assess the capacity of individuals with WS, DS and typically developing children to build allocentric and egocentric spatial representations in a real-world, controlled laboratory environment. For this aim, I tested the capacity of participants to remember one location among four potentially rewarded locations distributed in a 4 m x 4 m open-field arena. In the allocentric place learning condition, participants had to be able to learn and remember the reward location in relation to distal objects in the environment. In the egocentric response learning condition, participants had to be able to learn to find the reward by performing a fixed motor response. I found that 95% of typically developing children and 78% of participants with DS could solve the place learning task, thus showing basic allocentric capacities. In contrast, only 17% of participants with WS were capable of using a low-resolution allocentric spatial representation to learn and remember the location of one reward amongst four possible locations in the presence of visual information. For the egocentric task, whereas 72% of participants with WS and 56% of participants with DS could use a response learning strategy to learn and remember the location of one reward, only 16% of typically developing children did. These results provided answers to several questions raised by methodological issues inherent to previous studies. Moreover, my results lead to the elaboration of hypotheses regarding spatial learning strategies that may be used by individuals with WS and DS to successfully navigate in the real world, outside controlled laboratory conditions.

The second aim of my doctoral work was to characterize the capacity of individuals with WS, DS and typically developing children to use path integration to build egocentric and allocentric spatial representations in absence of vision. First, blindfolded participants were tested on their ability to return to a starting point after being led on straight and two-legged paths. Performance on this egocentric homing showed that participants could walk straight and return to their starting point when blindfolded. Second, I evaluated the capacity of these same participants to build an allocentric spatial representation without vision, in order to navigate between four objects placed in a large room. After an initial learning phase, participants were asked to walk directly to specific objects using novel paths (shortcuts), a hallmark of the capacity to create a cognitive map. In the homing task, I found that 96% of typically developing children, 84% of individuals with DS and 44% of individuals with WS could return to the starting point of the outbound journey consistently. In the cognitive mapping task, 64% of typically developing children and 74% of individuals with DS were able to take shortcuts and use never-traveled trajectories. In contrast, only one of eighteen individuals with WS demonstrated the ability to build a cognitive map, without vision, using vestibular and proprioceptive information. My findings rule out the possibility that the spatial impairments of individuals with WS arise from the integration of a corrupted signal from the dorsal visual stream. Instead, these results lead me to conclude that allocentric spatial memory capacities are impaired in the vast majority of individuals with WS, irrespective of the type of available sensory information.

3.2. Allocentric spatial memory deficits in WS

My studies showed that individuals with WS have severe allocentric spatial memory deficits, with and without vision. I used two different paradigms to assess allocentric memory in individuals with WS and typically developing children, both showing consistant results. Indeed, my findings that only one of 18 participants with WS (6%) was capable of using path integration to build a cognitive map in absence of visual information are consistent with findings in the open-field allocentric spatial memory task, which showed that only 3 of 18 participants with WS (17%) were capable of using a low-resolution allocentric spatial representation to learn and remember the location of one reward amongst four possible locations in the presence of visual information. These findings indicate that allocentric spatial memory is severely impaired in most individuals with WS, and that spatial impairments in WS are not simply due to visual impairments but are more likely due to an impaired capacity to form allocentric representations. Indeed, previous studies assessing spatial memory in WS tested spatial capacities in environments in which participants have access to visual cues, which may or may not have been associated with the movement of the participants. They showed that individuals with WS were impaired in tasks subserved by the dorsal stream (Atkinson & Braddick, 2011; Atkinson et al., 2003; Atkinson et al., 1997; Braddick et al., 2003). Moreover, neuroimaging findings in individuals with WS have reported structural and functional abnormalities in many different brain regions (Eckert et al., 2006; Menghini et al., 2011; Mobbs et al., 2007; Reiss et al., 2004), but in particular in the dorsal visual stream including the parietal and lateral occipital cortices (Bernardino et al., 2014; Meyer-Lindenberg et al., 2004; Meyer-Lindenberg et al., 2006). Thus, prior to my studies, it remained possible that impairments in the large-scale spatial capacities observed in WS derived from altered dorsal visual stream input. If true, this would imply that individuals with WS are able to use self-generated motion information to represent space in an allocentric frame of reference. It would also indicate that allocentric spatial capacities are relatively preserved in WS, and thus that the impairments previously observed in other spatial tasks were due to the reliance on altered visual stream inputs, rather than the result of abnormal processing by the hippocampus-dependent memory system. However, my cognitive mapping task, which evaluated the capacity of individuals with WS to use path integration to build allocentric spatial representations to navigate in a real-world environment without vision, revealed that cognitive mapping abilities were severely impaired in WS. In sum, the allocentric memory system is impaired in WS, irrespectively of the sensory input that is used to create the spatial representation.

