Brain (2000), **123,** 1051–1061

The cerebellum contributes to higher functions during development

Evidence from a series of children surgically treated for posterior fossa tumours

Daria Riva[1] and Cesare Giorgi[2]

[1]*Developmental Neurology Division and* [2]*Stereotactic and Functional Neurosurgery Unit, Carlo Besta National Neurological Institute, Milan, Italy*

Correspondence to: Daria Riva, MD, Developmental Neurology Division, Istituto Nazionale Neurologico C. Besta, via Celoria 11, 20133 Milano, Italy
E-mail: driva@istituto-besta.it

Summary

We present data on the intellectual, language and executive functions of 26 children who had undergone surgery for the removal of cerebellar hemisphere or vermal tumours. The children with right cerebellar tumours presented with disturbances of auditory sequential memory and language processing, whereas those with left cerebellar tumours showed deficits on tests of spatial and visual sequential memory. The vermal lesions led to two profiles: (i) post-surgical mutism, which evolved into speech disorders or language disturbances similar to agrammatism; and (ii) behavioural disturbances ranging from irritability to behaviours reminiscent of autism. These data are consistent with the recently acknowledged role of the cerebellum as a modulator of mental and social functions, and suggest that this role is operative early in childhood.

Keywords: cerebellum; social behaviour; frontal functions; language; intelligence; children

Abbreviations: MLU = mean length of utterance; PIQ = performance IQ; VIQ = verbal IQ; WCST = Wisconsin Card Sorting Test

Introduction

The cerebellum has been associated with motor control and the ability to learn highly complex motor sequences (Ghez and Fahn, 1985), but more recent studies have extended its contribution to non-motor functions, such as language, thought modulation, emotions and the ability to organize symbolic activities in a sequential manner (Schmahmann, 1991; Fiez *et al*., 1992; Leiner *et al*., 1993; Fiez, 1996). The role of the cerebellum in cognitive processing is mainly supported by anatomic demonstrations that the cerebellar hemispheres are indirectly connected to the associative areas of the frontal and parietal cortex (Asanuna *et al*., 1983; Stanton *et al*., 1988; Schmahmann and Pandya, 1993; Middleton and Strick, 1994). Furthermore, an increasing number of clinical studies have revealed both motor and cognitive deficits in adult patients with vascular or degenerative cerebellar disease (Grafman *et al*., 1992; Botez-Marquand *et al*., 1994; Silveri *et al*., 1994; Schmahmann and Sherman, 1998).

In children, it is well known that congenital hypoplasia of the cerebellum (and particularly the vermis) is often accompanied by a wide range of neurodevelopmental disorders (Gilberg and Coleman, 1992). In contrast, there are only rare descriptions of cognitive disturbances following acquired cerebellar lesions (Riva, 1998).

Schmahmann has hypothesized an internal topography of the cerebellum in which the regions of the vermis represent the cerebellar limbic system and are thought to be involved in the modulation of emotions and social behaviours, whereas the more lateral hemispheric regions are involved in modulating thought, language and the ability to plan (Schmahmann, 1991).

Speech disorders involving dysarthria to the point of mutism have been described in children after posterior fossa tumour surgery (Ferrante *et al*., 1990; van Dongen *et al*., 1994; Pollak *et al*., 1995; Van Calenbergh *et al*., 1995), but language organization disturbances have not yet been reported.

Alterations in cognitive functions have been repeatedly observed in children with medullablastomas; however, these have been attributed not to the site of the tumour removal

but to the effects of therapy (i.e. radiotherapy or chemotherapies) that usually involve the whole brain (Riva *et al*., 1989, 1991*b*; Duffner and Cohen, 1991). Studies of astrocytomas of the posterior fossa have revealed the presence of cognitive deficits after tumour removal (with greater impairment being observed in cases with a larger amount of residual tumour), or a selective slowing of attentional performances within the context of adequate mental functioning (Riva *et al*., 1989, 1991*b*; Riva, 1995*b*).

The behavioural changes observed after posterior fossa surgery have often been interpreted as symptoms of reactive depression. Pollack and colleagues described personality changes and emotional lability (Pollack *et al*., 1995) and, more recently, Levisohn and colleagues have reported expressive language and visuo-spatial problems in children who have undergone excision of posterior fossa tumours (Levisohn *et al*., 1997). Similar alterations have also been encountered in children with primary brainstem tumours.

We present here the results of neuropsychological evaluations of a consecutive series of children with hemispheric or vermal tumours who underwent surgery in our Institute between 1987 and 1993. The aim of the study was to examine the effects of the lesions on higher functions and to determine whether deficits vary depending on the site of the lesion (the vermis, or the left or right hemisphere of the cerebellum).

Methods

Clinical investigations

Between 1987 and 1993, 32 children underwent surgery for cerebellar astrocytoma, and 21 for cerebellar vermis medulloblastoma at the Carlo Besta National Neurological Institute in Milan. This study was approved by the Internal Ethics Committee of the Carlo Besta Neurological Institute, Milan.

Only those satisfying the following criteria were included in the study: (i) normal emotional and social behaviour before the onset of the disease. (ii) Normal academic and intellectual performances. (iii) Radiologically confirmed complete removal of the tumour. (iv) An individual score and total score less than 3 of the following major neurological cerebellar signs: (a) ocular disorders (nystagmus and alterations of saccadic movements); (b) movement disorders (dysmetria and intentional tremor); and (c) ataxia. The scores ranged from 0 (absent) to 3 (severe) (Riva *et al*., 1991*b*). (v) A willingness to collaborate during the examinations. (vi) Parental consent. (vii) The absence of a family history of psychiatric pathologies.

Each patient underwent a comprehensive neurological examination. MRI was performed according to the following standard protocol: T_2-weighted images in the axial or coronal views, and T_1-weighted images before and after contrast medium in the coronal, sagittal and axial views. The slice thickness was 4 mm. Standard EEG was performed using surface Ag–AgCl electrodes positioned according to the International 10–20 system. The EEG signals were acquired using a Micromed Computerized EEG system.

Patient characteristics

Twenty-six of the 53 patients met the selection criteria. Of these 26, 15 underwent surgery for left or right cerebellar astrocytoma and 11 for cerebellar vermis medulloblastoma.

The mean age of the 15 patients in the astrocytoma group was 10.2 years (range 7–12.6): seven (mean age 9.8, range 6.11–13.4 years) had right, and eight (mean age 10.6; range 7.2–13.1 years) had left cerebellar astrocytomas. The histological type was pylocytic in eight cases, protoplasmatic in three, fibrillar in two and mixed in two.

The mean age of the patients in the medulloblastoma group was 7.10 years (range 6–12.1). This sample was divided into two subgroups: the six children with speech/language disorders after surgery (two of whom had desmoplastic medulloblastomas) had a mean age of 7.2 years (range 6–8); the five children with post-surgery behavioural disorders had a mean age of 8.7 years (range 6.8–12.1).

