

Neuropsychological long-term sequelae after posterior fossa tumour resection during childhood

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Summary

The importance of the cerebellum for non-motor functions is becoming more and more evident. The influence on cognitive functions from acquired cerebellar lesions during childhood, however, is not well known. We present follow-up data from 24 patients, who were operated upon during childhood for benign cerebellar tumours. The benign histology of these tumours required neither radiotherapy nor chemotherapy. Post-operatively, these children were of normal intelligence with a mean IQ of 99.1, performance intelligence quotient (PIQ) of 101.3 and verbal intelligence quotient (VIQ) of 96.8. However, 57% of patients showed abnormalities in subtesting. In addition, more extensive neuropsychological testing revealed significant problems for attention, memory, processing speed and interference. Visuo-constructive problems were marked for copying the Rey figure, but less pronounced for recall of the figure. Verbal fluency was more affected than

design fluency. Behavioural deficits could be detected in 33% of patients. Attention deficit problems were marked in 12.5%, whereas others demonstrated psychiatric symptoms such as mutism, addiction problems, anorexia, uncontrolled temper tantrums and phobia. Age at tumour operation and size of tumour had no influence on outcome. Vermis involvement was related to an increase in neuropsychological and psychiatric problems. The observation that patients with left-sided cerebellar tumours were more affected than patients with right-sided tumours is probably also influenced by a more pronounced vermian involvement in the former group. In summary, this study confirms the importance of the cerebellum for cognitive development and points to the necessity of careful follow-up for these children to provide them with the necessary help to achieve full integration into professional life.

Keywords: cerebellum; posterior fossa tumour; cognition; intellect; behaviour

Abbreviations: FS IQ = full scale intelligence quotient; HAWIK-R and HAWIE-R = Hamburg–Wechsler intelligence scale for children (revision 1983) and adults (revision 1991); PIQ = performance intelligence quotient; RVDLT = Rey visual design learning test; VIQ = verbal intelligence quotient; VLMT = Verbal learning memory test

Introduction

The importance of the cerebellum for non-motor functions such as language, thought modulation, emotions and the ability to plan is becoming more and more evident (Schmahmann, 1991; Schmahmann and Sherman, 1998; Fiez *et al.*, 1992; Leiner *et al.*, 1993). In their study of adult patients, Schmahmann and colleagues introduced the term 'cerebellar cognitive affective syndrome', characterized by the four major problems of executive function, impaired spatial cognition, linguistic difficulties and personality changes. An increasing number of clinical studies have confirmed cognitive deficits in children with congenital or acquired cerebellar problems (Steinlin *et al.*, 1999; Riva and

Giorgi, 2000; Levisohn *et al.*, 2000; Karatekin *et al.*, 2000). In our previous study (Steinlin *et al.*, 1999), we could show that children with congenital non-progressive cerebellar ataxia have decreased full-scale IQ varying between 30 and 90. Patients with IQ above 60 revealed in further neuropsychological testing a better verbal than non-verbal performance and major problems in visuospatial tasks. Posterior fossa tumours are relatively common and account for half of all brain tumours in children. Many studies show outcome after cerebellar tumours, but results are influenced by further treatments such as radiotherapy or chemotherapy (Konrad *et al.*, 1998). Riva and Giorgi (2000) have shown neuropsy-

chological problems a few weeks after cerebellar tumour resection, prior to further treatment such as radiotherapy or chemotherapy. Their results reveal a localization related pattern, with problems of auditory sequential memory and language processing after right-sided cerebellar tumour and deficits in spatial and visual memory after left-sided tumour. Lesions to the vermis led to post-surgical mutism, which evolved into speech and language disorders as well as behavioural disturbances ranging from irritability to those reminiscent of mutism. Levisohn and colleagues presented a retrospective study of neuropsychological problems of children during the first 2 years after resection of a cerebellar tumour (Levisohn *et al.*, 2000). These children had problems comparable with the cognitive affective syndrome in adults with dysfunction of visual-spatial tasks, language sequencing, memory and regulation of affect. There was no localization related pattern as in the patients of Riva and Giorgi (2000). Karatekin *et al.* (2000) studied the effect of isolated cerebellar hemispheric tumours post-operatively and compared them with the effect of temporal tumours. After cerebellar lesions, children had a neuropsychological pattern characterized by executive function problems, which was different to those who had suffered temporal tumours. The aim of our study is to analyse long-term consequences of patients who have undergone isolated cerebellar tumour resection, without adjuvant chemotherapy or radiation therapy, during childhood. The main aims were to determine patterns of neuropsychological problems, the role of age at diagnosis/operation and the role of tumour localization.

Patients and methods

Patients

Between 1981 and 1998, 46 children underwent surgical resection of a cerebellar tumour without radiotherapy or chemotherapy at the Children's University Hospitals of Bern and Zurich. Thirty-five could still be contacted and 27 were willing to undergo more extensive neuropsychological testing. From these 27 children, two were excluded due to severe psychomotor retardation, which rendered neuropsychological testing impossible. In both children, cerebellar tumours were incidentally diagnosed during evaluation of longstanding developmental problems. In one, a pilocytic astrocytoma was resected 1 year after diagnosis. There had been no obvious tumour growth during that year. In the second case, the tumour was never removed and showed no changes over a 10-year follow up (probably haemangioblastoma). One patient was only 4.5 years at the time of the study. He had a full-scale IQ of 112 in Kaufman assessment battery for children testing, but was too young to undergo more extensive neuropsychological testing.

