

Does the Cerebellum Contribute to Human Navigation by Processing Sequential Information?

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Objective: Several authors have proposed that the cerebellum has an important role in functions of higher order as a general mode of sequence detection, independently from the nature of the information. The aim of this study was to verify whether the cerebellum mediates the processing of navigational sequential information and to determine whether it is influenced by the modality of the stimuli presentation. **Method:** We tested 12 cerebellar patients and 12 healthy age-matched participants in 2 comparable navigational tasks (Walking Corsi Test and the Magic Carpet) requiring to memorizing a sequence of spatial locations. The 2 tasks differ each other for the modality of stimuli presentation: in the Walking Corsi Test the sequence is shown by an examiner that walks on the carpet, whereas in the Magic Carpet it is shown by a computer that lights up the tiles in the sequence. We hypothesize that different mental processes are implicated between the Walking Corsi Test and the Magic Carpet. Indeed, whereas watching the examiner, who performs the sequence on the carpet, allows the patient to simulate the action mentally in the Walking Corsi Test, such simulation cannot be triggered in the Magic Carpet. **Results:** Our results showed that cerebellar patients obtained scores significantly lower than control participants only in the Magic Carpet. **Conclusions:** We interpreted the patients' performance as a specific deficit in detecting and ordering single independent stimuli as a sequence, when the maintenance of stimulus–response associations is more demanding.

General Scientific Summary

Cerebellum is involved in processing of sequential information also in spatial navigation. Patients with cerebellar pathology have a deficit in detecting and ordering single independent stimuli as a sequence, when the maintenance of stimulus–response associations is more demanding. Spatial information processing in cerebellar patients is influenced by the stimuli presentation modality.

Keywords: cerebellar diseases, spatial cognition, observation, sequencing, Walking Corsi Test

Spatial navigation is a cognitive function that can be defined as a dual process, integrating self-motion (vestibular, proprioceptive, optic flow, or motor command efference copy) and external sen-

sorimotor information (visual, olfactory, auditory, or tactile) to form an internal cognitive representation of the context in which the navigation takes place. A wide network of areas with clusters

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in the occipital, parietal, frontal and temporal lobes, especially in the parahippocampal cortex, has been described (Boccia, Nemmi, & Guariglia, 2014).

In rats and mice subcortical areas have also been identified to contribute in successful spatial navigation. In particular, studies on various strains of cerebellar mutant mice have reported spatial navigation deficits in the traditional Morris water maze paradigm, in which the animals are required to locate a hidden platform from random locations of departure (Caston, Vasseur, Delhaye-Bouchaud, & Mariani, 1997; Goodlett, Hamre, & West, 1992; Lalonde, Bensoula, & Filali, 1995; Le Marec et al., 1997; Rondi-Reig, Le Marec, Caston, & Mariani, 2002). Furthermore, it has been also described that in the Morris water maze hemisectomized rats show severe impairments in coping with spatial exploration, merely executing characteristic peripheral displacement namely, “circling” (Leggio et al., 1999; Mandolesi, Leggio, Graziano, Neri, & Petrosini, 2001; Petrosini, Leggio, & Molinari, 1998; Petrosini, Molinari, & Dell’Anna, 1996).

Some of these studies explicitly proposed that such notable impairments are linked to the inability to organize and execute complex and effective exploration behaviors (the procedural component of navigation) rather than to the failure to develop an internal map of the environment (the declarative component of navigation; Leggio et al., 1999; Mandolesi, Leggio, Spirito, & Petrosini, 2003). Burguière, Arabo, Jarlier, De Zeeuw, and Rondi-Reig (2010), consistent with Welsh et al. (2005), provided additional evidence that the cerebellar cortex underlies a basic and common process of conditioned motor response optimization, which is required when whole-body rotation responses in spatial navigation are necessary. In humans, the contribution of the cerebellum to spatial navigation remains a controversial issue (Rocheffort, Lefort, & Rondi-Reig, 2013).

Several clinical studies have confirmed the involvement of the cerebellum in spatial abilities and, in particular, in procedural learning of visuospatial sequences (Doyon et al., 1998; Gomez-Beldarrain, García-Moncó, Rubio, & Pascual-Leone, 1998; Molinari et al., 1997; Pascual-Leone et al., 1993). In 1998, Schmammann and Sherman (1998) first described the cerebellar cognitive affective syndrome (CCAS) that is characterized by a constellation of symptoms involving different affective and cognitive domains, among which is also the spatial domain. Indeed, patients with cerebellar lesions experience alterations in certain spatial domains, involving visuospatial memory and mental rotation (Malm et al., 1998; Molinari et al., 2004; Schmammann & Sherman, 1998)—cognitive processes that are important for human navigation (Nori, Grandicelli, & Giusberti, 2009; Palermo, Iaria, & Guariglia, 2008; Piccardi, Iaria, Bianchini, Zompanti, & Guariglia, 2011; Piccardi & Nori, 2011). Moreover, patients with deficits in these functions fail in navigation (Bianchini et al., 2010) and persons with excellent spatial abilities—specifically, good mental rotation—have a very good sense of direction (Verde et al., 2013).