My results also provide answers to several questions raised by methodological issues inherent to previous studies. As discussed in the introduction, very few real-world studies have met all the requirements necessary to unequivocally conclude that participants with WS are either able or unable to build and/or use an allocentric spatial memory representation. For example, real-world large-scale studies in WS participants have either favored (Foti et al., 2011; Smith et al., 2009) or did not preclude (Farran et al., 2010; Foti et al., 2015; Nardini et al., 2008) the use of egocentric or cue guidance strategies when the participants performed the tasks (Mandolesi et al., 2009). Plus, in essentially all previous studies, performance could be significantly influenced by impairments in other cognitive processes required to solve the task (e.g., working memory, higher order linguistic competence, mental rotation or visualization), which may confound the estimation of spatial memory impairments in individuals with WS. Therefore, there was a need to examine allocentric spatial memory of participants with

WS in controlled laboratory conditions in which the cues available to the subjects and the frame of reference in which space must be encoded are strictly controlled. In my open-field place learning task, egocentric strategies were precluded by having participants find the goal location from multiple starting locations. Indeed, participants never entered the arena through a door which they had just exited on the immediately preceding trial. Additionally, the local cue condition, in which a red cup indicated the location of the reward, allowed us to gauge participants' motivation to participate and evaluate if they understood the goal of the task. I found that all participants from the three different groups (individuals with WS, individuals with DS and typically developing children) were able to discriminate the rewarded location in presence of the local cue, in both the place learning and response learning tasks. Thus, individuals with WS (and DS) understood the objectives of the task, could initiate and sustain a selective search and could inhibit searching unrewarded locations when they knew the location of the hidden reward. Therefore, because all my participants succeeded in this control task, I am confident that my results showing severe impairments in allocentric memory in WS are not due to motivation or inhibition difficulties.

The allocentric condition of my open-field experiment also precluded the use of a cue guidance strategy to memorize the location of the reward. In laboratory testing paradigms, these visual cues may be items such as doors, windows, chairs, and wall heaters, located adjacent to or directly behind the goal, thus allowing subjects to make the visual or verbal association that the reward is ‘‘by the radiator’’ or ‘‘in line with the window’’. I showed, with my control task, that when a local cue (a red cup) indicated the location of the reward, participants with WS succeeded in finding the goal location, confirming that individuals with WS are able to use a cue guidance strategy. Therefore, it is crucial to control the proximal visual landmarks in spatial paradigms aimed at assessing allocentric memory in WS in order to avoid cofounding different strategies that may be used by the subjects to learn and memorize the location of the target. In the allocentric condition of my open-field task, the goal and the three decoy locations were identical, a white paper plate covered by an inverted white plastic cup. No coincident distinguishing visual cues were provided. Moreover, the arena was enclosed with three opaque curtains, thus eliminating the possibility to easily use visually aligned guidance cues. Thus, in my open-field allocentric place learning task, I precluded participants from using alternative strategies to find the reward location. Thus, in the allocentric spatial condition, participants could only rely only on an allocentric representation to find the goal location. Therefore, my results provide unequivocal evidence of severe allocentric spatial memory deficits in WS.

