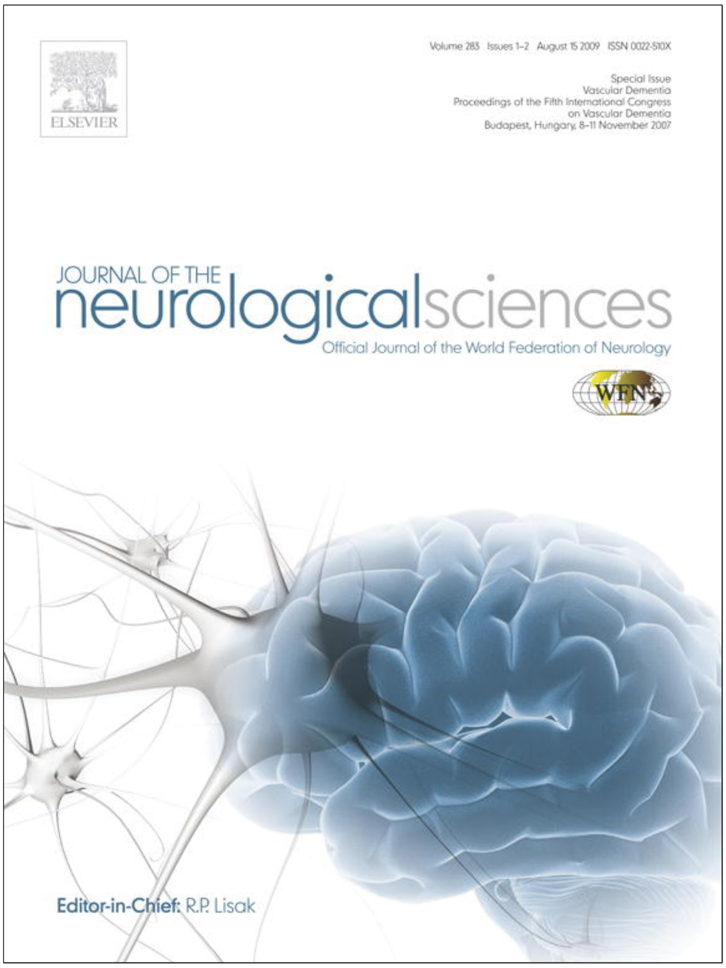
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“Real life” executive deficits in patients with focal vascular lesions affecting the cerebellum

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ABSTRACT

The aim of this study was to investigate everyday executive functioning abilities in patients with focal cerebellar lesions using an executive battery sensitive for the detection of damage to the prefrontal cortex, including a “real life” situation task. Eleven patients with focal cerebellar infarcts were studied prospectively after their injury. All subjects underwent a complete neurological, neuropsychiatric, and neuropsychological examination, as well as a specific computerized battery (Test of Attentional Performance), and an “ecological” test: the Multiple Errands Task-hospital version (MET-hv, adapted version). Significant differences were found between patients and normal controls in language and executive functions tasks. Significant differences were observed in the flexibility subscale of the Test of Attentional Performance and several subscales of the MET-hv (total amount of failures, interpretation failures, task completion score, and inefficiencies subscale). This study supports previous reports showing a pattern of cognitive abnormalities following focal cerebellar damage that includes impairments of executive function. Moreover, it suggests that the ecological test used in this investigation might be useful for the detection of deficits in real-life executive functioning among this patient population.

1. Introduction

Anatomical and clinical evidence, as well as functional neuroimaging studies, indicate that the cerebellum contributes to the processing of higher cognitive functions, such as executive functions, visuospatial functions, and linguistic abilities [1]. As well, there are well defined behavioral conditions with cerebellar anomalies such as autism [2], schizophrenia [3,4], attention deficit hyperactivity disorder [5,6], and dyslexia [7]. Different studies have shown that cerebellar stroke impairs cognition [8,9]. However, marked impairment in everyday life executive functioning, including planning and problem solving following cerebellar lesions is not often described, and experimental studies are yet to be conducted to investigate this in depth.