However, despite the evidence of a cerebellar role in visuospatial domain, its specific involvement in human spatial navigation remains to be established. Studies using fMRI have reported that the cerebellum is also activated during mental and virtual navigation tasks (Ino et al., 2002; Maguire et al., 1998; Moffat, Elkins, & Resnick, 2006) and that there is functional coactivation between the cerebellum and hippocampus during spatial navigation tasks (Iglói et al., 2015). Undoubtedly, these data suggest an involve-

ment of the cerebellum in cognitive aspects of navigation and a functional interaction between the cerebellum and the hippocampus within spatial memory. Nevertheless, the specific role of the cerebellum in the declarative and procedural components of the human navigation has not been addressed, making it difficult the comparison with the animal literature. According to Rocheffort, Lefort, and Rondi-Reig (2013) “the cerebellum contributes to spatial navigation at two levels, first in processing self-motion information to build spatial representation . . . , and second in using this spatial representation to perform an optimal trajectory toward a goal” (p. 2). Thus, detecting and simulating patterns of temporally or spatially structured events, the cerebellum creates internal models that are able to generate a prediction of the sensory consequences of the intended movement (Ito, 2008). In other words, the cerebellum, at least in the motor domain, mediates implementation of forward internal models, integrating predictions about the consequences of a motor action with sensory feedback to fine-tune motor behavior (Ebner & Pasalar, 2008; Ito, 2008).

Several groups have proposed that independent of the sensory (Bower, 1997), motor (Thach, Goodkin, & Keating, 1992), and behavioral (Leggio et al., 2008) nature of the information, the sequencing of incoming sensory patterns and processing of outgoing responses are the principal functions of the cerebellar circuits (Braitenberg, Heck, & Sultan, 1997; Ivry, 1997; Mauk, Medina, Nares, & Ohyama, 2000), and a “sequence detection theory” has been advanced to describe the general operational mode of cerebellar processing (Leggio, Chiricozzi, Clausi, Tedesco, & Molinari, 2011). The spatial procedural acquisition deficit observed in hemisectomized rats has been attributed to difficulties in detecting and generating the appropriate behavioral sequences (e.g., recognition of spatial environment, putting explorative strategies into action, building a spatial map template, and so on; Petrosini, Leggio, & Molinari, 1998). Indeed, to allow an efficient spatial navigation, behavioral sequences need to be generated by integrating environmental (sensory) information and exploration (motor) acts.

In an observation-learning paradigm, when rats were allowed to observe only single procedures, but not the entire sequence of explorative steps, and then were hemisectomized, they acquired only the observed step without developing competence of the complete procedural sequence (Graziano et al., 2002). This datum highlights on one side spatial navigational as composed of behavioral units sequentially arranged, and on the other side the cerebellum as instrumental for sequential processing.

Furthermore, it has to be considered that the cerebellum has been involved in both of the main navigational strategies: the place-based strategy, which relies on allocentric representation, and the sequence-based strategy, which depends on sequential egocentric representations that are based on the memory of temporal relations between specific navigational choice points and temporal sequences of body turns (Arleo & Rondi-Reig, 2007; Iglói et al., 2015; Iglói, Zaoui, Berthoz, & Rondi-Reig, 2009; Rondi-Reig et al., 2006).

Taking into account the increasing evidence of a cerebellar role in sequence processing in different cognitive domains and the absence of clear data regarding the cerebellar processing modality in human navigation, the aim of the present study was to verify whether the cerebellum mediates the processing of sequential information also in a navigational space and determine whether

this involvement is influenced by the modality of presentation of spatial sequences. To this purpose, we measured the performance of patients affected by cerebellar damage by using two navigational tasks: the Walking Corsi test (WalCT; Piccardi et al., 2008, 2013) and the Magic Carpet, a modified electronic version of WalCT (E-WalCT; Meilinger, Berthoz, & Weiner, 2011; Perrochon et al., 2014). Both tasks are sensitive tools to measure visuospatial memory during a locomotor navigation task (Bi-anchini et al., 2010, 2014; Demichelis, Olivier, & Berthoz, 2013; Meilinger et al., 2011; Perrochon et al., 2014; Piccardi et al., 2010, 2011, 2014a), but whereas in the WalCT the sequence of places is traveled by an examiner on a carpet, in the E-WalCT it is indicated by a computer that lights up the tiles in the sequence.