In all of my spatial tasks, individuals must move around in the environment and thus have access not only to visual information, but also to vestibular and proprioceptive information with which to create spatial representations. As discussed in the introduction, the construction of spatial representations, especially allocentric representations, is associated with the movement of an individual through its environment and integrates inputs from all of sensory modalities, not only vision (Etienne & Jeffery, 2004). Accordingly, removing vestibular and proprioceptive information decreases spatial memory performance in humans (Ruddle & Lessels, 2006). Only a few studies have investigated allocentric spatial memory in a paradigm in which participants with WS must move around (Farran et al., 2010; Foti et al., 2011; Lakusta et al., 2010; Mandolesi et al., 2009; Smith et al., 2009). However, because some aspects of their paradigms were not controlled or were not designed to directly assess allocentric spatial memory, their results could not be used to state whether allocentric spatial memory was impaired or not in WS. Whereas more studies have investigated spatial capacities in WS using virtual reality paradigms, results obtained in virtual environments may also be inconclusive because the participant’s body remains static, thus making inputs from the different sensory modalities incoherent and possibly leading to abnormal competitive interactions between sensory cues (Ravassard et al., 2013). Therefore, a failure of participants with WS and typically developing children to succeed in virtual environments cannot be considered as unequivocal evidence of the absence or impairment of spatial capacities. Similarly, the results of Nardini et al. (2008) could be interpreted as suggesting that individuals with WS may have failed some conditions of their spatial task because self-motion information was incoherent with the position of the array that participants saw. In contrast, in my open-field place learning task, I can unequivocally rule out the possibility that the observed failure of individuals with WS to form an allocentric spatial representation is due to a mismatch between visual information and proprioceptive and vestibular cues. Thus, my results provide unequivocal evidence showing that individuals with WS are incapable of using an allocentric representation, in the presence of coherent integration of visual, vestibular and proprioceptive information, to learn and remember the location of one reward amongst four potential reward locations.

Finally, my cognitive mapping task, which also assessed the capacity to create allocentric representations, tested the capacity of individuals with WS to take a shortcut in a previously explored environment, hallmark evidence for the presence of a cognitive map of the environment. However, in contrast to my open-field task, participants had only access to vestibular and proprioceptive information in order to create spatial representations. Therefore, this paradigm can serve to test the capacity of individuals with WS to form allocentric representations using only idiothetic information. First, my egocentric homing task showed that, even though they performed less well than typically developing children and individuals with DS, 44% of individuals with WS could return to the starting point of the outbound journey consistently, using vestibular and proprioceptive information. Importantly, of the 8 out of 18 individuals who passed the homing task, only 1 was passed the cognitive mapping task. This indicates that whereas about half of the individuals with WS are likely able to use vestibular and proprioceptive information in order to create egocentric spatial representations, the vast majority are unable to use vestibular and proprioceptive information to create an allocentric spatial representation. Therefore, these results complement and confirm the results of the open-filed task and lead to the conclusion that the allocentric spatial memory system is impaired in most individuals with WS.

3.3. Preserved allocentric spatial memory in DS

My results showed that allocentric spatial memory, in the presence and absence of visual input, is preserved in DS. I used two different spatial paradigms to test allocentric spatial memory in DS and the results from both tasks are coherent. Indeed, my findings that 74% of participants with DS were capable of using path integration to build a cognitive map of the four objects' locations in absence of visual information are very similar to my findings from the open-field allocentric spatial memory task showing that 78% of participants with DS were able to learn and remember the location of one reward amongst four identical locations in presence of visual information. Successful performance on both tasks depends on the ability to form and use a low-resolution allocentric spatial representation of the environment, and my findings are consistent with the view that the allocentric spatial memory system is preserved in DS. My studies complement the study of Banta Lavenex et al. (2015) who also proposed that overall individuals with DS have preserved low-resolution allocentric spatial capacities. In contrast, the authors showed that the capacity of individuals with DS to build high-resolution allocentric representations is impaired. Indeed, in their paradigm only two individuals with DS (out of 20) were able to reliably identify the other two rewarded locations located on the middle and inner arrays, which required the ability to build a high-resolution spatial representation of the environment. Overall, these results suggest that low-resolution place learning is relatively preserved in individuals with DS (e.g., as compared to TD children), whereas high-resolution place learning is more impacted (e.g., as compared to TD children).