None of the children had a score of 3 for any of the three cerebellar signs considered in the selection criteria, and the sum of the three scores was never greater than 3. None of these children had a pathological EEG.

The MRI examinations did not reveal any brain lesions other than cerebellar tumours, the mean diameter of which was 2.8 cm (range 2–4 cm). Their locations were the vermis in the case of the patients with medulloblastomas (marginally involving the right cerebellar hemisphere in two cases), and the cerebellar hemispheres in the patients with astrocytomas (the right cerebellar lesions were mainly anterior in three cases, and mostly posterior in four; the left cerebellar lesions were anterior in three cases, and posterior in five). The vermis was not involved in any of these cases.

Pre- and post-operative MRI of a case with posterior left hemispheric cerebellar astrocytoma is shown in Fig. 1 and of a case of vermis medulloblastoma in Fig. 2.

All the children were assessed by means of a neuropsychological battery which included: (i) general intelligence, measured with the Wechsler Scale verbal IQ (VIQ) and non-verbal items as performance IQ (PIQ) (Wechsler, 1986); (ii) language, in terms of (a) lexical production (Boston Naming Test) (Kaplan *et al*., 1983) and comprehension (Peabody's Picture Vocabulary Test) (Dunn and Dunn, 1981), (b) syntax (Token Test) (De Renzi and Vignolo, 1962), and (c) verbal production based on the mean length of utterance (MLU) deduced from the description of a story based on visual stimuli (MacWhinney, 1991); (iii) executive abilities, reflected in (a) auditory and visual sequential memory using the Illinois Test of Psycholinguistic Abilities (ITPA) (Kirk *et al*., 1968), (b) abstract reasoning and the ability to adapt cognitive strategies in response to a controlled change in environmental contingencies using the Wisconsin Card Sorting Test (WCST) (Grant and Berg,

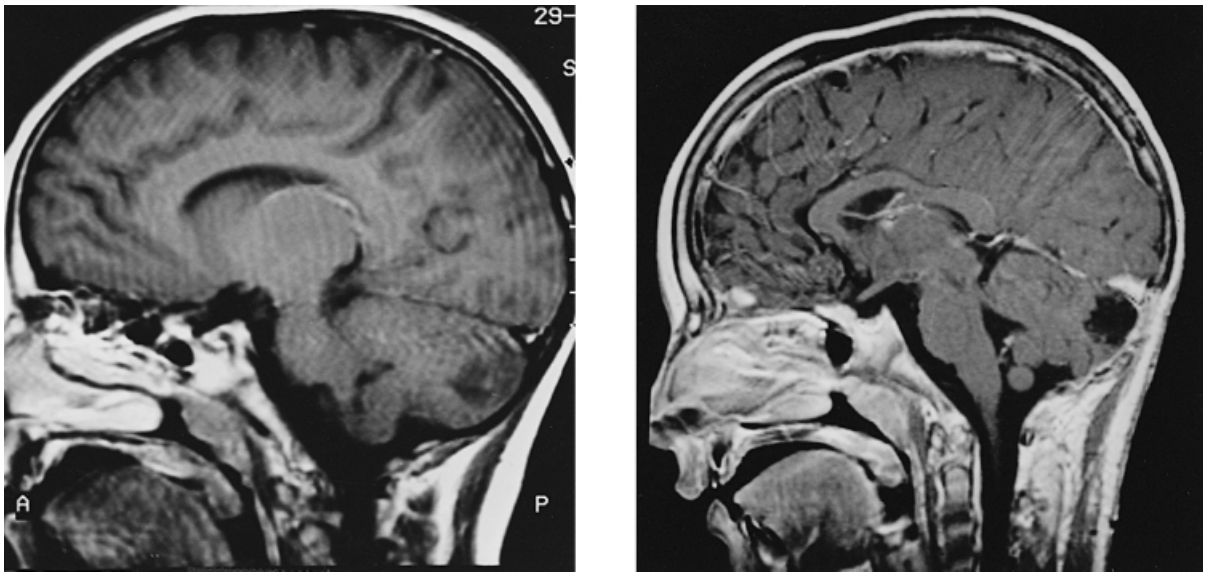

Fig. 1 T_1-weighted sagittal MRI: pre-operative showing an astrocytoma of the posterior left cerebellar hemisphere (*left panel*) and post-operative showing the site and extent of excision (*right panel*).

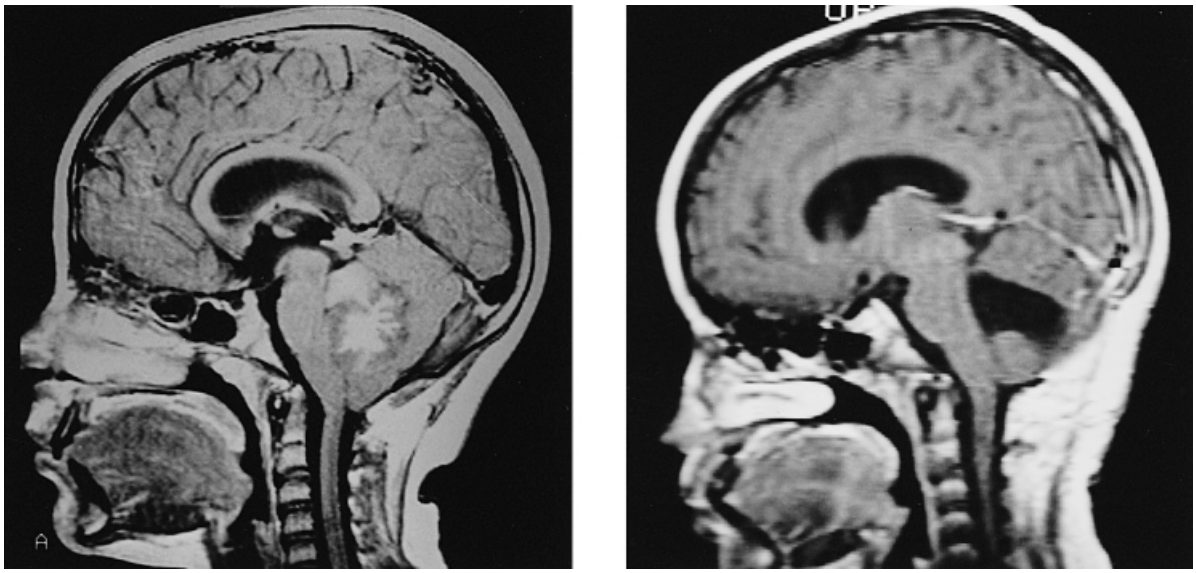

Fig. 2 T_1-weighted sagittal MRI: pre-operative showing a medulloblastoma of the IV ventricle with intense enhancement (*left panel*) and post-operative showing a large demolition of the inferior vermis lobules that was associated with an autistic-like picture (*right panel*).