The processes of planning, decision-making, anticipation, judgement, and reasoning are essential in our daily life. Commonly, problems arise that need to be solved, or immediate and appropriate decisions need to be taken. To carry out these processes efficiently, it is necessary to be constantly monitoring the environment, pay attention to the required information, absorb the sought data, recover information related to past memories, assemble and manipulate it, and ultimately, relay information to other cerebral areas. It is also necessary to suppress the distribution of irrelevant information to inappropriate cerebral areas, and to inhibit certain actions in order to carry out others in a temporally co-ordinated fashion following a specific sequence. Functions resulting from a combination of said processes have been termed executive functions [10]. Assessment of executive functions under laboratory conditions can be very challenging [11] and the performance on such office-based tests fails to predict real world consequences [12]. Given the nature of the executive functions with their inherent focus on managing and coordinating cognitive and behavioral activities in response to real-world demands, ecological tests are particularly important in their assessment.

In the present study, we attempted to enhance the traditional cognitive assessment with the addition of tasks of greater complexity, applied for the first time in patients with cerebellar lesions, in order to detect specific and subtle deficits, thus increasing sensitivity for the detection of real life executive dysfunction. Overall, the purpose of this experiment was to evaluate the MET-hv (Multiple Errands Test Hospital Version), as a test that presents tasks in a “real life” situation subjected to minor casual inconveniences, in patients with focal vascular lesions affecting the cerebellum.

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2. Patients and methods

Eleven patients with cerebellar infarctions were studied prospectively at least 6 months after the injury (Table 1). Patients were matched by sex, age, and years of education with the control group. All participants gave their informed consent prior to neuropsychological assessment. Seven patients had infarctions in the territory of the posterior inferior cerebellar artery (PICA; 4 right, 1 left, 2 bilateral), three patients had had infarctions in the territory of the left superior cerebellar artery (SCA), and one had infarction in both territories, PICA and SCA. Patients who had non-cerebellar white matter hyperintensities on MRI or damage of brain regions other than the cerebellum were excluded from the study. All subjects underwent a standard examination, including complete neurological and neuropsychological examination, as well as a specific computerized battery (Test of Attentional Performance) and the MET-hv test (adapted version).

All patients completed a thorough neuropsychological battery assessing: estimated premorbid IQ with the Word Accentuation Test — Buenos Aires (WAT-BA) [13]; attention with the forward digits span task of the Weschler Memory Scale — Revised (WMS-R) [14], and the Trail Making Test Part A (TMT-A) [15]; verbal memory through the Rey auditory verbal learning test (RAVLT) [16], and the logical memory subtest of the WMS-R [14], and non-verbal memory with the Rey Complex Figure test [16]; executive function using the backward digits span test [14], part B of the Trail Making Test [15], the letters and numbers ordering test [14], and the modified version of the Wisconsin Card Sorting Test (WCST) [17]. None of the participants had a history of drug or alcohol use, head trauma, or previous neurological or psychiatric disorders. Individuals with poor schooling level were excluded, as well as subjects with anxiety or depression as assessed by formal psychiatric interview.

2.1. Specific executive battery

2.1.1. Test of Attentional Performance

This is a computerized battery [18] that includes reaction time tasks of low complexity that allow for the assessment of very specific attentional deficiencies. In the present study we assessed divided attention, inhibitory control (go–no go), working memory, and flexibility of focused attention.

2.1.2. Multiple Errands Test Hospital Version [Adapted from 19]

The purpose of this test, which is frequently administered at the hospital and its surroundings, is for participants to carry out a number of tasks simulating "real life" situations where minor inconveniences may take place. While still inside the hospital, the patient is given a card with four sets of simple tasks totaling 12 subtasks. The first set requires participants to attain 6 specific goals which include purchasing three items (a coke, a postcard and a card), collecting an envelope from the lobby, using the internal phone, and posting something to an external address. The second set involves obtaining and jotting down pieces of information (the area code of Argentine city 'Chivilcoy', the price of a menu, the last transfer shuttle to Buenos Aires). In the third set, the participant is required to phone the test proctor 20 min after the beginning of test and state the time over the phone. The final task asks the participant to inform the proctor when every task has been completed. Nine rules are clearly stated in the instruction sheet. Participant's behavior while carrying out the tasks is monitored by two observers in order to record performance. At the end of the test, each participant was prompted to rate the question: "How well do you think you did with the task?" using a 10-point scale. Errors in this test were categorized using the same definitions set by Shallice and Burgess [20], namely: 1) inefficiencies — for cases when a more effective strategy could have been applied; 2) rule breaks — for cases when a specific rule (social, or one of the nine explicitly defined within the test) was broken; 3) interpretation failures — when the requirements of a task were misunderstood; 4) task failures — when any of the twelve tasks were not fully completed; and 5) total failure — the sum of scores 1 through 4.