Method

Participants

Twelve patients (Cb group: 4 females, 8 males; mean age 49.33 years \pm 9.10) with cerebellar lesions were recruited from the IRCCS Santa Lucia Foundation Rehabilitation Hospital. Patients were affected by focal or diffuse cerebellar damage (for details, see Table 1). No participants with focal lesions presented with any clinical or radiological evidence of extracerebellar involvement or increased intracranial pressure at the time of testing. The lesions in participants with focal cerebellar damage are characterized in Table 2 and Figure 1. Three of the 7 patients with cerebellar atrophy had a genetic diagnosis (Cb9 and Cb11: spinocerebellar ataxia type 2, Cb7: spinocerebellar ataxia type 8) and 4 presented idiopathic forms.

Each patient underwent a comprehensive neurological examination and MRI scan. Motor impairment was quantified using the International Cooperative Ataxia Rating Scale (ICARS; Trouillas et al., 1997), which ranges from 0 (*the absence of any deficit*) to 100 (*the presence of all deficits to the highest degree*) and evaluates four aspects of the symptomatology of ataxia (postural and gait disturbances, kinetic disturbances, speech disorders, and ocu-

Table 1
Clinical Characteristics of the Cerebellar Patients

Patient ID	Diagnosis	ICARS score			
		Posture & Gait	Kinetic	Speech	Oculomotor
Cb1	Ischemic	1	5	2	2
Cb2	ICA	9	7.5	2	1
Cb3	ICA	14	8	0	2
Cb4	Surgical	10	3	1	3
Cb5	Ischemic	0	0	0	0
Cb6	ICA	15	13.5	2	1
Cb7	SCA8	26	10	2	4
Cb8	ICA	7.5	18	3	3
Cb9	SCA2	10	6.5	2	1
Cb10	Ischemic	2	1	3	1
Cb11	SCA2	1	8	1	4
Cb12	Ischemic	6.5	11.5	0	2

Note. ICARS = International Cooperative Ataxia Rating Scale; Cb = patients affected by cerebellar pathologies; ICA = idiopathic cerebellar ataxia; SCA 8 = spinocerebellar ataxia type 8; SCA2 = spinocerebellar ataxia type 2.

Table 2
Lesion Characteristics in Participants with Focal Cerebellar Lesions

Participant ID	Cb1	Cb4	Cb5	Cb10	Cb12
Side	R	R	R	R	L
PICA		x	x		
AICA					
SCA	x			x	x
DCN	x	x			x
ANT	x			x	x
POST	x	x	x	x	x
Hem	x	x	x	x	x
Vermis	x				
Lobule					
I-IV				x	x
V	x			x	x
VI	x			x	x
Crus I	x		x		
Crus II		x	x		
VIIIb		x	x		
VIIIa		x	x		
VIIIb		x	x		
IX		x	x		
X					

Note. Cb = patients affected by cerebellar pathologies; R = right; L = Left; PICA = posterior inferior cerebellar artery; AICA = anterior inferior cerebellar artery; SCA = superior cerebellar artery; DCN = deep cerebellar nuclei; ANT = anterior cerebellar lobe; POST = posterior cerebellar lobe; Hem = cerebellar hemisphere.

lomotor disorders; Trouillas et al., 1997; see Table 1). All patients were able to walk without aids, and patients who were affected by a focal cerebellar lesion had a chronic clinical deficit (>3 months post onset).

A random sample of 12 healthy participants (5 females, 7 males), matched for age (51.42 years \pm 9.91), and education (12.58 years \pm 3.34) with no history of neurological disease or psychiatric disorders, formed the control group (C group). By independent samples *t* test, we confirmed that the C group did not differ from the Cb group with regard to age ($t = -0.536, p = .60$) or years of education ($t = 0.817, p = .42$).

The experimental procedures were approved by the ethical committee of IRCCS Santa Lucia Foundation. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). Written consent was obtained from each participant.

Neuropsychological Assessment

All patients were examined extensively through a neuropsychological protocol, comprising Raven's 47 progressive matrices (Raven, 1947), word fluency (Borkowsky, Benton, & Spreen, 1967), the Wisconsin Card Sorting Test (Heaton, Chelune, Talley, Kay, & Curtiss, 2000), the Stroop test (Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2002a; Golden, 1978; Venturini, Lombardo Radice, & Imperiali, 1983), forward and backward digit span (Orsini et al., 1987; Wechsler, 1945), supraspan verbal learning (Buschke & Fuld, 1974), Rey-Osterrieth figure copy and memory (Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2002b), immediate visual memory (Caltagirone et al., 1995), multiple-features target cancellation task (Marra et al., 2013), and a test of constructional apraxia