1993), and (c) creative fluency in the production of: (1) words on the basis of categorical semantic stimuli (Benton and Hamsher, 1989), and (2) unverbalizable drawings (Jones-Gotman and Milner, 1977); and (iv) attention, using the Cancellation Test involving the crossing out as quickly as possible of a series of simple stimuli (Lezak, 1995).

In our Division, all children with neurological diseases undergo neuropsychological evaluation. The protocol used in the present study was specifically designed to study the behaviour and higher functions of children with cerebellar lesions, and is part of a broader protocol that evaluates late neuropsychological effects in children with brain tumours undergoing different treatment modalities. All of the tests are administered in their Italian versions. Standard norms have been published for some of them: the Boston Naming Test and Verbal Fluency Test (Riva *et al*., 2000), the Token Test (Vender *et al*., 1979; Riva *et al*., 1999), and the Illinois Test of Psycholinguistic Abilities (Nardocci *et al*., 1997). For the Design Fluency test, Peabody Picture Vocabulary Test and Cancellation Test, the normative data have been collected by our group.

The WCST perseverations were based on American norms but, given the independence of this test from language or other cultural factors, it is unlikely that the use of American norms had any effect on the results, and this is also confirmed by our ongoing data collection. All of the children were evaluated after surgery because their general pre-operative condition did not allow a reliable evaluation to be made due

Table 1 *Intelligence, language and executive performances (Z scores) of 15 children with right and left hemispheric cerebellar tumours*

	Right cerebellar tumours (n = 7)	Left cerebellar tumours (n = 8)
VIQ	−1.4	+0.2
PIQ	+0.3	−1.3
Lexical naming	−1.5	−1.4
Lexical comprehension	−1.3	−1.9
Token Test	−1.6	+1.4
MLU	−2.3	+1.4
Visual sequential memory	+0.8	−1.7
Auditory sequential memory	−1.8	+1.2
WCST (perseverations)	+2.5	+2.1
Design fluency	ND	−2.4
Verbal fluency	−2.9	−1.7
Attention	−3.1	−3.2

ND = no data.

to their neurological status and/or apprehension related to the severity of their disease. In all cases, the evaluations were carried out at least 5–6 weeks after surgery.

The patients with malignant tumours requiring further radio- or chemotherapy were always evaluated before the initiation of adjunctive treatment.

Procedures

The neuropsychological tests were performed by two clinical psychologists working in the Neuropsychology Laboratory of the Developmental Neurology Division; some of the patients were still hospitalized, whereas the others were seen as outpatients.

All of the tests were administered in a quiet room, and interrupted whenever this was requested by the patient.

The children suffering from mutism or behavioural disturbances secondary to the operation were only observed and not tested during the days immediately following surgery because they were in no condition to undergo formal testing. The laboratory tests were undertaken only after a sufficient period of post-surgical recovery.

Statistics

All of the test results were '*Z*' normalized (mean value = 0 and standard deviation = 1). *Z* scores provide a standard from which all other scores can be derived, and they reflect the extent to which a score deviates from the mean population score. The individual *Z* scores were then averaged in order to allow rapid between-test and between-group comparisons (Cristante *et al*., 1992). *Z* scores $\geqslant 2$ correspond to an area of probability that is outside 95% of the normal distribution and so were considered statistically significant.

Results

Cerebellar hemisphere astrocytomas

The mean *Z* scores of the right and left lesioned subjects are shown in Table 1. The subjects with *right cerebellar lesions* showed a slight but non-significant decline in verbal performance (–1.4). The results of all the language tests revealed an impairment, which was less pronounced in the case of tests of lexicon, such as naming (–1.5) and comprehension (–1.3), and most marked in relation to measures of complex aspects of language, such as receptive syntax (Token Test, –1.6) and formulation of sentences as reflected in the MLU (mean length of utterance) (–2.3). Executive functions as assessed by tests of verbal fluency and WCST were deficient (–2.9 and 2.5, respectively), although sequential memory was impaired only verbally (–1.8).

The children with *left cerebellar lesions* showed a decline in non-verbal performance (–1.3). In the language domain, only the lexical components were impaired (naming, –1.4; comprehension, –1.9), whereas the more complex aspects such as syntax comprehension and MLU were preserved. In the domain of executive function, there was a high percentage of perseverative errors on the WCST (2.1). Verbal fluency was impaired (–1.7), and there was a decrease in design fluency (–1.7); sequential memory was deficient only visually (–1.7).

Both groups showed a slowing of more than 2 SD in executing the time-based attention tests (left, –3.2; right, –3.1).

Cerebellar vermis medulloblastomas

Of the 21 children who underwent surgery for cerebellar vermis medulloblastoma between 1989 and 1993, only 11 children for whom we had a detailed record of post-operative behaviour and a baseline neuropsychological assessment that included evaluations of language and executive functions were included in the study. All of the children had the cerebellar vermis sectioned along the midline for its entire length. One of them underwent the excision of a large part of the VI, VII and VIII lobules, and to lesser extent the IX and X lobules.

The post-surgical clinical pictures could be divided into two groups: the first characterized by obvious mutism without any clear behavioural alterations (six children), and the second by obvious alterations in behaviour and some neuropsychological dysfunctions (five children).

Post-operative mutism

The mean age of the first sub-group of six children (two of whom had desmoplastic medulloblastomas) was 7.2 years (range 6–8). The disturbances in verbal production were represented by a post-surgical mutism that evolved in such a way as to allow the identification of two distinct types of

Table 2 *Intelligence, language and executive performances (Z scores) in six children with vermis medulloblastoma presenting mutism after surgery*

	Mutism with subsequent speech disturbances (n = 4)	Mutism with subsequent language disturbances (n = 2)
VIQ	+0.5	+0.8
PIQ	−0.1	+0.4
Lexical naming	−0.5	−0.5
Lexical comprehension	+0.1	−0.8
Token Test	+0.6	−2.7
MLU	+0.9	−2.5
Visual sequential memory	+1.8	ND
Auditory sequential memory	+1.6	−2
WCST (perseverations)	+0.5	+2.8
Design fluency	ND	−2.08
Verbal fuency	−2.8	−3.2
Attention	−2.9	−3.1

ND = no data.