3.4. Dissociation of allocentric and egocentric capacities in WS and DS

Individuals with WS and DS exhibited a dissociation between their allocentric place learning and egocentric response learning capacities. The performance of individuals with WS in the place learning task and cognitive mapping task was severely impaired. In contrast, individuals with WS exhibited facilitated response learning abilities, compared to typically developing children. Indeed, 13 of 18 individuals with WS performed above chance level on the response learning task, whereas only 3 of 19 typically developing children did. Although response learning emerges earlier (well before 2 years of age) than place learning in TD infants (Acredolo, 1978; Cornell & Heth, 1979; Newcombe et al., 1998; Ribordy Lambert et al., 2013), my study shows that by 4 years of age incidental response learning is extremely difficult. In contrast, individuals with DS exhibited preserved low-resolution allocentric place learning capacities, as compared to individuals with WS, and somewhat facilitated response learning capacities, as compared to TD children. With respect to response learning, specifically, when no cue indicated the location of the reward, individuals with DS exhibited a level of performance that was intermediate between those of mental age-matched TD children and typically developed adults: More individuals with DS performed above chance level (15/27; 56%) than typically developing children (3/19; 16%), and fewer individuals with DS performed above chance level than typically developed adults (17/21; 81%). The dissociation between place and response learning capacities in WS, and typically developing children is reminiscent of the dissociation shown previously in human and rodents with hippocampal or striatal lesions (Chang & Gold, 2003; Packard & McGaugh, 1996; Poldrack & Packard, 2003). Indeed, experiments carried out in rats have shown that response learning is dominant and even facilitated when the hippocampus is inactivated (Chang & Gold, 2003; Packard & McGaugh, 1996). My findings showing that both individuals with WS and individuals with DS exhibit facilitated response learning, as compared to TD children matched for mental age, suggest that impaired “hippocampus-dependent” place learning may facilitate “striatum-dependent” response learning in WS and DS.

In WS, the fact that most individuals with WS exhibit severely impaired allocentric spatial memory is consistent with a severe deficit in hippocampal function. Indeed, allocentric spatial memory has been shown to be dependent on the hippocampal formation in rodents, monkeys and humans (Banta Lavenex et al., 2006; Morris et al., 1982; O'Keefe & Nadel, 1978; Olton et al., 1978). Moreover, in WS, some aspects of hippocampal physiology, morphology and function have been shown to exhibit abnormalities (Haas et al., 2014; Meyer-Lindenberg, Mervis, & Berman, 2006; Meyer-Lindenberg et al., 2005). In DS, the majority of individuals with DS demonstrate relatively preserved low-resolution place learning capacities (similar to typically developing children, but impaired as compared to typically developed adults), and severely impaired high-resolution place learning capacities (as compared to typically developing children). These behavioral findings support the hypothesis that some specific hippocampal circuits may be particularly impacted in DS. Indeed, different functional pathways within the hippocampal formation are thought to contribute to complementary but partially dissociable spatial coordinate systems (Rolls & Kesner, 2008). A direct projection from the entorhinal cortex to CA1 is thought to be able to subserve basic allocentric spatial processing (Brun et al., 2002; Lavenex & Banta Lavenex, 2013). By contrast, imaging studies in humans, neurophysiological studies in rats, and computational models, have established that the dentate gyrus, together with its connections to CA3, subserve a process known as pattern separation, which enables the discrimination of spatial locations that are close to one another (Kesner, 2007). The fact that individuals with DS have relatively preserved low-resolution place learning capacities, but impaired high-resolution place learning capacities suggest that the function of CA1 may be relatively preserved, whereas the function of the dentate gyrus/CA3 region may be more generally and severely impaired. Indeed, although structural MRI studies have reported smaller hippocampal volumes in children (Pinter et al., 2001) and adults (Aylward et al., 1999; Raz et al., 1995) with DS, neuropathological findings suggest possibly greater abnormalities in the dentate gyrus (Contestabile et al., 2010). Taken together, my findings indicate that response learning may be more easily expressed in individuals with a variety of neurodevelopmental learning disorders associated with abnormal hippocampal function. The comparison of the performance of individuals with WS and individuals with DS leads me to further hypothesize that greater impairments in “hippocampus-dependent” place learning may be associated with greater facilitation of “striatum-dependent” response learning.