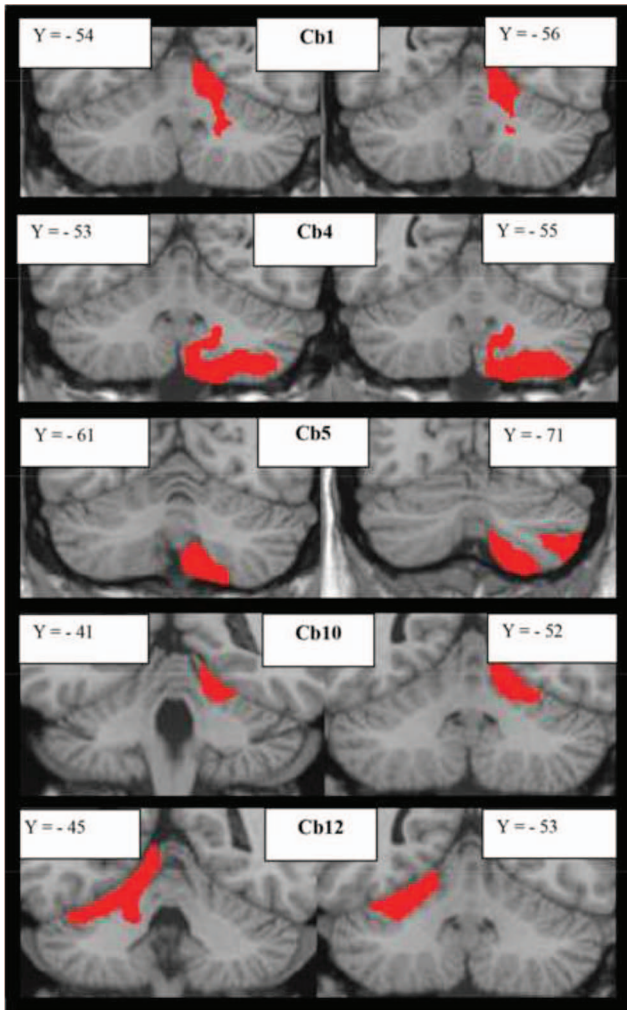


Figure 1. Participants with focal cerebellar lesions. Lesion extensions were assessed on the 3D-T1-MPRAGEs after spatial normalization and overlaid onto the coronal T1-weighted template from the MRI Atlas of the human cerebellum (Schmahmann, Dojon, Toga, Petrides, & Evans, 2000). For each participant, the lesion is presented in two representative coronal sections. See the online article for the color version of this figure.

with planning elements (Gainotti, Miceli, & Caltagirone, 1977). The results of the neuropsychological assessment are reported as standard scores in Table 3.

Experimental Testing

Spatial working memory tests. To exclude deficits in visuospatial working memory and compare the spatial span between Cb and C groups, the Corsi Block Tapping Test (CBT; Corsi, 1972) was administered to both groups.

The CBT is used extensively in experimental studies and is probably the most important neuropsychological nonverbal test that is used to assess short-term and long-term spatial memory. It is composed of nine wooden blocks (3×3 cm) that are fixed on a baseboard (30×25 cm) in a randomized array. The blocks are numbered on the examiner's side for easy identification. Following

a recently proposed administration protocol that was developed to allow one to make direct comparisons between the CBT and WalCT (Piccardi et al., 2008, 2010, 2011, 2013), the examiner taps a sequence of blocks at a rate of one block every 2 s, and the participant is invited to reproduce the sequence. Sequences increase in length until the participant fails to reproduce three of five trials of a given length. The span score is calculated, corresponding to the longest sequence that the participant is able to reproduce correctly.

Navigational tests.

WalCT. The WalCT (Piccardi et al., 2008, 2013) comprises nine black tiles (30×30 cm) that are placed on a light gray carpet (2.50×3 m), scaled up from the CBT (10:1 scale). At the edge of the carpet, a 10th tile shows the participant's position during the presentation (Figure 2a). The examiner presents each sequence of tiles by walking on the carpet and stopping on each tile for 2 s. Then, the participant must walk on the carpet and repeat the sequence.

Magic Carpet (i.e., E-WalCT). The E-WalCT, developed in Paris by the Berthoz group (Meilinger et al., 2011; Perrochon et al., 2014), has the same dimensions as the WalCT (2.50×3 m), with nine white tiles (30×30 cm) placed on the carpet in the same array. Each tile is 10-mm thick with a luminous white surface of 75×95 mm on top and 6 pressure sensors that are regularly spaced under the surface. As in the WalCT, at the edge of the carpet, a tenth tile shows the participant's position during the presentation (see Figure 2b). The tiles are connected to an electronic device that turns the luminous surface on or off and detects the sensors that are activated by a participant walking on the tiles. A laptop is connected to the device to administer each sequence at a rate of 2 s per tile and record the participant's performance—specifically, the number of correct tiles that is reached in the correct order. The sequence that is to be memorized is presented by lighting up the tiles in the sequence consecutively at 1 tile per 2 s (each tile lights up for 2 s and then shuts off before the following tile is lit). At the end of presentation, an acoustic warning signals the participant that he must reproduce the sequence that was observed by walking in the E-WalCT.