Table 3 *Intelligence, language and executive performances (Z scores) of children with behavioural alterations after surgical vermis incision* (n = *4) and autistic-like picture after large demolition of the inferior vermis lobules* (n = *1)*

	Minor behavioural disturbances (n = 4)	Autistic behaviour (n = 1)
VIQ	−0.6	−1.8
PIQ	−0.8	−3.4
Lexical naming	−1.2	−3.4
Lexical comprehension	−0.9	ND
Token Test	−0.9	−2.1
MLU	−1.1	−2.3
Visual sequential memory	ND	ND
Auditory sequential memory	−0.9	−2.9
WCST (perseverations)	+1.3	+2.4
Design fluency	ND	−2.6
Verbal fuency	−1.1	−3.6
Attention	ND	ND

ND = no data.

disorder: four cases had severe speech anarthria and two others suffered from a severe intrinsic language disturbance Their mean *Z* scores are shown in Table 2.

The first four patients were perfectly capable of understanding language and providing clear linguistic responses immediately after surgery but, within a period of 3–5 days, none of them could emit any sound despite the fact that there was no evidence of any cranial nerve deficit and their brainstem-evoked responses were normal. All had normal involuntary palatal, lip and tongue movements, but none of them could imitate tongue or lip movements on command. During the course of the subsequent 3–4 weeks, they recovered their ability to emit sounds first by phonating when they laughed or cried, and then by producing single words; after 5–6 weeks, they were capable of producing grammatically correct but highly dysarthric sentences. The clinical findings were confirmed by their normal performance on all tasks given to them under laboratory conditions (with the exception of the verbal fluency task, where their score was below 2 SD due to verbal slowness secondary to dysarthria). The children fully recovered their ability to use expressive language 3–6 months after the operation, but their speech patterns continued to be dysarthrically monotonous. During the course of the following 6–24 months, all of them completely re-acquired their normal speech.

In contrast, the mutism observed in the other two patients evolved to a true language disorder. After the recovery of word production, their language was not dysarthric but slow and monotonous, and lacked its previous prosodic intonations. Furthermore, despite a normal tendency towards communication and the absence of dysarthria, these children made use of a telegraphic language often structured in the form of simple noun/verb sentences that frequently omitted grammatical elements and often included uninflected verbs. Their language was reminiscent of the agrammatical language frequently encountered in aphasic patients (including children) with acquired left frontal lesions.

When it was possible to make an evaluation under laboratory conditions, the children had an excellent ability to understand and repeat fluently even complicated sentences (thus demonstrating they were not dysarthric), but suffered from a severe lack of spontaneity in terms of active language, and tended to speak very little even after being encouraged to do so. These findings were confirmed by their poor syntactic comprehension on the Token Test (–2.7) and their poor performance in terms of auditory sequential memory (–2) and MLU (–2.5). Their executive auditory sequential memory and design fluency scores also fell 2 SD below the norm, and their WCST perseverative errors were >2 SD above the norm (2.8).

The picture evolved positively over time, but its evolution was much slower than that of the other four patients described above: even as late as 3 years after the operation, their language quality was poor even though it was grammatically correct.

Post-operative behavioural disturbances

The five children suffering post-operative behavioural disturbances had a mean age of 8.7 years (range 6.8–12.1). The surgery involved the incision of the lower part of the vermis in all cases; in one, the inferior lobules were largely excised.

All of the patients presented with different degrees of post-surgical behavioural disturbances. In addition to a precise daily record of their behaviour being kept and performing the neuropsychological evaluation described in the Methods section, the patients were also evaluated using the DSM IV (Diagnostic and Statistical Manual of Mental Disorders,

fourth edition) diagnostic criteria for autism (Andreoli *et al*., 1996). Their mean *Z* scores are shown in Table 3.

In four cases, the picture was characterized by frank irritability, a decreased ability to remain in the company of others (including family members), and a general tendency to avoid physical and eye contact. Their language was not dysarthric, but moderately monotonous or partially lacking in emotional inflections, and was rarely used as a means of communication; in brief, it reflected the behavioural picture of contact avoidance. All of their performances on the tests fell within normal limits, although their scores tended to be 1 SD below the average (Table 3). The behavioural alterations gradually subsided and returned to normal within a period of 3–4 weeks, as assessed by their parents and the physician who followed them during the course of their hospitalization (D.R.).

However, the picture in the fifth case was quite dramatic (MRI in Fig. 2). Immediately after the operation, this girl had a very mild right cerebellar hemisyndrome (mild hypotonia and hyposthenia), and her behaviour changed in a startling manner: she had complete gaze aversion and a severe intolerance of the approach of others (including her mother). She presented with complex rhythmic rocking stereotypical movements of the trunk and hands, and a series of untranslatable linguistic eccentricities devastated her communication. Spontaneous language for the purposes of communication was practically absent during the first few days after the intervention, and was limited to bizarre stereotypic linguistic repetitions. Her behaviour satisfied the DSM IV diagnostic criteria for autism and was associated with disinhibition, including the production of scurrilous words and obscenities that were not at all usual for her.

Her behavioural disturbances made it impossible to carry out any neuropsychological evaluation during the first few days following the operation. After 1 week, a formal assessment revealed deficient lexical naming (–3.4) and syntactical comprehension (–2.1), with a very marked reduction in both free (MLU, –2.3) and semantically stimulated verbal fluency (–3.6). Furthermore, semantic cues triggered an unstoppable confabulatory mechanism. All of the frontal test results were severely impaired: auditory sequential memory (–2.9); design fluency (–2.6); WCST perseverations (2.4) (Table 3). One month after surgery, her behaviour settled down: she became more tolerant of the physical approach of others and could once again accept eye contact. Although she remained generally introverted, her language was contextual and not telegraphic. However, she had a clear general lack of empathy with others, including children of her own age. The longitudinal description of this case will be published elsewhere.

Discussion

This study describes the cognitive and behavioural disorders observed in children affected by cerebellar tumours. These deficits can be clinically detected by means of specific tests, making it possible to identify different behavioural patterns related to the tumour location.

The tumours of the right cerebellar hemisphere correlated to an alteration in the processing of verbal intelligence and complex language tasks; those of the left cerebellar hemisphere correlated to a diminished capacity to process non-verbal tasks and, in some cases, an impairment in prosodic intonation. Regardless of the laterality of the lesions, there was a slight worsening in naming and comprehension, and difficulties with the processing of executive and time-based attention tests.

None of the children presented with frank behavioural disturbances. In the group with hemispheric tumours, the deficits tended to be hemisphere dependent, and were similar to those observed in children with acquired unilateral lesions of the cerebral hemispheres. The slight deficits in relation to lexical production and comprehension found in our patients with right or left cerebellar tumours were also similar to those found in children with right or left unilateral cerebral lesions (Aram and Whitaker, 1988; Riva *et al*., 1991*a*). The left–right distinction also applied to the low frontal executive test scores: sequential auditory memory was deficient in patients with right cerebellar lesions and sequential visual memory in those with left cerebellar lesions (Marlowe, 1992).