2.2. Statistical analysis

When variances were homogeneous (tested with Levene's test), independent *t*-test was used; all other variables were tested using a *U*

Table 2a
Results of standard neuropsychological assessment.

Neuropsychological evaluation	Patients mean (SD)	Controls mean (SD)	*p*
MMSE	29.36 (0.92)	29.45 (0.69)	n.s.
ACE	90.82 (5.15)	94.55 (4.57)	n.s.
Vocabulary subtest (WAIS III)	39.91 (6.76)	39.91 (5.65)	n.s
Raven's Progressive Matrices	30.00 (5.85)	29.82 (2.64)	n.s
Logical memory subtest (WAIS III)			
Immediate recall	22.64 (5.50)	26.27 (7.55)	n.s
Delayed recall	18.27 (6.74)	22.36 (8.94)	n.s
Rey–Osterreith Complex Figure Test (CFT)			
Immediate copy	35 (1.79)	34.36 (2.01)	n.s.
Delayed recall	19.81 (6.85)	20.36 (6.14)	n.s
Boston Naming Test	18.82 (1.17)	19.82 (0.40)	0.019
Semantic Verbal Fluency	15.36 (3.41)	21.64 (6.41)	0.021
Phonological Verbal Fluency (letter P)	12.82 (3.60)	15.73 (3.52)	n.s
Token Test abbreviated version	23.64 (1.36)	24.82 (1.40)	n.s
Pyramids and Palm tree test	50.82 (1.08)	51.00 (1.18)	n.s
Block Design abbreviated version(WAIS III)	5.55 (1.04)	5.91 (0.30)	n.s
Digit Span Forward	6 (1.41)	6.73 (0.90)	n.s
Digit Span Backward	4 (1.26)	4.18 (0.60)	n.s
Trail Making Test Part A	41.18 (15.33)	34.64 (9.96)	n.s
Trail Making Test Part B	116.82 (72.63)	83.36 (49.00)	n.s
Wisconsin Card Sorting Test Categories	4.91 (1.38)	5.82 (0.6)	0.032

Table 1
Demographic, clinical and neuroimaging findings of patients with cerebellar infarctions.

Patient	Age (years)	Gender	Handedness	Education (years)	Clinical signs	Arterial territories involved
F.C.	55	M	Right	12	Nystagmus, dysarthria, ipsilateral limb ataxia, gait ataxia, contralateral hypalgesia and thermoanesthesia.	L. SCA
M.L	35	M	Left	17	Nystagmus, ipsilateral limb ataxia and tremor. Gait ataxia.	L.SCA
M.S.C.	28	F	Right	18	Dystarthria, ipsilateral limb ataxia, axial lateropulsion.	L. SCA
N.H.	52	M	Right	12	Nystagmus, dysarthria, ipsilateral limb ataxia, truncal and gait ataxia.	L SCA + PICA
J. V.	50	M	Right	9	Nystagmus, dysarthria, ibilateral limb ataxia, truncal and gait ataxia.	L + R. PICA
J.G.	52	M	Right	12	Nystagmus, dysarthria, bilateral limb ataxia, truncal and gait ataxia.	L + R. PICA
M.C.	40	F	Right	12	Truncal ataxia.	R. PICA
M.G.	56	M	Right	12	Nystagmus, ipsilateral limb ataxia.	R. PICA
P.S.	63	M	Right	8	Nystagmus, axial lateropulsion, gait ataxia.	R. PICA
E.P.	57	M	Right	12	Nystagmus, ipsilateral limb ataxia, truncal ataxia.	L. PICA
L.B.	69	M	Right	13	Ipsilateral limb ataxia.	R. PICA

L: left. R: right. SCA: superior cerebellar artery. PICA: posterior cerebellar artery.

Table 2b
Results of specific executive battery.