As in the CBT, in both navigational tasks, sequences increase in length until the participant fails to reproduce three of five trials of a given length. The span scores are then calculated for each task, corresponding to the longest sequence that the participant is able to reproduce correctly. The order in which the WalCT and E-WalCT were administered was counterbalanced across the participants in each group. The participants were tested individually in a quiet laboratory room with artificial lighting and without any landmarks.

Statistical Analysis

Pearson correlation coefficients between motor scores and WalCT and E-WalCT span scores were calculated to verify the relationship between motor and cognitive performance. Linear regression models were used to identify significant associations between span scores and motor scores. Student's *t* test for independent samples and the Wilcoxon signed-ranks test were used, when appropriate, to detect differences between cerebellar patients and control participants. SPSS was used to analyze the data.

Table 3
Neuropsychological Assessment

Test	Cb1	Cb2	Cb3	Cb4	Cb5	Cb6	Cb7	Cb8	Cb9	Cb10	Cb11	Cb12	Cut off ^a
Raven's 47 (progressive matrices)	32.8	—	35.8	31.8	30.8	33.8	20.8	28.8	24.2	32.3	22.8	18.8	18.96
Word Fluency	44.5	24.5	43.1	17.3	42.5	19.3	11.9	20.3	17.3	32.9	41.3	32.3	18.35
Token Test	34	32	33	33	33	33	34	33	32	33	33	33	32
Wisconsin Card Sorting Test (total errors)	138	119	108	100	119	138	108	92	10	138	138	92	<85–91
Wisconsin Card Sorting Test (perseverative errors)	138	119	108	100	138	138	119	92	10	138	138	81	<85–92
Stroop Test interference effect time	12	23.75	3.25	—	14.25	13.5	41.25	19.25	23.5	26	16.5	11.5	36.91 [†]
Stroop Test interference effect errors	.5	1.25	1	—	3.75	-1.25	.75	.25	1.25	2.5	-.25	-.25	4.23 [†]
Forward Digit Span	9	6	5	6	—	6	5	9	5	6	6	6	5
Backward Digit Span	7	4	4	5	—	6	3	5	3	3	4	3	3
Supra-span Verbal Learning (Long-term memory)	—	97	80	215	99	72	52	111	195	33	86	50	37
Supra-span Verbal Learning (non-casual recall)	—	85	60	92	78	51	18	94	68	11	63	33	3
Supra-span Verbal Learning (delay memory)	—	6.75	7.43	7.5	8	4.75	7.25	—	7.5	4.75	4.75	8.75	2.25
Rey-Osterrieth figure (memory)	—	—	—	18.75	25	15.25	5	14.5	7.75	13.5	12	12.5	9.47
Immediate Visual Memory	19.6	19.6	22.8	19.8	18.6	20.4	16	20.1	18.8	20.3	18.4	20.4	13.85
Features targets cancellation task	1	.96	.96	1	.97	1	.96	.92	.97	1	.96	1	.869
Copying drawings	11.2	8.2	10	10.7	11.2	10.5	10.4	8.4	8.7	11.3	6.6	10.6	7.18
Copying drawings with landmarks	69.8	63.8	69.9	68.1	68.8	68.6	69.1	61.1	60.1	67.9	64.5	68.5	61.85
Rey-Osterrieth figure (copy)	—	—	—	33.75	34.5	34.5	29.25	27.25	32.75	35	33.25	28.75	28.88

Note. For each patient the standardized neuropsychological scores are reported. Values in bold are pathological values. Dashes indicate “not tested.” The cut off scores are two standard deviations from the standard norm's mean. Cb = patients affected by cerebellar pathologies.

^a Pathological values are inferior to cut off levels in all tests with exception of those with [†] beside the score.

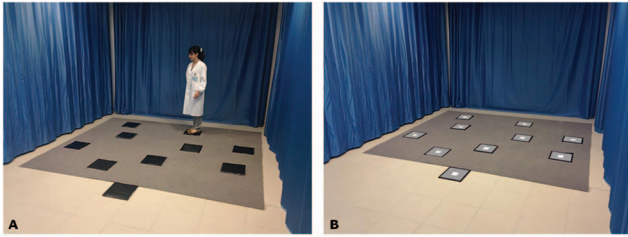


Figure 2. Experimental setting. (a) WalCT is composed of nine black tiles (30 × 30 cm) placed on a light gray carpet (2.50 × 3 m). The examiner presents each sequence of tiles by walking on the carpet and stopping on each tile for 2 s. (b) E-WalCT is composed of nine luminous tiles placed on a light gray carpet (2.50 × 3 m). The tiles light up in the sequence consecutively at one tile per 2 s. See the online article for the color version of this figure.