The limited nature of our data obviously means that they need to be confirmed but, in any case, all of the patients with cerebellar hemispheric involvement showed more perseverative errors on the WCST compared with their normal peers, and their average production of a story presented in picture form was inferior.

The children with vermal lesions had two distinct profiles that could be identified easily even on a clinical basis: a profile of outright mutism, or a profile of affective and social behavioural alterations, the severity of which varied in terms of clinical expression. The profile of mutism was distinct and well differentiated.

After the resolution of the mutism, the children with a speech disorder suffered from dysarthric speech that continued for months after the surgical intervention, but they nevertheless retained an intrinsically intact language structure in terms of the lexical and syntactic components, and the organization of complex utterances. Their spontaneous language was creative and natural, and did not require any solicitation. Furthermore, they did not present any executive deficits.

After being described in a large number of reports (Rekate *et al*., 1985; Ferrante *et al*., 1990; van Dongen *et al*., 1994; Pollak *et al*., 1995; Van Calenbergh *et al*., 1995), this picture was categorized by van Dongen and colleagues as the ‘mutism and subsequent dysarthria syndrome’ (MSD), a speech disorder whose dysarthric characteristics may be so severe as to reach the level of anarthria, but which always has a favourable evolution (van Dongen *et al*., 1994).

In addition to mutism, Pollack and colleagues found pseudo-bulbar signs and emotional changes and/or decreased initiation of voluntary movements (Pollack *et al*., 1995). The

causes are thought to be a transient bilateral dysfunction of the afferent and/or efferent dentate/thalamic pathways or their cells of origin due to MRI-detectable bilateral oedema of the brachium pontis (van Dongen *et al*., 1994).

The second type of mutism was similar to agrammatism (Riva, 1995*a*, *b*, 1998), with a marked deficit on complex linguistic tests despite an excellent ability to repeat even highly complex sentences. As previously described by Silveri and colleagues in an adult patient affected by a right cerebellar stroke (Silveri *et al*., 1994), and by us in a child with cerebellitis (Riva, 1998), the condition is characterized by agrammatical and hypospontaneous language even after the resolution of the symptoms. The deficient executive test performances of these children once again highlight the important relationship between executive function and the programming of linguistic output—a typically sequential function.

The poor performance of the two children with mutism and subsequent language disorders on the test of fluency in the production of unverbalizable drawings, deserves special mention as it probably reflects the use of verbal strategies when performing visuo-perceptual tasks, a behaviour that is not infrequent in children (Stiles-Davis *et al*., 1988).

The differences between the two profiles of mutism described above can be accounted for by the fact that the first four children underwent the partial excision of the vermis alone (causing an alteration in the mechanical processes of phonation or the initiation of articulatory movements and subsequent anarthria), whereas the last two children presented a real language disturbance secondary to the additional partial excision of the right cerebellar hemisphere, which leads to alterations in linguistic processes including language organization. The right cerebellar hemisphere participates in language processing as a result of its cross-connections, particularly with the frontal associative areas of the left cerebral hemisphere via the thalamus (Barker *et al*., 1991; Kim *et al*., 1994; Silveri *et al*., 1994, 1998; Schmahmann and Pandya, 1997*a*).

Vermal lesions mainly involving the postero-inferior lobules cause disturbances in social and communicative behaviour of varying severity. Cerebellar vermis alterations in psychiatric and schizophrenic patients have been anecdotally described in the past (Schmahmann, 1991) and, more recently, also in groups of carefully selected patients (Heath *et al*., 1979; Martin and Albers, 1995).

Experimental studies of animals with an ablated cerebellar vermis have revealed primitive defence and isolation behaviours, as well as alterations in sexual conduct (Berman *et al*., 1974). A large number of radiological and autopsy studies have demonstrated that lobules VI and VII of the vermis are involved in the pathogenesis of infantile autism (Courchesne, 1991, 1997).

These studies, not confirmed by others (Bauman and Kemper, 1997; Piven *et al*., 1997), suggest that the vermis (particularly its lower lobules) plays a role in the processing of complex social and emotional behaviours, a processing that takes place in a complex network involving other associative areas that are important in the mediation of social cognitive behaviour, such as the frontal lobes and the limbic system (Courchesne, 1991, 1997; Saitoh *et al*., 1995; DeLong and Heinz, 1997).

Our surgical cases seem to support this view, particularly in relation to the role of the lower vermis. The dramatic picture of autistic-like behaviour presented by the girl who underwent the excision of the lower part of the cerebellar vermis (in comparison with the other five children, who did not present with a picture of autistic-like behavioural alteration) may have been due to the abrupt disconnection of the vermis from the supratentorial circuits, particularly those that process emotions and complex social behaviours (Middleton and Strick, 1994; Schmahmann and Pandya, 1997*a*, *b*).

All of the children were slow in performing the time-based tests, which could be more precisely quantified by the results of the Cancellation Test (the only test that led to reduced levels of performance of more than three standard deviations). We have previously observed a similar slowness in carrying out this task in a study of children with cerebellar astrocytomas. This was interpreted as an effect of the proximity of the lesions or the surgical approach routes to the ascending activating reticular system of the brainstem (Riva *et al*., 1989). However, it can also be hypothesized that this slowness of execution may depend on the poor functioning of the intrinsic structure of the cerebellum, which is constituted in a crystalline manner by a micromodular structure that works in parallel. Each of these modules can be considered the equivalent of microprocessors: in large numbers, this parallel array leads to an extremely powerful network capable of high-speed processing and learning. The progressive possibility of recruiting modules in rapid succession establishes a network that can reach exceptional speeds of execution, and it is therefore clear that any lesion affecting a part of this network reduces the efficiency of recruitment and thus the speed of executing tests (Ito, 1984; Ghez and Fahn, 1985). If a lesion is extensive, as in the case of cerebellitis, this processing slowness affects all tests. We have recently reported the case of a girl with cerebellitis who, in addition to specific neuropsychological disorders affecting language and sequential organization, was also extremely slow in performing even the successfully completed tests. After the resolution of the clinical picture, the only remaining sign was her considerable slowness in performing all activities, including spontaneous ones (Riva, 1998).

The presence of cerebellar signs such as dysmetria and tremor may worsen time-based performances, but this does not seem likely here because all of the patients with major signs of motor impairment were excluded from the study, and it must be remembered that the neurological signs in children with posterior fossa tumours are always very slight because of the exceptional adaptability of a child's brain, as well as the early diagnosis of the lesions.

