Acta Neurochir (Wien) (2008) 150: 545–550
DOI 10.1007/s00701-008-1562-5
Printed in The Netherlands

Acta Neurochirurgica

Clinical Article

Cerebellar lesions: is there a lateralisation effect on memory deficits?

S. de Ribaupierre[1,3], C. Ryser[2], J.-G. Villemure[1], S. Clarke[2]

[1] Neurosurgery Department, CHUV, Lausanne, Switzerland
[2] Neuropsychology Department, CHUV, Lausanne, Switzerland
[3] Department of Clinical Neurological Sciences, London Health Sciences Centre, University of Western Ontario, London, ON, Canada

Received 27 August 2007; Accepted 21 February 2008; Published online 30 May 2008

Summary

Background. Until recently, neurosurgeons eagerly removed cerebellar lesions without consideration of future cognitive impairment that might be caused by the resection. In children, transient cerebellar mutism after resection has lead to a diminished use of midline approaches and vermis transection, as well as reduced retraction of the cerebellar hemispheres. The role of the cerebellum in higher cognitive functions beyond coordination and motor control has recently attracted significant interest in the scientific community, and might change the neurosurgical approach to these lesions. The aim of this study was to investigate the specific effects of cerebellar lesions on memory, and to assess a possible lateralisation effect.

Methods. We studied 16 patients diagnosed with a cerebellar lesion, from January 1997 to April 2005, in the ''Centre Hospitalier Universitaire Vaudois (CHUV)'', Lausanne, Switzerland. Different neuropsychological tests assessing short term and anterograde memory, verbal and visuo-spatial modalities were performed pre-operatively.

Results. Severe memory deficits in at least one modality were identified in a majority (81%) of patients with cerebellar lesions. Only 1 patient (6%) had no memory deficit. In our series lateralisation of the lesion did not lead to a significant difference in verbal or visuo-spatial memory deficits.

Findings. These findings are consistent with findings in the literature concerning memory deficits in isolated cerebellar lesions. These can be explained by anatomical pathways. However, the cross-lateralisation theory cannot be demonstrated in our series. The high percentage of patients with a cerebellar lesion who demonstrate memory deficits should lead us to assess memory in all patients with cerebellar lesions.

Keywords: Cerebellum; cognitive functions; memory.

Introduction

In contrast to the resection of a lesion in an eloquent supratentorial area, plans for resection of an infratentorial lesion do not generally take into account the possibility of disrupting higher cognitive functions. Since cerebellar mutism is more often encountered in children than in adults, midline approaches with splitting of the vermis have become progressively less popular with paediatric neurosurgeons. Surgeons actively attempt to avoid the cerebellar nuclei in order to minimise the occurrence of cerebellar syndromes with coordination problems, dysarthria, ataxia and dysmetria but do not consider preserving the cerebellar hemispheres to minimise deficits of higher cognitive function. Even though the cerebellum was not considered an eloquent area at first, different researchers have proved the role of the cerebellum in different cognitive functions. At first, with

Correspondence: Sandrine de Ribaupierre, Departments of Neurosurgery and Clinical Neurological Sciences, Victoria Campus – Rm E6 320, 800 Commissioners Rd E, London, Ontario N6A 5W9, Canada.
e-mail: s_derib@hotmail.com

the concept of diaschisis, different studies demonstrated the implication of the cerebellum in different cognitive tasks [2, 7, 15, 16, 29]. Lesional and functional studies have also demonstrated the role sustained by the cerebellum in cognition [1, 9–12, 17, 21, 25, 31, 37, 41], and their results are supported by anatomical animal studies [24, 32–34].