3.5. Within group variations in cognitive performance

An important point to consider is that even though a coherent pattern of cognitive functions emerges, not all individuals with the same genetic syndrome exhibit the same performance. Indeed, even though as a group, individuals with WS are impaired on allocentric spatial tasks, 3 out of 18 (17%) individuals with WS succeeded at solving the basic allocentric place learning task with vision and 1 individual out of 18 (6%) individuals with WS was able to solve the cognitive mapping task in absence of visual information. In contrast, although as a group individuals with DS exhibited relatively preserved allocentric spatial capacities, 6 out 27 (22%) participants with DS were not able to solve the allocentric place learning task and 5 out of 19 (26%) participants with DS failed to solve the cognitive mapping task in absence of visual information. Thus, individual variations exist within groups affected by the same genetic condition. In previous studies, those individual variations in neurodevelopmental disorders might have been underestimated because researchers often rely on a group’s average performance to represent the behavior of the individuals belonging to the same group. Reporting the group’s average performance (or any other single statistic) may not be sufficient and might neglect important individual variations. Therefore, in my thesis work I also reported the performance of each participant for each task, in order to present a broad view of the memory performance of individuals with WS and DS.

Only few studies in WS and DS have reported the performance of individual participants and confirmed that individual variations in cognitive performance are inherent to both WS and DS (Courbois et al., 2013; Foti et al., 2015). In most studies investigating spatial memory, when the scores of the WS or DS groups were significantly different compared to typically developing children (e.g., average number of errors, average number of correct choices, average time spent to find a reward), the authors generally stated that the individuals with WS or DS were impaired in spatial processing (Broadbent et al., 2014; Farran et al., 2010; Lakusta et al., 2010; Nardini et al., 2008; Pennington et al., 2003; Purser et al., 2015; Toffalini et al., 2018). Although this methodology may be statistically sound and commonly used in most experimental studies, it can only answer group-level questions, and often neglects individual variation. Thus, it does not reveal the level of performance, or whether individuals are capable or not to solve the task, or the variability of the performance within the same group of individuals. Indeed, it is possible that individuals with WS or DS were capable of solving a certain spatial task but not at the level of the control group. For example, they might have produced more errors throughout the task, yet they might be able to locate a reward at an above chance level, suggesting a preservation of the spatial capacity investigated. Reporting the group's average performance might also neglect whether all individuals behave the same, whether they have a similar level of performance or if there was individual variability within the group of participants, with some individuals exhibiting impaired performance and others exhibiting preserved performance equivalent to that of participants matched for mental age or even chronological age.

In this context, in my open-field place learning experiment, I first compared the number of correct first choices (i.e., choosing the reward location as their first choice upon entering the arena) between individuals with DS and control participants. When no local cue marked the reward location, as a group, individuals with DS made significantly fewer correct choices (M = 0.793) than typically developing children (M = 0.955). This gives us a first indication that, on average, individuals with DS perform less well than typically developing children. However, as mentioned, it gives no indication as to whether specific individuals with DS are able to solve the task or not; the average number of correct choices alone is not sufficient to represent how individual participants behave. Indeed, when analyzing each participants individual performance on the last 8 allocentric spatial trials, I discovered that 14 out of 27 individuals with DS exhibited perfect performance, and only 5 out of 27 individuals with DS exhibited more than 3 errors on the last 8 trials, which was our criterion for a failing performance. This analysis thus suggests that most individuals with DS exhibit very good performance and are capable of using an allocentric strategy. Thus, to further investigate the individual scores of my participants, I compared, for each individual, the number of correct first choices (visiting a rewarded location) and the number of incorrect first choices (visiting a nonrewarded location) for the last eight allocentric spatial trials to determine above chance performance. I found that 21 out of 27 individuals with DS performed the allocentric place learning task at above chance levels. This shows that the performance of this group is best described by a bimodal performance distribution, with one group consisting of the majority of individuals with DS making very few or no errors on the place learning task combined with a number of individuals that make a few errors but nonetheless perform above chance level, and a second group consisting of a minority of individuals that did not succeed on the task. Note that being able to solve the task at above chance levels does not mean that their performance is perfect, but rather that individuals with DS can build an allocentric spatial representation to find a location in an environment, even though as a group they tend to make more mistakes as compared to the control group. Limiting my analyses to the average number of correct choices made by each group, as is often done, would have led to the conclusion that individuals with DS were impaired in our allocentric spatial memory task because they performed less well than the control group. This would have ignored the fact that not all individuals within the group behave the same and that the majority of participants with DS are indeed capable of solving this place learning task. Consequently, it is critical to look at the distribution of individual scores and the relation of those scores to chance performance, in addition to the average score of the group, when investigating cognitive capacities in intellectual disability.