The cognitive and behavioural alterations observed in this

study confirm those found in individual adult patients (Silveri *et al*., 1994, 1998) and in groups of patients with cerebellar pathologies of various kinds (Grafman *et al*., 1992; Botez-Marquand *et al*., 1996; Schmahmann and Sherman, 1998). Although the heterogeneity of the patients involved in these studies has not always made it possible to identify constellations of symptoms associated with the site of the lesion, the results did make it possible to conclude that the vermal lesions were associated with major affective alterations, whereas those involving the cerebellar hemispheres (particularly the posterior lobes) were crucial for the generation of altered cognitive behaviours (Silveri *et al*., 1994, 1998; Botez-Marquand *et al*., 1996; Schmahmann and Sherman, 1998).

Neurocognitive and/or behavioural alterations of varying severity are found in children with (global or only vermal) congenital cerebellar hypoplasias, whether these are isolated or form part of complex cerebral malformations; however, precisely because of their often severe intellectual deficits and the difficulty of establishing a relationship that is reliable enough to allow a complete evaluation, no more detailed pictures have yet been described (Baraitser, 1990; Guzzetta *et al*., 1993).

The literature contains very few descriptions of normally intelligent children with an acquired cerebellar pathology: the children with surgically induced lesions described by Pollak *et al*. and Levisohn *et al*. had cognitive and affective deficits if the vermis was involved (Pollak *et al*., 1995; Levisohn *et al*., 1997); the child with cerebellitis described by us showed a deficit in the sequential organization of symbolic activities (particularly language), but the lesion involved both hemispheres (Riva, 1998).

Nevertheless, even these few cases highlight the important fact that the cerebellum plays a fundamental role in constructing the harmonious organization of higher cognitive and social behaviours. Furthermore, the results of the present study make it possible to identify patterns that are compatible with the site of the lesion, and this differentiation of patterns supports the hypothesis advanced by Schmahmann concerning the functional topography of the cerebellum (Schmahmann, 1991).

The fact that vermal lesions (particularly of the inferior lobules) are correlated to different degrees of behavioural disturbances that go from irritability to a general tendency towards avoidance that may even reach the stage of transitory autism supports the role of the vermis as a cerebellar limbic system. Furthermore, the fact that lesions of the cerebellar hemispheres lead to deficits in complex mental activities supports the role of these hemispheres in the modulation of thought, language and executive abilities. Although this conclusion needs to be advanced with caution, the two cerebellar hemispheres may have a right–left specialization similar to that of the cerebral hemispheres.

The results described above also make it possible to hypothesize that, given the young age of some of the children included in our study, this inter-cerebellum specialization develops early, as is also shown by the fact that congenital vermis abnormalities or hypoplasia are accompanied by a wide range of developmental disorders (including autism) (Baraitser, 1990; Gilberg and Coleman, 1992; Bauman and Kemper, 1997).

The early specialization of the cerebral areas has been widely demonstrated in animals (Kennard, 1940) and in children presenting specific deficits after focal cerebral lesions acquired at an early age and affecting different sites (Riva and Cazzaniga, 1986; Aram and Whitaker, 1988), even though its maturation times vary from region to region (Thatcher *et al*., 1987; Simonds and Scheibel, 1989).

Furthermore, the neuropsychological anomalies encountered in these children with cerebellar lesions are the same as those found in children with supratentorial cortical lesions, including the executive function deficits of children with lesions in the right and left pre-frontal associative regions (Marlowe, 1992), and alterations in communications and social relations in children with lesioned limbic structures (Chugani *et al*., 1996; DeLong and Heinz, 1997).

The reciprocal links connecting the cerebellum to these structures have been elucidated in a large number of studies (Schmahmann and Sherman, 1998): reciprocal connections between the cerebellum and cortical areas (here we shall consider only the frontal and pre-frontal areas, and the limbic regions) have been demonstrated from the frontal cortex to the cerebellum through the pons (Schmahmann and Pandya, 1995, 1997*a*, *b*) and vice versa through the thalamus (Schmahmann and Pandya, 1990, 1997*a*, *b*; Middleton and Strick, 1994, 1997), and reciprocal anatomical connections have been found between the para-hippocampal structures (Schmahmann and Pandya, 1993), the cingulate gyrus (Vilensky and van Hoesen, 1981) and the hypothalamus (Snider, 1950; Haines and Dietrichs, 1984).

The fact that the cerebellum forms part of a network of cerebro-cerebellar and cerebello-cerebral connections that process and mediate complex social and cognitive behaviours has been confirmed by studies of normal subjects performing different tasks (Barker *et al*., 1991; Schmahmann, 1991), and this makes it likely that the disorders following cerebellar pathologies are the consequence of the malfunctioning of a network of complex connections.

The fact that cerebellar damage causes deficits in the long term has been demonstrated by PET studies that have revealed areas of hypoperfusion in associative cortical areas (Botez-Marquand *et al*., 1996; Schmahmann and Sherman, 1998) and hypoperfusion in cerebellar areas in case of cerebral lesions (Pantano *et al*., 1986; Gomez Beldarrain *et al*., 1997).

It follows that it is impossible to determine whether the deficits described here are directly due to the cerebellar lesion or to the diaschisis arising from the sudden interruption of the reciprocal connections between the different cerebral regions and the cerebellum. The degree to which age-dependent factors affect the extent and duration of diaschisis has not yet been determined, but the improvement in function

observed in some of our cases (particularly those with vermal lesions) clearly shows that the alterations caused by cerebellar lesions are transient.

If the deficits in higher functions observed after cerebellar lesions can be interpreted as an effect of a major and more or less abrupt diaschisis of the cerebellar circuits of the supratentorial structures, it has to be concluded that the system of reciprocal cerebro-cerebellar connections is also operative in childhood (Jacobson, 1991).

Conclusions

Our results confirm the cognitive and behavioural deficits following cerebellar lesions reported in previous studies, but the more precise localization and homogeneity of the pathology has also made it possible to identify different neurobehavioural patterns related to the vermal or hemispheric site of the lesions themselves. These findings support the hypothesis of Schmahmann concerning a functional topography within the cerebellum (Schmahmann, 1991), and suggest that this topography becomes operative at an early stage. The existence of cognitive and social alterations profiles related to cerebellar tumours implies that these lesions are causally related to the generation of the deficits.

However, it cannot be concluded that the lesions *per se* are the direct cause, as it may be that their primary effect is to deprive the complicated network of interconnections between the cerebellum and the associative cortical areas of its ability to modulate the cerebellum itself, and thus its capacity to harmonize the behaviour of the various domains.

Furthermore, it needs to be remembered that many children have undergone the similar type of surgery for the same pathology without experiencing any post-surgical cognitive or behavioural alterations, or alterations that were so slight as to go unobserved. This means that the question must be even more complex, and that the more or less dramatic response to a cerebellar lesion and the associated problems of diaschisis from other supratentorial associative structures may also depend on a genetically different inter-subject neuronal organization.