Cognitive deficits have been described following the diagnosis of pure cerebellar lesions [17, 21, 37]. The systematic examination of patients with damage limited to the cerebellum revealed deficits in executive functions, memory, spatial cognition, and language, as well as personality and affective changes, which have been proposed to be part of the ''cerebellar cognitive affective'' syndrome [17, 30, 36, 41]. While some studies showed a crossed lateralisation effect with verbal deficits in right-sided [37] and non-verbal deficits in left-sided cerebellar lesions [19], other studies displayed global dysfunction [30] or a lack of lateralisation [31], while others showed a significant increase in cognitive impairments in right cerebellar lesions in right handed patients as compared to left sided lesions [21].

The aim of this study was to investigate the specific effects of cerebellar lesions on memory and to assess a possible lateralisation effect.

Material and methods

We reviewed all adult patients (>18 years old) admitted between January 1997 and April 2005 to the Neurosurgery Department of the University Hospital (CHUV, Lausanne, Switzerland) with cerebellar tumours. The patients preceding February 2002 were retrospectively analysed and those admitted from February 2002 to April 2005 were reviewed prospectively.

Initially, 89 patients were identified. Those with underlying pathology which might lead to cognitive dysfunction, such as a history of chronic systemic hypertension, hydrocephalus, supratentorial lesions, and alcohol abuse were excluded. None of the patients had a history of depression or needed to be treated for this condition in the follow-up period. The lack of detailed medical or neuropsychological data also resulted in patient exclusion. As we were interested in the ''crossed-lateralisation'' effect, only hemispheric cerebellar lesions, either intra-axial or extra-axial, with a mass effect on the cerebellar hemisphere were included; cerebellar midline lesions (fourth ventricle or vermis) were discarded. For the reason regarding on certainty of the dominant hemisphere, another two patients who were not right-handed (one was left-handed, the other ambidextrous) were excluded.

Sixteen patients were eventually studied (age range = 18 to 72 years old; mean age = 47 years; Table 1). There were 11 men and 5 women, all right-handed. Eleven patients had right cerebellar hemispheric lesions, while 5 had left-sided lesions. There were 5 metastases, 3 haemangiomas, 2 meningiomas, 2 pilocytic astrocytomas, 2 medulloblastomas (both were exophytic, lateralised and growing into the ponto-cerebellar angle), 1 glioblastoma, and 1 cavernous angioma.

Table 1. *Patient population*

	Age (years)	Gender	Side of lesion	Type of lesion	VSTM	VSSTM	AVM	AVSM
1	45	M	R	haemangioblastoma	L	N	D	D*
2	63	M	R	haemangioblastoma	D	D	N	N
3	61	M	R	metastasis	N	N	D	D
4	49	F	R	metastasis	L		D	
5	18	M	R	pilocytic astrocytoma	N	D	N	N
6	57	M	R	meningioma	N	N	D	N
7	72	F	R	glioblastoma	N	D	N	N*
8	25	M	R	medulloblastoma	N		D	
9	49	M	R	metastasis	L	N	L	N
10	67	F	R	metastasis	N		L	
11	36	M	R	pilocytic astrocytoma	N			N*
12	52	M	L	medulloblastoma	N	N	D	D
13	47	F	L	cavernous angioma	D	N	D	N*
14	31	M	L	haemangioblastoma	N	N	N	D
15	52	F	L	meningioma	N	N	D	N
16	39	M	L	metastasis	N		D	D*

Patients included in this study and their performance in verbal (VSTM) and visuo-spatial (VSSTM) short term memory as well as anterograde verbal (AVM) and visuo-spatial memory (AVSM). * Indicates the patients who had the faces/landscapes recurrent images series.
M Male, *F* female, *R* right, *L* left *N* normal, *D* deficient (<10 percentile), *L* at lower limit of normal performance (10–20 percentile). Patient 1 (Fig. 2), patient 16 (Fig. 3) and patient 12 (Fig. 4) are illustrated.

All patients had a pre-operative assessment followed by 1 or 2 post-operative assessments, consisting of a global neuropsychological assessment which included (language (spontaneity, repetition, fluency, comprehension) writing and reading skills, calculations, construction and ideo-motor praxias, gnosias, executive tasks, verbal and non-verbal memory and a neurological examination.