Specific executive battery	Patients mean (SD)	Controls mean (SD)	p
Multiple Errands Test (MET-hv)			
Total failures	6.73 (3.04)	1.45 (1.44)	0.001
Aim interpretation	0.82 (0.60)	0.09 (0.3)	0.003
Fulfillment of tasks	1.36 (0.92)	0.09 (0.3)	0.001
Inefficiencies	2.00 (1.00)	0.09 (0.3)	0.000
Rule transgression	2.55 (2.11)	1.27 (1.49)	n.s
Test for Attentional Performance			
Divided attention	92.76 (5.9)	87.08 (9.2)	n.s
Working memory	94.09 (13.19)	98.18 (3.37)	n.s
Go–no go	96.59 (5.8)	95.45 (11.5)	n.s
Flexibility	67.08 (27.71)	89.60 (15.1)	0.045

Mann–Whitney non-parametric test. Tests that evolved throughout time were analysed using a two-way ANOVA with repeated measures, followed by simple effect tests to analyse differences between groups for each time as well as differences throughout time for each group. Correlation between variables was measured with Spearman's rank correlation coefficient.

3. Results (Tables 2a and 2b).

Groups were successfully matched for age ($t_{20}=.656$, $p>.05$) and years of education ($t_{20}=.085$, $p>.05$). There were no significant differences between patients and controls on most tests of the neuropsychological battery, with the exception of the Boston Naming Test ($U=29.0$, $p=.019$) and Semantic Verbal Fluency ($U=25.5$, $p=.021$).

On the executive battery, significant differences were found between the groups for their performance on the Wisconsin Card Sorting Test ($U=33.5$, $p=.032$), the flexibility subscale of the Test of Attentional Performance ($U=30.0$, $p=.045$), and several subscales of the MET-hv, including the total amount of failures ($U=10.0$, $p=.001$), the interpretation failure ($U=14.0$, $p=.003$), the fulfillment of tasks score ($U=14.0$, $p=.001$), and the inefficiencies subscale ($U=7.0$, $p<.001$). Noticeably, the WCST correlated significantly with the fulfillment of tasks score of the MET-hv ($r=-.474$, $p=.04$).

4. Discussion

It becomes clear from our study that patients with focal vascular lesions affecting the cerebellum are impaired on everyday executive functioning abilities. The specific executive tests employed in this study have been previously shown to be sensitive to frontal lobe dysfunction and included both a computerized battery (Test of Attentional Performance), and an "ecological" test: the MET-hv (adapted version). Patients with cerebellar lesions were impaired on their performance on the flexibility subscale of the Test of Attentional Performance. On the MET, significant differences were found on the total amount of failures, interpretation failures, inefficiencies, and on the total tasks score, suggesting timing, task planning, and organization deficits. The results of the standard neuropsychological evaluation also indicate that cerebellar patients were impaired on verbal tasks and classical tasks of executive function (WCST), in agreement with previous reports [1]. The number of items produced in the fluency tasks was extremely low for this group of patients. Deficits in fluency after cerebellar lesions have consistently been described by different authors [21,22].

Ecological validity refers to the degree to which performance on neuropsychological tests corresponds with real world performance. Although the literature investigating the ecological validity of standard neuropsychological tests of executive functioning has been inconsistent, in our study, the WCST correlated significantly with the fulfillment of tasks score of the MET-hv. The executive deficits in our cerebellar patients cannot be, therefore, due simply to motor disturbances. None of the patients had paretic limbs and if other motor impairment were present, deficits should have been seen in all executive tasks.

Within the executive functions are included diverse processes such as selective attention, decision-taking, planning, response inhibition, strategy development, and a working memory that allows information to be maintained temporarily and manipulated online during diverse cognitive demands. The prefrontal cortex (PFC) is vital for these processes, as damage to this area degrades the executive control and, as a result, impairs judgement, decision-making, and planning [23,24]. On the whole, patients with PFC lesions present normal IQ values, their long-term memory is spared, and they fail to display any perceptual or motor ability deficits. Stored or well-established information is unaffected by prefrontal damage. However, when intellectual operations call for the creation of an action program and a choice from between several alternatives, the cognitive activity of patients with frontal syndrome is severely impaired [23,25].