Given the complexity of the problem, studies of larger samples of patients at different ages, including patients with no or minor symptoms, but with homogeneous lesions whose location can be precisely defined, are necessary before any definite conclusions can be drawn concerning the functional organization of the different areas of the cerebellum.

Acknowledgements

We wish to thank Dr Kevin Smart for helping with the English and Dr Vargha-Khadem for supervising the paper.

References

Andreoli V, Cassano GB, Rossi R, editors. DSM IV: Manuale diagnostico e statistico dei disturbi mentali. Milano: Masson; 1996.

Aram DM, Whitaker HA. Cognitive sequelae of unilateral lesions acquired in early childhood. In: Molfese DL, Segalowitz S, editors. The developmental implications of brain lateralization. New York: Guidford Press; 1988. p. 417–36.

Asanuna C, Trach WT, Jones EG. Distribution of cerebellar terminations and their relation to other afferent terminations in the ventral lateral thalamic region of the monkey. Brain Res 1983; 286: 237–65.

Baraitser M. Cerebellar syndromes. In: Baraitser M, editor. The genetics of neurological disorders. 2nd ed. 1990; p. 71–211.

Barker WW, Yoshii F, Loewenstein DA, Chang JY, Apicella A, Pascal S, et al. Cerebrocerebellar relationship during behavioral activation: a PET study. J Cereb Blood Flow Metab 1991; 11: 48–54.

Bauman ML, Kemper TL. Is autism a progressive process [abstract]? Neurology 1997; 48 (3 Suppl 2): A285.

Benton AL, Hamsher K de S. Multilingual Aphasia Examination. Iowa City (IA): AJA Associates; 1989.

Berman AF, Berman D, Prescott JW. The effect of cerebellar lesions on emotional behavior in the rhesus monkey. In: Cooper IS, Riklan M, Snider RS, editors. The cerebellum, epilepsy and behavior. New York: Plenum Press; 1974. p. 277–84.

Botez-Marquard T, Lèveillè J, Botez MI. Neuropsychological functioning in unilateral cerebellar damage. Can J Neurol Sci 1994; 21: 353–7.

Chugani HT, Da Silva E, Chugani DC. Infantile spasms: III. Prognostic implications of bitemporal hypometabolism on positron emission tomography. Ann Neurol 1996; 39: 643–9.

Courchesne E. Neuroanatomic imaging in autism. [Review]. Pediatrics 1991; 87: 781–90.

Courchesne E. Brainstem, cerebellar and limbic neuroanatomical abnormalities in autism. [Review]. Curr Opin Neurobiol 1997; 7: 269–78.

Cristante F, Lis A, Sambin M. Statistica per psicologi. Firenze: Giunti Barbera; 1992.

DeLong GR, Heinz ER. The clinical syndrome of early-life bilateral hippocampal sclerosis. Ann Neurol 1997; 42: 11–7.

De Renzi E, Vignolo LA. The Token Test: a sensitive test to detect receptive disturbances in aphasics. Brain 1962; 85: 665–78.

Duffner PK, Cohen ME. The long-term effects of central nervous system therapy on children with brain tumors. [Review]. Neurol Clin 1991; 9: 479–95.

Dunn LM, Dunn LM. Peabody Picture Vocabulary Test—Revised. Circle Pines (MN): American Guidance Service; 1981.

Ferrante L, Mastronardi N, Acqui M, Fortuna A. Mutism after posterior fossa surgery in children: report of three cases. [Review]. J Neurosurg 1990; 72: 959–63.

Fiez JA. Cerebellar contribution to cognition. Neuron 1996; 16: 13–5.

Fiez JA, Peterson SE, Cheney MK, Raichle ME. Impaired non-motor learning and error detection associated with cerebellar damage. A single case study. Brain 1992; 115: 155–78.

Ghez C, Fahn S. The cerebellum. In: Kandel ER, Schwartz JH, editors. Principles of neural science. 2nd ed. New York: Elsevier; 1985. p. 502–22.

Gillberg C, Coleman M. The biology of the autistic syndromes. London: MacKeith Press; 1992.

Gomez Beldarrain M, Garcia-Monco JC, Quintana JM, Llorens V, Rodeno E. Diaschisis and neuropsychological performance after cerebellar stroke. Eur Neurol 1997; 37: 82–9.

Grafman J, Litvan I, Massaquoi S, Stewart M, Sirigu A, Hallett M. Cognitive planning deficit in patients with cerebellar atrophy. Neurology 1992; 42: 1493–6.

Grant DA, Berg EA. Wisconsin Card Sorting Test. Odessa (FL): Psychological Assessment Resources; 1993.

Guzzetta F, Mercuri E, Bonanno S, Longo M, Spano M. Autosomal recessive congenital cerebellar atrophy: a clinical and neuropsychological study. Brain Dev 1993; 15: 439–45.

Haines DE, Dietrichs E. An HRP study of hypothalamo-cerebellar and cerebello-hypothalamic connections in squirrel monkey (Saimiri sciureus). J Comp Neurol 1984; 229: 559–75.

Heath RG, Franklin DE, Shraberg D. Gross pathology of the cerebellum in patients diagnosed and treated as functional psychiatric disorders. J Nerv Ment Dis 1979; 167: 585–92.

Ito M. The cerebellum and neural control. New York: Raven Press; 1984.

Jacobson M. Developmental neurobiology. 3rd ed. New York: Plenum Press; 1991.

Jones-Gotman M, Milner B. Design fluency: the invention of nonsense drawings after focal cortical lesions. Neuropsychologia 1977; 15: 653–74.

Kaplan E, Goodglass H, Weintraub S. The Boston Naming Test. Philadelphia: L & Febiger; 1983.

Kennard MA. Relation of age to motor impairment in man and subhuman primates. Arch Neurol Psychiat 1940; 44: 377–97.

Kim SG, Ugurbil K, Strick PL. Activation of a cerebellar output nucleus during cognitive processing. Science 1994; 265: 949–51.

Kirk SA, McCarthy JJ, Kirk WD. Illinois Test of Psycholinguistic Abilities. Urbana (IL): Stoelting University of Illinois Press; 1968.

Leiner HC, Leiner AL, Dow RS. Cognitive and language functions of the human cerebellum. [Review]. Trends Neurosci 1993; 16: 444–7.

Levisohn L, Cronin-Golomb A, Schmahmann JD. Neuropsychological sequelae of cerebellar tumors in children [abstract]. Soc Neurosci Abstr 1997; 23: 496.

Lezak MD. Neuropsychological assessment. 3rd ed. New York: Oxford University Press; 1995.

MacWhinney B. The CHILDES project: tools for analyzing talk. Hillsdale (NJ): Lawrence Erlbaum; 1991.

Marlowe WB. The impact of a right prefrontal lesion on the developing brain. Brain Cogn 1992; 20: 205–13.