Results

Cerebellar patients did not present any evidence of mental decay in the general neuropsychological assessment, although pathological scores were recorded on certain tests in a few patients affected by degenerative (Cb7, Cb8, Cb9, Cb11) or focal damage (Cb10, Cb12; see Table 3 for details). To make a descriptive correlation between lesion site and pathological performances, we specifically analyzed the 2 patients with focal lesion. In particular, Cb10, whose lesion was localized in the right hemiserebellum (see Figure 1, Table 2), failed in Supraspan Verbal learning tasks (language/working memory domain), whereas Cb12, whose lesion was localized in the left hemiserebellum (see Figure 1, Table 2), failed in Wisconsin Card Sorting Test, making more perseverative errors (executive domain), Raven's 47 Progressive Matrices and Rey-Osterrieth figure copy (visuospatial domain). The lobules involved in each lesion for each patient affected by focal lesion are reported in detail in Table 2. By *t* test, there was no significant difference on the CBT between the Cb (mean ± *SD* = 5 ± 0.85) and C (mean ± *SD* = 4.83 ± 0.72) groups (*p* > .05). With regard to the navigational tasks, by Wilcoxon signed-ranks test, performance differed significantly between the Cb and C groups on the E-WalCT (*T* = 2, *Z* = 2.24, *p* = .02) but not on the WalCT (*T* = 15.5, *Z* = 0.83, *p* = .41). The E-WalCT and WalCT span scores in the Cb (E-WalCT: *M* ± *SD* = 3.91 ± 0.79; WalCT: *M* ± *SD* = 4.33 ± 1.23) and C (E-WalCT: *M* ± *SD* = 5 ± 1.13; WalCT: *M* ± *SD* = 4.75 ± 1.05) groups are reported in Figure 3. By Pearson correlation, with regard to motor and cognitive scores, there was a significant relationship between the Postural & Gait Disturbances score and both the WalCT and E-WalCT scores (WalCT: *r* = −0.78, *p* = .003; E-WalCT: *r* = −0.82, *p* = .001; see Table 4 for details). The graphic of linear regression is reported in Figure 4.

Discussion

In this study, we aimed to verify the specific function of cerebellum in processing sequential information in spatial navigation. Our results demonstrate that compared with healthy controls, the Cb group was impaired only in the E-WalCT, performing comparably with the control group on the WalCT.

When dealing with patients affected by cerebellar pathologies, it is mandatory to rule out the influence of the motor impairment on the cognitive performances. Indeed, the correlation between the

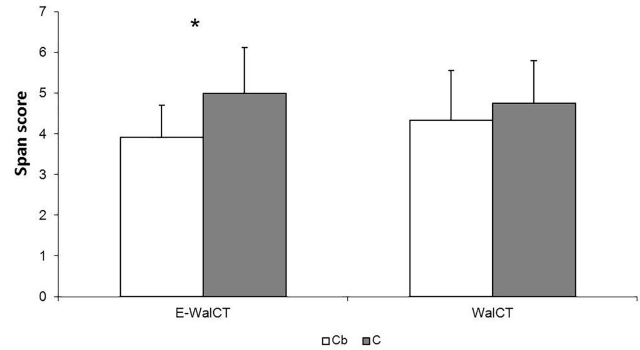


Figure 3. E-WalCT and WalCT performance. Mean span score and standard deviation of patient (Cb) and control group (C) performance on the E-WalCT and WalCT. * *p* < .05

ICARS Postural & Gait Disturbances subscale and both navigational tasks demonstrates that motor impairments affect the performances on both the WalCT and E-WalCT. However, the motor performance that is required by the participant—that is, walking on tiles on the carpet and reproducing the sequence that they have just seen—is the same in both tasks. Thus, the poor performance on the E-WalCT cannot be attributed to cerebellar ataxia. Furthermore, two recent studies (Piccardi et al., 2015; Verde et al., 2016) found that only spatial environmental interference hampers navigational working memory, in contrast to motor interference, which does not affect performance.

Even the poor performance of the Cb group on the E-WalCT cannot be ascribed to the presence of general cognitive decay. The neuropsychological assessment revealed the presence of selective and very slight impairments in some Cb patients but did not show clear evidence of general mental deterioration. Although the absence of deficits on the domains of the CCAS (Kozioł et al., 2014; Schmahmann, & Sherman, 1998) sounds unusual for cerebellar patients, this result is consistent with finding that patients who are affected by cerebellar damage do not present with intellectual deterioration (Tedesco et al., 2011). Indeed, mostly standard norms of testing do not detect cognitive impairments in cerebellar cohorts because cerebellar patients' symptoms are present in selective domains of the CCAS and very often they can be detected only when the patients are compared to matched healthy controls. Still, it has to be considered that in the present study the patients have different types of lesion with a large heterogeneity in the cerebellar damage and therefore this aspect might influence the overall outcome of the entire cerebellar cohort (Stoodley & Schmahmann, 2009, 2010).