Short-term memory was assessed by the Digit Span Test [5, 26, 28, 38, 42] for verbal modality and the Corsi Block-Tapping Test [39, 40] for visuo-spatial modality. Anterograde verbal memory was tested either with a 15 word list (Clapared-Rey) [6, 8, 28] or with a recurrent word series. Visuo-spatial memory was tested either with the complex figures of Rey (11 patients) [3, 14, 28], or with faces/landscapes recurrent images series (5 patients) [4, 13, 28]. Patient scores were compared to the normal population (adjusted for age and gender) and those equal to the mean ± 2 standard deviations (SD) were graded as normal performance. Performance between the 10 and 20th percentile was considered the limit of normal performance. Lower performance ($<10^{th}$ percentile) was considered a severe deficit.

Results

Thirteen patients (81%) presented with severe memory deficits (percentile ≤ 10) in at least one of the tasks and an additional two patients (13%) scored at the lower limit of normal (percentile 10–20). Only 1 patient (6%) had no memory deficits. The deficits were either isolated or associated with executive dysfunction, but none of the patients had global cognitive dysfunction.

The laterality of the lesion did not influence verbal short term memory scores, as 9% of patients (1/11) with right-sided and 20% of patients (1/5) with left-sided cerebellar lesions were deficient in verbal short term memory ($p = 0.55$). Visuo-spatial short term memory was deficient in 43% of patients (3/7) with right-sided lesions and in none of the patients with left-sided lesions ($p = 0.16$). Therefore, 28% of patients (3/11) with right-sided and 20% of patients (1/5) with left-sided cerebellar lesions ($p = 0.74$) had a deficit in short term memory (either verbal or visual). A combined severe verbal and visuo-spatial short term memory deficit was found in 1 patient (9%) with a right-sided cerebellar lesion.

Anterograde memory was more often affected than short-term memory. In patients with right-sided cerebellar lesions, anterograde verbal memory was deficient in 50% (5/10) while it was affected in 80% of patients (4/5) with left-sided lesions ($p = 0.28$). Anterograde visuo-spatial memory was deficient in 25% of patients (2/8) with a right-sided cerebellar lesion and 60% of patients (3/5) with a left sided lesion ($p = 0.23$). Deficits in either verbal or visuo-spatial anterograde memory were present in 45% of patients (5/11) with right-sided but 100% (5/5) of patients with left-sided lesions ($p = 0.05$). A combined verbal and visuo-spatial anterograde memory deficit was found in 18% of patients (2/11) with right-sided and 40% (2/5) of patients with left-sided lesions ($p = 0.36$).

Combined short term and anterograde severe memory deficits were found in one patient.

In the results previously described we only included the severe memory deficits. If the moderate deficits were also included, the number of patients presenting with a deficit would be even more striking. 31% of the patients had a verbal short term memory deficit (5/16), 27% a visuo-spatial short term memory deficit (3/11), 73% a verbal anterograde memory deficit (11/15), and 38% a visuo-spatial anterograde memory deficit (5/13).