Martin P, Albers M. Cerebellum and schizophrenia: a selective review. [Review]. Schizophr Bull 1995; 21: 241–50.

Middleton FA, Strick PL. Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. Science 1994; 266: 458–61.

Middleton FA, Strick PL. Cerebellar output channels. [Review]. Int Rev Neurobiol 1997; 41: 61–82.

Nardocci F, Stella G, Ferrari E, Gibertoni M, Ciotti F, Papperini M. Italian translation of the Illinois Test of Psycholinguistic Abilities. Turin: OMEGA; 1997.

Pantano P, Baron JC, Samson Y, Bousser MG, Derouesne C, Comar D. Crossed cerebellar diaschisis: further studies. Brain 1986; 109: 677–94.

Piven J, Saliba K, Bailey J, Arndt S. An MRI study of autism: the cerebellum revisited. Neurology 1997; 49: 546–51.

Pollack IF, Polinko P, Albright AL, Towbin R, Fitz C. Mutism and pseudobulbar symptoms after resection of posterior fossa tumors in children: incidence and pathophysiology. [Review]. Neurosurgery 1995; 37: 885–93.

Rekate HL, Grubb RL, Aram DM, Hahn JF, Ratcheson RA. Muteness of cerebellar origin. Arch Neurol 1985; 42: 697–8.

Riva D. Le lesioni cerebrali focali. In: Sabbadini G, editor. Manuale di neuropsicologia dell'età evolutiva. Firenze: Zanichelli; 1995a. p. 484–504.

Riva D. Technical Report of the Ministry of Health: criteri prognostici neuropsicolgici per la scelta del trattamento dei tumori cerebrali infantili. 1995b.

Riva D. The cerebellar contribution to language and sequential functions: evidence from a child with cerebellitis. Cortex 1998; 34: 279–87.

Riva D, Cazzaniga L. Late effects of unilateral brain lesions sustained before and after age one. Neuropsychologia 1986; 24: 423–8.

Riva D, Pantaleoni C, Milani N, Fossati Belani F. Impairment of neuropsychological functions in children with medulloblastomas and astrocytomas in the posterior fossa. Childs Nerv Syst 1989; 5: 107–10.

Riva D, Pantaleoni C, Milani N, Devoti M. Late sequelae of right versus left hemispheric lesions. In: Martins IP, editor. Acquired aphasia in children: acquisition and breakdown of language in the developing brain. Dordrecht: Kluwer Academic Publishers; 1991a. p. 213–24.

Riva D, Milani N, Pantaleoni C, Ballerini E, Giorgi C. Combined treatment modality for medulloblastoma in childhood: effects on neuropsychological functioning. Neuropediatrics 1991b; 22: 36–42.

Riva D, Nichelli F, Devoti M. Una batteria di valutazione del linguaggio orale nel bambino afasico: normative italiane e considerazione neuroevolutive (European Comunity Project: BIOMED '1': Developmental disorders). Giornale di Neuropsichiatria Infantile dell'Età Evolutiva 1999; 4: 321–32.

Riva D, Nichelli F, Devoti M. Developmental aspects of verbal fluency and confrontation on naming in children. Brain Lang. In press 2000.

Saitoh O, Courchesne E, Egaas B, Lincoln AJ, Schreibman L. Cross-sectional area of the posterior hippocampus in autistic patients

with cerebellar and corpus callosum abnormalities. Neurology 1995; 45: 317–24.

Schmahmann JD. An emerging concept: the cerebellar contribution to higher function. [Review]. Arch Neurol 1991; 48: 1178–87.

Schmahmann JD, Pandya DN. Anatomical investigation of projections from thalamus to posterior parietal cortex in the rhesus monkey: a WGA-HRP and fluorescent tracer study. J Comp Neurol 1990; 295: 299–326.

Schmahmann JD, Pandya DN. Prelunate, occipitotemporal, and parahippocampal projections to the basis pontis in rhesus monkey. J Comp Neurol 1993; 337: 94–112.

Schmahmann JD, Pandya DN. Prefrontal cortex projections to the basilar pons in rhesus monkey: implications for the cerebellar contribution to higher function. Neurosci Lett 1995; 199: 175–8.

Schmahmann JD, Pandya DN. The cerebrocerebellar system. [Review]. Int Rev Neurobiol 1997a; 41: 31–60.

Schmahmann JD, Pandya DN. Anatomic organization of the basilar pontine projections from prefrontal cortices in rhesus monkey. [Review]. J Neurosci 1997b; 17: 438–58.

Schmahmann JD, Sherman JC. The cerebellar cognitive affective syndrome. Brain 1998; 121: 561–79.

Silveri MC, Leggio MG, Molinari M. The cerebellum contributes to linguistic production: a case of agrammatic speech following a right cerebellar lesion. Neurology 1994; 44: 2047–50.

Silveri C, Di Betta AM, Filippini V, Leggio MG, Molinari M. Verbal short-term store-rehearsal system and the cerebellum. Evidence from a patient with a right cerebellar lesion. Brain 1998; 121: 2175–87.

Simonds RJ, Scheibel AB. The postnatal development of the motor speech area. Brain Lang 1989; 37: 42–58.

Snider RS. Recent contributions to the anatomy and physiology of the cerebellum. Arch Neurol Psychiat 1950; 64: 196–219.

Stanton GB, Goldberg ME, Bruce CJ. Frontal eye field efferents in the macaque monkey: II. Topography of terminal fields in midbrain and pons. J Comp Neurol 1988; 271: 493–506.

Stiles-Davis J, Janowsky J, Engel N, Nass R. Drawing ability in four young children with congenital unilateral brain lesions. Neuropsychologia 1988; 26: 359–71.

Thatcher RW, Walker RA, Giudice S. Human cerebral hemispheres develop at different rates and ages. Science 1987; 236: 1110–3.

Van Calenbergh F, Van de Laar A, Plets C, Goffin J, Casaer P. Transient cerebellar mutism after posterior fossa surgery in children. [Review]. Neurosurgery 1995; 37: 894–8.

van Dongen HR, Catsman-Berrevoets CE, van Mourik M. The syndrome of 'cerebellar' mutism and subsequent dysarthria. Neurology 1994; 44: 2040–6.

Vender C, Anghini DA, Cumer Bruno S, Borgia R, Zardini G. Contributo allo studio del Token Test in età evolutiva. Neuropsichiatria Infantile 1979; 215: 436–9.

Vilensky JA, van Hoesen GW. Corticopontine projections from the cingulate cortex in the rhesus monkey. Brain Res 1981; 205: 391–5.

Wechsler D. WISC-R: Scala d'intelligenza per bambini riveduta. Firenze: Organizzazioni Speciali; 1986.

Received November 8, 1999. Revised January 28, 2000.
Accepted January 31, 2000