Indeed, in our sample only one patient with right cerebellar lesion (Cb10) and one patient with left cerebellar lesion (Cb12)

Table 4
Pearson Correlation

Task	Postural & Gait	Kinetic	Dysarthria	Oculomotor
E-WalCT	−.82**	−.47	−.05	−.09
WalCT	−.78**	−.30	−.07	−.06

** *p* < .01.

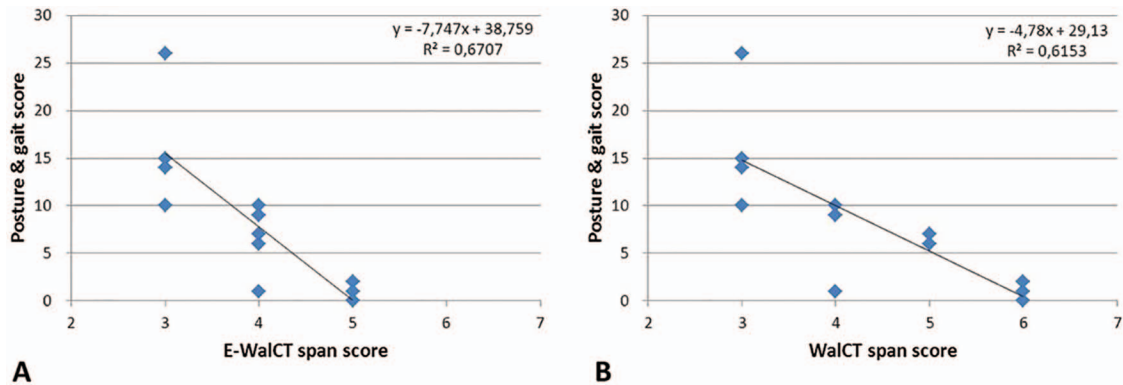


Figure 4. Linear regression of E-WalCT and WalCT performance against Motor score. Panel A: Scatter plot and curve estimation of E-WalCT span scores against Postural & Gait scores of the ICARS (Trouillas et al., 1997) in cerebellar patients. Panel B: Scatter plot and curve estimation of WalCT span scores against Postural & Gait scores of the ICARS (Trouillas et al., 1997) in cerebellar patients. See the online article for the color version of this figure.

showed scores below the cut off levels (see Table 3). Their performances were in line with the language versus visuospatial processing functions dichotomy described for right versus left hemispheric cerebellar lesions (Stoodley & Schmahmann, 2009, 2010). Furthermore, Cb10 lesion also involved right lobule VI and Cb12 lesion also involved left lobule VI and Crus I. These lobules are reported as involved respectively in language and spatial as well as executive domains in the Ale activation maps (Stoodley & Schmahmann, 2009). The deficit shown in performing the E-WalCT is not related to a deficit in spatial working memory, because in the CBT the patients did not differ from the control group. Even if several studies have demonstrated clear involvement of the cerebellum in verbal working memory (Chiricozzi, Clausi, Molinari, & Leggio, 2008; Silveri, Di Betta, Filippini, Leggio, & Molinari, 1998), there is no consensus on cerebellar function in spatial working memory (Gottwald, Wilde, Mihajlovic, & Mehdorn, 2004; Leggio et al., 2008; Tavano et al., 2007). In this vein, our results did not evidence the presence of a deficit in visuospatial working memory. Moreover, the lack of difference in performing the WalCT between the Cb and control groups suggests that also navigational working memory is not impaired in patients affected by cerebellar pathology.

Both walking tests assess a special domain of spatial memory that is specifically linked to the ability to memorize routes, which is not tapped by other tests on sequential spatial memory, such as the CBT. Walking in the environment to reproduce a sequence also requires idiothetic memory, based on vestibular and proprioceptive information relative to whole-body movements. In a recent study, Piccardi et al., (2014b) suggested that navigational working memory, as measured by the WalCT, requires proper functioning of the inner scribe of Logie's multicomponent model (Logie, 1995, 2003). This model assumes that spatial working memory is divided into two major components: a passive visual storage system (visual cache) and an active spatial rehearsal mechanism (inner scribe). The contents of the visual cache are refreshed through the operation of the active inner scribe, which is also implemented during the planning and execution of movement. Our results indicate that cerebellar patients, despite their motor impairments, are unaffected

by deficits in the inner scribe that handles navigational working memory. However, the correct functioning of the inner scribe is required also by the E-WalCT because participants have to plan and to execute movements. The only difference between the two tasks is given by the presence/absence of the examiner that show or not the sequence to reproduce. It is possible to hypothesize that this difference in administration of the two tasks may elicit differences in information processing. Indeed, taking into account that both WalCT and E-WalCT aimed at assessing working memory in a navigational space, alternative interpretations are needed to explain the difference in the performance of these patients.