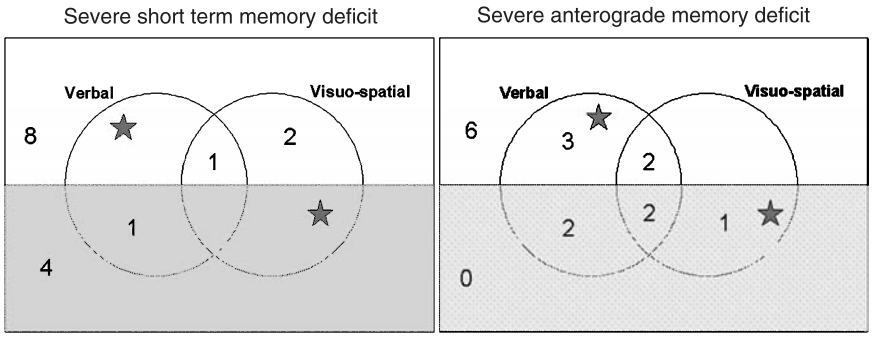

Fig. 1. Distribution of short-term (*left panel*) and anterograde (*right panel*) memory deficits on the function of the side of the cerebellar lesion (*white box* right sided lesions, *grey box* left sided lesions). Numbers written in the circles indicate the number of patients with severe deficits in the verbal or/and visuo-spatial domains, respectively. Numbers outside the circles indicate patients without deficits. A *star* indicates domains where most deficits would be expected if cross-lateralisation for memory was present, i.e., if verbal deficits occurred with right side and visuo-spatial deficits with left side cerebellar lesions

Twenty-five percent (4/16) present had both a short term and an anterograde memory deficit, while 69% (11/20) presented with one of the two deficits, only one patient having no deficit at all.

Fig. 2. Patient 1: T2-axial sequence with a predominantly cystic right hemispheric cerebellar lesion (haemangioblastoma) with minimal mass effect on the midline structures. This patient had severe deficits in anterograde verbal and visuo-spatial memory

Fig. 3. Patient 16: CT-head with contrast revealing a contrast enhancing lesion (metastasis) in the lateral portion of the left cerebellar hemisphere with moderated mass effect on the midline structures. This patient had severe deficits in anterograde verbal and visuo-spatial memory

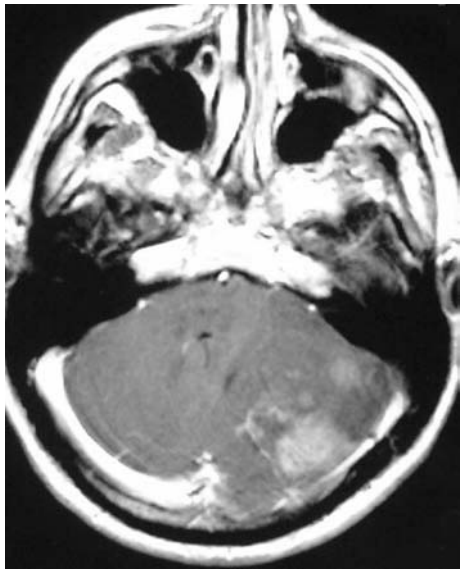

Fig. 4. Patient 12: Axial T1 sequence with gadolinium, showing a heterogeneous lesion situated in the lateral portion of the left cerebellum (exophytic medulloblastoma) with moderate mass effect on the midline structures. This lesion was associated with severe deficits in anterograde verbal and visuo-spatial memory

Discussion

As previously demonstrated in the literature by case reports [30, 37, 43] or series [17, 19, 31], the cerebellum seems to have a role in higher cognitive functions. The high incidence of memory deficits in our series provides more evidence for this function. None of the patients of the series complained of depression or were treated before or afterwards for symptoms of depression. However, depression was not actively searched for with a formal depression assessment in this series. It is well known that severe depression might affect cognitive functions such as attention and memory [22, 27]. It is controversial whether depression impacts on a wide range of neuro-cognitive parameters [27] or whether it affects memory predominantly. Studies evaluating memory among those with moderate to severe depression, reported minimal changes in memory performance compared to non-depressed patients [22]. Therefore even though we cannot formally rule out that some kind of depressive disorder might have affected our results, we tend to believe that the specific findings discussed here are due to the cerebellar lesion.