Although the presence of executive deficits is usually considered a sign of frontal lobe dysfunction, it should not be surprising to find impairment of executive deficits in association with cerebellar lesions. The cerebellum is an integral node in the distributed neural circuits subserving sensorimotor, cognitive, autonomic and affective processing. The cerebellar cortex is anatomically homogeneous, but different regions of the cerebellum modulate different functional domains [26–28]. There are regions of the cerebellum devoted to cognitive processing rather than to motor coordination. The cerebellum appears to be a critical modulator of prefrontal systems mediating executive function [26]. In an elegant study, Schmahmann and Pandya [28] determined the extent to which higher order corticopontine projections, the feed-forward limb of the cerebrocerebellar system, are derived from prefrontal associative cortices by injecting anterograde tracers into multiple prefrontal regions in rhesus monkeys. Moreover, Middleton and Strick [29], using retrograde transneuronal transport of herpes simplex virus type 1 (HSV1), identified neurons labeled in restricted regions of the dentate nucleus of the cerebellum from area 46 of the primate prefrontal cortex (an area involved in spatial working memory). These findings showed an anatomical substrate for the cerebellar output in higher cognitive functions. The single cerebellar infarct documented with magnetic resonance imaging and showing no other lesions remains certainly one of the best models for the study of cognitive cerebellar functions. The sudden removal of areas of functioning brain, as what occurs with strokes, may produce distant effects in functionally connected neural structures. This phenomenon is often termed diaschisis. Thus, we hypothesized that the executive deficits in our cerebellar patients could be the result of diaschisis (functional disconnection between the cerebellum and frontal cortex). An alternative interpretation is that these executive tasks that are conventionally coined as "prefrontal functions" might be functions that are distributed in a network of interconnected regions. Lesions in the cerebellum disrupt this interconnected network, thus causing the deficits [30]. We must also acknowledge the possibility that the impairments could be non-specific effects of the factors just listed, rather than resulting specifically from a deficit in the cognitive processes that subserve executive functions. Future work should include a 'disease control group', to control for the non-specific effects of illness.

Using ecological tasks in the field of neuropsychology has become an increasingly important strategy over the past decade. One of the most problematic aspects of assessment of executive functioning is that the actual testing environment typical of neuropsychological assessment may be a poorly conductive arena for eliciting executive deficits. Someone with an executive deficit may have no real world problems if his or her environment places have little demand on a particular skill. Conversely, even minor executive deficits coupled with a highly demanding environment could cause extreme functional impairment. The focus of ecological tests, today, is devoted to the detection of how well the test captures the essence of cognitive demands in the everyday environment. Shallice and Burguess [20] described the *Multiple Errands Test* (*MET*) with the purpose of capturing a range of "daily life" activities within a "real life" environment. They demonstrated that patients with frontal lobe damage may be specifically impaired in everyday situations which require planning and multitasking, despite normal performance on tests of speech, perception, memory, and executive functioning. These investigators argued that the MET captures a range of "real-life" activities within the context of a "real-life" environment. Alderman et al. [19] described a simplified MET designed for use in hospital settings. They found that subjects with acquired brain injury were found to make more errors than neurologically healthy controls. In our study, a clear pattern of failure in the MET-hv was detected, with performance in cerebellar patients characterized by a greater number of errors (interpretation failures, inefficiencies).

From a clinical perspective, our results showed that focal cerebellar lesions may impair real-life problem-solving performance and this may be reflected on impairments in daily life functioning. This poor performance is of great importance because of the strong impact it may have on daily life. The capacity to quantify the extent of executive deficits in patients with focal cerebellar lesions would greatly facilitate the design of appropriate rehabilitation strategies with the objective of improving the impact of these deficits in patients' daily living.

In summary, the present findings are in accordance with previous reports showing that there is a pattern of cognitive abnormalities after focal cerebellar damage that specifically includes impairments of executive functions. Moreover, it shows that the ecological executive test used in this investigation might be a sensitive instrument for the detection of deficits in real life executive functions in these patients. Deficits in problem solving capacity suggest a functional link between the cerebellum and the frontal lobe. Further studies in patients with cerebellar damage are necessary to investigate whether the profile of these deficits correlates with the localization of cerebellar lesions.

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