This issue has important clinical implications for therapists working with individuals with WS and DS. For example, when a therapist working with individuals with DS proposes to use learning strategies that a majority of persons with DS may be able to use to orient in space, s/he must be aware that whereas the proposed strategy may work for most individuals with DS, it might not work for all individuals with DS. Moreover, it emphasizes the fact that despite being affected by a neurodevelopmental disorder of the same genetic origin, cognitive profiles might vary among individuals. Thus, therapists must be aware that the cognitive profiles of individuals with WS or DS are not homogenous and careful descriptions of individual cognitive capacities are needed. Moreover, it emphasizes the fact that it is not the syndrome that necessarily characterizes each person. This is the reason why we have been using the formulation "individuals with WS" or "individuals with DS", and not WS individuals and DS individuals.

3.6. Outside the laboratory

Deficits in real-world spatial memory capacities can have a strong impact on daily life, and individuals with intellectual disabilities must frequently depend on family members or caregivers for their displacements (e.g., going to and from work, grocery shopping, and social gatherings). Consequently, individuals with intellectual disabilities are often excluded from social life and suffer from a lack of individual autonomy. Therefore, characterizing the spatial memory profile of individuals with intellectual disabilities can not only help to identify which memory processes are impaired, but more importantly can help to identify preserved spatial memory capacities. Focusing on individuals' strengths can encourage their independence and provide critical navigational skills, giving them control of their own displacements, developing their self-efficacy and raising their self-esteem. Therefore, in the next paragraphs, I will elaborate some hypotheses regarding strategies that can be used by individuals with WS and DS to successfully navigate in the natural environment in typical life situations, outside the laboratory.

It is true that navigation in the real world, outside the laboratory, is far more complex than the individual basic processes that I evaluated with my experiments. However, it was necessary to investigate these basic spatial processes before evaluating more complex behaviors. For example, when individuals learn a route in the real world, they often learn a sequence of several left and right turns in order to find their location/destination. In contrast, in my response learning task, participants had to learn that they could find the reward by performing only one fixed right or left turn. Logically, however, it is critical to investigate if the capacity to perform one simple motor response is preserved in individuals with WS and DS, before attempting to evaluate whether they can learn a sequence containing several left and right turns. Knowing which basic spatial processes are preserved or impaired in individuals with WS and DS can help to identify which more complex learning strategies these individuals might be capable of using in the real world. Thus, my results and concordant results from other experiments could be used to infer how individuals may be able to orient in the real world, outside controlled laboratory conditions.

In order to see how the results from my thesis work can help clinicians, first imagine being a therapist helping a young adult with DS. Marco lives with his parents in the city of Sion, in a house located near the train station. Marco found a part-time job in a small grocery store in the old town, north of the city. Marco can commute by foot and would be very proud to do so without his parents' help. How can you, Marco's therapist, help him to learn his way to his job and to return back home safely? In laboratory conditions, I found that most individuals with DS were capable of creating a cognitive map of the environment. Thus, Marco might be able to represent different distal landmarks of the city of Sion (e.g., a castle, a mountain, a big tree, a specific building) in relation to each other, independently of his own point of view, in order to find a location. Thus, from the first day of training with Marco, you could encourage him during his journey to work and back, to pay attention to the distal landmarks along the way: from the castles of Valère et Tourbillon, to the north hill known as Mont d'Orge, on the opposite side is Nendaz mountain, and to the west is the cathedral bell tower (Fig. 17). You could encourage Marco to think about these landmarks in relation to each other and in relation to his house and workplace: "*See, the Castle is there (pointing your finger at it), you can see it directly once you go outside your home. On this side, if you turn your head in that direction (pointing your finger to the other location), you can see the village of Nendaz. On the opposite side of Nendaz, on this side of the mountain, you can see Mont d'Orge. Look carefully at where the Castle is in relation to Mont d'Orge (point your finger back and forth between the two locations)*".

Figure 17. Representation of the distal visual landmarks that Marco can use to orient in space. From Marco's home, all the landmarks can be seen.

From time to time, Marco might want to stop for a drink with his colleagues after work. Even though Marco will not take his usual home-work itinerary, he will be able to find his way back home, since he can rely on the distal landmarks to locate himself and find the way to his home, possibly using an itinerary he has never taken before.