The underlying pathophysiology of such deficits can be derived from anatomical evidence from animal studies which also support cerebellar involvement in cognition, such as the cerebello-frontal and cerebello-parietal loops [23, 24, 34], and connections between the medial

mamillary bodies and the deep layers of the superior colliculus within the cerebellum [18]. The existence of a cortico-cerebellar loop, consisting of crossed projections from the frontal, posterior parietal, superior temporal and limbic cortex to the pontine nuclei, also strengthens this theory [35]. The uncrossed ponto-cerebellar projections, crossed cerebello-thalamic and thalamo-cortical pathways form a feedback loop, which involve not only the sensori-motor areas but also the fronto-parietal associative cortex [33]. In humans, activation studies such as PET and fMRI have demonstrated cerebellar activation, predominantly on the right, in verbal anterograde memory tasks [1, 9–11, 20], in addition to the left supramarginal gyrus and Broca's area.

Even though cross lateralisation has been described, and there is evidence of anatomical crossed projections as well as crossed activations, we were not able to find any significant differences in the type of memory affected with regard to the side of the lesion. The only result tending to a significant difference was the incidence of anterograde memory deficits between right-sided and left-sided lesions (63% of all, 45% of right-sided lesions, and 100% of left-sided lesions, $p = 0.05$). The incidence of short-term memory deficits (25% in all; 28% of right-sided and 20% of left-sided, $p = 0.74$) was not significantly different.

Consistent with other studies, we observed several examples of right cerebellar lesions (3) associated with a selective verbal memory deficit, and one patient with a left cerebellar lesion associated with a selective visuo-spatial memory deficit. However, we also observed two patients with right-sided lesions and selective visuo-spatial deficits, and 2 patients with left-sided lesions who were affected by verbal deficits. The lack of right-verbal and left-visuo-spatial association was more evident for short term memory than for anterograde memory. In the literature, some studies have shown a cross-lateralisation effect [17, 19, 37], but others such as in Ravizza *et al.* [31] described verbal working memory deficits with either right or left-sided lesions. Gottwald *et al.* [17] observed a partial effect, in which patients with right-sided lesions had more deficits than those with left-sided lesions. A case report of a visuo-spatial deficit in a patient with a right-sided cerebellar lesion has also been described [43].

Conclusion

Our study confirms that memory deficits can be seen in isolated cerebellar lesions. As previously demonstrated in the literature by case reports [30, 37, 43] or series [17, 19, 21, 31], the high incidence of memory deficits in patients with cerebellar lesions proves that the cerebellum functions in higher cognition tasks. Patients with cerebellar lesions should have a neuropsychological assessment to evaluate their memory pre-operatively, and might benefit from post-operative assessment and rehabilitation.

Our data does not support the cerebellar cross lateralisation view, which has been described and demonstrated in other studies. We were not able to find significant differences between right and left-sided lesions in the incidence of either anterograde or short-term memory deficits.