These tasks share dimensions of the apparatus, testing procedure, and the method to produce the response but not the manner in which the sequence is presented. Thus, we hypothesize that differences in performance are influenced by the modality of presentation of stimuli. It has been proposed that the modality of presentation alters the strategy of solving the two tasks (e.g., see Piccardi et al., 2014c; Perrochon et al., 2014). In the WalCT, by walking into the environment, the examiner demonstrates not only the sequence of positions that the participant must remember but also the trajectory with praxis references. In contrast, in the E-WalCT, the participant does not see the examiner presenting the sequence by walking on the carpet; instead, the path is defined by a succession of tiles that light up consecutively. Thus, the WalCT and E-WalCT may elicit disparate effects and could be performed differently by the same population of patients (Perrochon et al., 2014). Previous studies have reported that in the WalCT, to remember subsequent spatial positions correctly, participants visualize the pathway on the carpet by imagining an ideal line that joins the squares that are shown by the examiner (i.e., participants memorize the various positions of the examiner as a single route; Piccardi et al., 2008).

Alternatively, in the E-WalCT, participants must memorize the tiles that are lit and perform a succession of independent simple egocentric responses that requires sequential ordering of individual events (Perrochon et al., 2014). Belmonti et al. (2015) suggested that several strategies and brain networks can be used to solve a task like the E-WalCT. These authors showed that the E-WalCT

fosters a switch from egocentric to allocentric spatial encoding, but it can also be solved, although less efficiently, by egocentric updating. These strategies rely on different brain networks, the former centered on hippocampal and prefrontal areas, the latter on posterior parietal and premotor cortices. Dissociable cortical networks have been described to be involved in recognizable and nonrecognizable biological movement (Pavlova, Lutzenberger, Sokolov, & Birbaumer, 2004).

It has been demonstrated that the left lateral cerebellum interacts with the cortical structures subserving visual processing of biological motion (Sokolov et al., 2012; i.e., in the WalCT), allowing to learn by observation how to solve the task and to understand the relations between specific actions and outcomes (Graziano et al., 2002; Leggio et al., 2000; Torriero et al., 2007). Differently, moving visual signal processing (i.e., in the E-WalCT) mainly engages vermal lobule VI and right-hemispheric lobule X and the recruitment of the cerebellum is related to the perceptual demands of the task (Baumann et al., 2015).

Despite a possible cerebellar involvement in both tasks, the fact is that patients affected by cerebellar damage are not impaired in performing the WalCT. This is in accordance with recent data that indicate an excellent recovery of visual body motion processing following neurosurgical left cerebellar lesion removal and suggest that reorganization in the cerebellum may trigger topographic shifts in the communicating cortical areas (Sokolov et al., 2014). Differently, the E-WalCT cannot rely on the neural circuitry that have been demonstrated to be involved in observational learning, that is the fronto-parietal mirror neuron system that interacts with dorsolateral prefrontal cortex and motor preparation areas during imitative learning of novel actions (Buccino et al., 2004; Iacoboni, 2005; Petrosini, 2007). All in all, considering the characteristics of the E-WalCT task and the significant involvement of the cerebellum in sequence processing (Leggio et al., 2008, 2011), we hypothesize that the Cb group performed worse than control participants on the E-WalCT, because it requires a higher load to detect and order single, independent stimuli as a sequence.

The present findings are in line with the theory proposed by Spencer and Ivry (2009). These authors hypothesized that the cerebellum works with cortical regions “to sustain representations of the stimulus-response mappings, a form of action-based working memory” (p. 1302). Indeed, the cerebellum would interact with the prefrontal and premotor cortices in order to prepare the required movements and to anticipate their sensory consequences. Its role would be particularly required when the stimulus-response translation is more demanding. In the navigational tasks a spatial mapping requires a translation from stimulus space onto response space. This translation process entails higher processing costs in the E-WalCT than in the WalCT. As a consequence, an impaired cerebellar function affects the maintenance of stimulus-response associations in working memory, preventing the sequence elaboration.

Although, this latter interpretation is interesting and may contribute to shed some light on the role of the cerebellum in human navigation, some limits should be pointed out. More specifically, it has been proposed that the left and right lobules VIIA Crus I of the cerebellum are part of two functional loops involved respectively in place-based and sequence-based navigation (Iglói et al., 2015). Unfortunately, the high heterogeneity in the cerebellar damage of our cohort of patients did not allow to analyze possible

relationships between site of cerebellar lesion and navigational performance. Future studies will require an enlargement of the sample of patients affected by cerebellar pathology to verify whether a lesion of the left or right lobules VIIA Crus I differently affects place-based and sequence-based navigation.

Furthermore, it has been proposed that the cerebellum facilitates perception by monitoring and coordinating the acquisition of sensory information and by creating “internal models” of sensory events (Baumann et al., 2015). The present study did not allow to determine whether the impaired performances of the patients with cerebellar damage during observation of a navigational task are due to deficits in analyzing sensory information or using them to mentally build an internal model of the navigational sequence. Further studies are needed to analyze these specific aspects of cerebellar function in spatial navigation.

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