However, it is important for the therapist to keep in mind that not all individuals with DS have the capacity to create a cognitive map of their environment. Indeed, I found that 22% of participants were not able to learn and remember the reward location in relation to distal objects in the environment. Thus, the therapist might also teach Marco another strategy in order to help him find and remember his way to work and back home. I found that half of the individuals with DS that I tested had relatively preserved egocentric capacities in the open-field task suggesting that Marco might also be able learn at least one egocentric directional change to learn an itinerary. Moreover, another recent real-world study further showed that individuals with DS could learn more than one right or left turn to remember a route (Meneghetti et al., 2020). Even though the maximum number of moves that could be remembered by individuals with DS was not specified by Meneghetti et al. (2020), participants made on average 3.5 correct left, right or straight moves per trial. Finally, results from virtual reality paradigms are in agreement with these results and confirm that individuals with DS are capable of learning an itinerary composed of four left and right turns (Courbois et al., 2013; Farran et al., 2015). Consequently, Marco might be able to learn 3-4 sequential right or left turns in the city of Sion in order to get to work and back home. To do so, one could encourage Marco to learn the right and left turns, in combination with visual landmarks, of his home-work itinerary as such: *"walk straight until you arrive at the music store, then turn right and walk straight until the statue, then left and walk straight until the church"*.

Now imagine that you have to help his friend, Mathias, a young adult with WS. In laboratory conditions, I found that individuals with WS were not able to create a cognitive map of their environment. Thus, as Mathias' therapist, you should probably not insist that Mathias tries to use a place learning strategy since he will most likely not be able to succeed, even though I showed that there are some rare exceptions. Instead, I found that 72% of individuals with WS were able to learn an egocentric directional change to find a goal location. Results from virtual reality are consistant with this finding and suggest that most individuals with WS can learn more than one simple motor response. Indeed, Farran et al. (2015) reported that 65% of individuals with WS can learn at least one of two different routes requiring four changes of direction. Moreover, as discussed above, in environments containing visual landmarks such as the city of Sion, individuals with WS can usually rely on local environmental cues or landmarks to navigate in space (Bostelmann et al., 2017; Broadbent et al., 2015; Farran et al., 2010). Consequently, it is likely that Mathias can use proximal landmarks as beacons (i.e., buildings, statues, etc.) and might associate these cues with left and right turns. Moreover, since Farran et al. (2010) showed that verbal labeling of landmarks improved the performance of individuals with WS in route learning, you should provide clear verbal instructions such as: "*When you come out of the train station by the McDonald's, look for the church and walk towards it. When you get to the church look for the statue and then walk towards it…*". However, since Mathias will learn his way to work and back in an inflexible manner, and he will likely not be able to build a configural representation of the city of Sion, he must have a back-up plan in place in case his environment changes and he becomes lost. Mathias can be taught what to do in such situations, such as to ask a passerby for help in finding his destination or calling a caregiver for help. He could also use a mobile phone and activate his GPS to find his way to work or home, even though the ability of individuals with WS to use this strategy needs further empirical evidence.

In conclusion, when charged with helping individuals with intellectual disabilities develop autonomy, therapists must thoroughly investigate the strengths and weaknesses of each individual in order to identify which specific spatial learning processes may be more preserved or more impaired, and then adapt the specific learning strategies to that specific individual.

3.7. Conclusion

Even though individuals with WS and DS have similar mental ages, my experimental findings provide unequivocal evidence that they exhibit clearly distinct spatial memory profiles, confirming that space is not a unitary process and that it is not uniformly impacted by all neurodevelopmental disorders. I have provided experimental evidence describing the state of the most basic spatial capacities in a number of individuals with WS and DS. Overall, allocentric spatial learning is severely impacted in WS, whereas it is relatively preserved in DS. In contrast, spatial abilities subserved by egocentric learning are preserved and may even facilitated in WS and DS. My work has shown that a detailed and systematic evaluation of individual spatial memory capacities may help to infer the specific cognitive processes that may be impacted or preserved in individuals with DS or WS. Each individual's spatial cognitive profile should be defined and considered carefully when designing training paradigms to improve navigational capacities that can lead to greater autonomy, self-confidence and social inclusion.

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