References

1. Andreasen NC, O'Leary DS, Paradiso S, Cizadlo T, Arndt S, Watkins GL, Ponto LL, Hichwa RD (1999) The cerebellum plays a role in conscious episodic memory retrieval. Hum Brain Mapp 8(4): 226–234
2. Barker WW, Yoshii F, Loewenstein DA, Chang JY, Apicella A, Pascal S, Boothe TE, Ginsberg MD, Duara R (1991) Cerebro-cerebellar relationship during behavioral activation: a PET study. J Cereb Blood Flow Metab 11(1): 48–54
3. Bennett-Levy J (1984) Determinants of performance on the Rey-Osterrieth Complex Figure Test: an analysis, and a new technique for single-case assessment. Br J Clin Psychol 23(Pt 2): 109–119
4. Benton AL (1980) The neuropsychology of facial recognition. Am Psychol 35(2): 176–186
5. Blackburn HL, Benton AL (1957) Revised administration and scoring of the digit span test. J Consult Psychol 21(2): 139–143
6. Boake C (2000) Edouard Claparede and the auditory verbal learning test. J Clin Exp Neuropsyc 22(2): 286–292
7. Boni S, Valle G, Cioffi RP, Bonetti MG, Perrone E, Tofani A, Maini CL (1992) Crossed cerebello-cerebral diaschisis: a SPECT study. Nucl Med Commun 13(11): 824–831
8. Boone KB, Salazar X, Lu P, Warner-Chacon K, Razani J (2002) The Rey 15-item recognition trial: a technique to enhance sensitivity of the Rey 15-item memorisation test. J Clin Exp Neuropsyc 24(5): 561–573
9. Cabeza R, Nyberg L (2000) Imaging cognition II: an empirical review of 25 PET and fMRI studies. J Cognitive Neurosci 12(1): 1–47
10. Chen SH, Desmond JE (2005) Cerebro-cerebellar networks during articulatory rehearsal and verbal working memory tasks. Neuroimage 24(2): 332–338
11. Desmond JE (2001) Cerebellar involvement in cognitive function: evidence from neuroimaging. Int Rev Psychiatry 13: 283–294
12. Dolan RJ (1998) A cognitive affective role for the cerebellum. Brain 121(Pt 4): 545–546
13. Farah MJ (1996) Is face recognition 'pecial'? Evidence from neuropsychology. Behav Brain Res 76(1–2): 181–189
14. Fastenau PS, Denburg NL, Hufford BJ (1999) Adult norms for the Rey-Osterrieth Complex Figure Test and for supplemental recognition and matching trials from the Extended Complex Figure Test. Clin Neuropsychol 13(1): 30–47
15. Feeney DM, Baron JC (1986) Diaschisis. Stroke 17(5): 817–830
16. Garcia-Bunuel L (1988) Cerebellar diaschisis. Lancet 1(8597): 1282

17. Gottwald B, Wilde B, Mihajlovic Z, Mehdorn HM (2004) Evidence for distinct cognitive deficits after focal cerebellar lesions. J Neurol Neurosurg Psychiatry 75(11): 1524–1531
18. Haines DE, Dietrichs E (1984) An HRP study of hypothalamo-cerebellar and cerebello-hypothalamic connections in squirrel monkey (Saimiri sciureus). J Comp Neurol 229(4): 559–575
19. Hokkanen LS, Kauranen V, Roine RO, Salonen O, Kotila M (2006) Subtle cognitive deficits after cerebellar infarcts. Eur J Neurol 13(2): 161–170
20. Hubrich-Ungureanu P, Kaemmerer N, Henn FA, Braus DF (2002) Lateralised organization of the cerebellum in a silent verbal fluency task: a functional magnetic resonance imaging study in healthy volunteers. Neurosci Lett 319(2): 91–94
21. Kalashnikova LA, Zueva YV, Pugacheva OV, Korsakova NK (2005) Cognitive impairments in cerebellar infarcts. Neurosci Behav Physiol 35(8): 773–779
22. Kessels RP, Ruis C, Kappelle LJ (2007) The impact of self-reported depressive symptoms on memory function in neurological outpatients. Clin Neurol Neurosur 109(4): 323–326
23. Leiner HC, Leiner AL, Dow RS (1986) Does the cerebellum contribute to mental skills? Behav Neurosci 100(4): 443–454
24. Leiner HC, Leiner AL, Dow RS (1987) Cerebro-cerebellar learning loops in apes and humans. Ital J Neurol Sci 8(5): 425–436
25. Leiner HC, Leiner AL, Dow RS (1993) Cognitive and language functions of the human cerebellum. Trends Neurosci 16(11): 444–447
26. Marchand Y, Lefebvre CD, Connolly JF (2006) Correlating digit span performance and event-related potentials to assess working memory. Int J Psychophysiol 62(2): 280–289
27. Mondal S, Sharma VK, Das S, Goswami U, Gandhi A (2007) Neuro-cognitive functions in patients of major depression. Indian J Physiol Pharmacol 51(1): 69–75
28. Nolin P, Laurent J-P (2004) Neuropsychologie, cognition et développement de l'enfant. PUQ, Québec
29. Pantano P, Baron JC, Samson Y, Bousser MG, Derouesne C, Comar D (1986) Crossed cerebellar diaschisis. Further studies. Brain 109(Pt 4): 677–694
30. Paulus KS, Magnano I, Conti M, Galistu P, D'Onofrio M, Satta W, Aiello I (2004) Pure post-stroke cerebellar cognitive affective syndrome: a case report. Neurol Sci 25(4): 220–224
31. Ravizza SM, McCormick CA, Schlerf JE, Justus T, Ivry RB, Fiez JA (2006) Cerebellar damage produces selective deficits in verbal working memory. Brain 129(Pt 2): 306–320
32. Schmahmann JD, Pandya DN (1989) Anatomical investigation of projections to the basis pontis from posterior parietal association cortices in rhesus monkey. J Comp Neurol 289(1): 53–73
33. Schmahmann JD, Pandya DN (1990) Anatomical investigation of projections from thalamus to posterior parietal cortex in the rhesus monkey: a WGA-HRP and fluorescent tracer study. J Comp Neurol 295(2): 299–326
34. Schmahmann JD, Pandya DN (1995) Prefrontal cortex projections to the basilar pons in rhesus monkey: implications for the cerebellar contribution to higher function. Neurosci Lett 199(3): 175–178
35. Schmahmann JD, Pandya DN (1997) The cerebro-cerebellar system. Int Rev Neurobiol 41: 31–60
36. Schmahmann JD, Sherman JC (1998) The cerebellar cognitive affective syndrome. Brain 121(Pt 4): 561–579
37. Silveri MC, Di Betta AM, Filippini V, Leggio MG, Molinari M (1998) Verbal short-term store-rehearsal system and the cerebellum. Evidence from a patient with a right cerebellar lesion. Brain 121(Pt 11): 2175–2187
38. Tolor A (1958) Further studies on the Bender-Gestalt test and the digit-span test as measures of recall. J Clin Psychol 14(1): 14–18
39. Vandierendonck A, Kemps E, Fastame MC, Szmalec A (2004) Working memory components of the Corsi blocks task. Br J Psychol 95(Pt 1): 57–79
40. Vecchi T, Richardson JT (2001) Measures of visuospatial short-term memory: the Knox Cube Imitation Test and the Corsi Blocks Test compared. Brain Cogn 46(1–2): 291–295
41. Vokaer M, Bier JC, Elincx S, Claes T, Paquier P, Goldman S, Bartholome EJ, Pandolfo M (2002) The cerebellum may be directly involved in cognitive functions. Neurology 58(6): 967–970
42. Wilde N, Strauss E (2002) Functional equivalence of WAIS-III/WMS-III digit and spatial span under forward and backward recall conditions. Clin Neuropsychol 16(3): 322–330
43. Willert C, Schaumann-Kuchling C, Adamaszek M, Spitzer C (2005) Neuropsychological dysfunction after cerebellar stroke. Nervenarzt 76(8): 988–991

Comments

There has been a growth in interest in cognitive and behavioural functions of the cerebellum in recent years. The current paper adds to the literature on the cognitive effects of lateralised cerebellar lesions, and has useful practical implications for managing neurosurgical patients. The study is not fully prospective, and the cognitive battery that was used to assess patients varied from case to case. The current report focuses on memory problems associated with cerebellar lesions, and does not give information about other deficits that may have been present such as problems of language, attention and executive functions. It would be very interesting to see a prospective study of such cases using tests chosen to identify more specifically the nature of cognitive impairment caused by cerebellar lesions. The authors are right to flag up memory problems, as a currently under-recognized consequence of cerebellar lesions.

Lindsay Wilson
Stirling University

This manuscript underlines the fact that cognitive deficits represent a critical parameter in the management of cerebellar lesions. Without any doubt, such studies are useful since data about cognitive deficits in this field remain rare and taking in account that these deficits remain well underestimated.

Mathieu Vokaer
Université Libre de Bruxelles