Hence 24 patients (seven girls/women and 17 boys/men) entered the study. They were aged between 7.6 and 26.7 years with an average of 15.04 years. Age at operation/diagnosis (tumour biopsy was performed in one child only) was

between 3.6 and 15.5 years with an average of 8.25 years. Follow-up after tumour operation was between 2.1 and 18.25 years with an average of 7.5 years. The social class of the patients was defined as in the study by De Spiegelare and colleagues (De Spiegelare *et al.*, 1998): group 1 parents were members of upper management and professional groups; group 2 were white collar workers; group 3 were self-employed individuals and technicians; group 4 were manual workers; and group 5 were unemployed. Of the 24 patients, five belonged to group 1, three to group 2, four to group 3 and 12 to group 4.

Detailed clinical neurological data are summarized in Table 1, together with the results of a standardized neuromotor assessment, as suggested by Largo to quantify the motor handicap of the limbs (Largo *et al.*, 2000). Fine motor testing with a pegboard was performed twice with each hand. Despite only minimal fine motor problems at clinical examination (as mild tremor) and almost no subjective problems, this test yielded an overall mild motor handicap. Fifteen of the 22 tested patients showed at least two out of the four tests to be >1 SD from the norm. The two results of the dominant hand are listed in Table 1.

Informed consent was given by patients and/or parents and the study was approved by the ethics committee of the Canton of Bern, Switzerland.

Brain tumours

Histology of the brain tumours revealed pilocytic astrocytomas in all but five patients. There were two children with choroid plexus papilloma originating from the fourth ventricle and one child each with astrocytoma grade II, gangliocytoma and haemangioblastoma. These data are summarized in Table 2, together with pre- and post-operative imaging findings. Subgroups of localization were defined as follows: (i) right-sided tumour resection without damage of the vermis; (ii) right-sided tumour resection with damage of the vermis; (iii) left-sided tumour resection with damage of the vermis (Fig. 1); and (iv) vermis resection showing atrophy without significant hemispheric damage (Fig. 2).

Neuropsychological assessment

Neuropsychological assessment was performed in all patients by two neuropsychologists (S.I. and P.Z.) during one or two sessions of 2–4 h each at the hospital. Sessions lasting longer than 2 h were interrupted by a break of ~30 min. The different tests were always performed in the same order.

Due to the diversity of age and gender in our group, evaluation of results was correlated with published reference values for age and transferred to *z*-values for comparison. Subtests of intelligence quotient are given in points (mean 10; SD ± 3).

Table 1 Summary of clinical findings

| Patient | Age at diagnosis | Age at test | Pre-operative findings | Follow-up | FM FU |
|---------|------------------|-------------|--|--|-------|
| 1 | 4 3/4 | 7 1/2 | HA, VO, R-sided ataxia | R-predom dysdiadocho | 0/1 |
| 2 | 3 1/2 | 8 | HA, VO, HT, PO, mild truncal ataxia | minimal truncal ataxia | – |
| 3 | 5 3/4 | 8 1/3 | VO, PO | mild truncal ataxia | 3/3 |
| 4 | 8 | 8 3/4 | HA VO PO mild truncal ataxia, dysmetria | normal | 3/3 |
| 5 | 5 | 8 3/4 | HA, VO, appetite ↓, vigilance ↓ | mild truncal ataxia | 1/1 |
| 6 | 5 3/4 | 10 1/2 | HA, HT hemi R, aggressive po: extended somnolence, VI palsy | mild hemi R | – |
| 7 | 6 1/2 | 12 | HA, VO, PO, VII + VI L, ataxia L-predom | increased processing time | 1/1 |
| 8 | 7 3/4 | 12 | HA, VO, PO po: extended somnolence, VII bil, VI L, affect lability, ataxia | depressive, mutism mild truncal ataxia, tremor bil | 0/0 |
| 9 | 12 1/4 | 12 3/4 | Diplopia, limited gaze to R | nystagmus to R | 0/0 |
| 10 | 5 3/4 | 13 1/4 | HA, VO, diplopia, mild truncal ataxia | R dysmetria | 2/2 |
| 11 | 9 1/2 | 14 | tired, aggressive, V, VI, VII L, mild truncal and R-sided ataxia | ADHD mild V+ VII L mild ataxia L | 2/1 |
| 12 | 12 | 14 | HA, PO?, ataxia R-predom | phobias, fears, tremor R | 2/1 |
| 13 | 7 3/4 | 15 1/3 | VO, mild truncal + L sided ataxia | slow, stiff movements | 1/1 |
| 14 | 4 1/4 | 15 1/2 | HA, VO, HT, PO, mild truncal ataxia | minimal dysmetria | 0/0 |
| 15 | 11 3/4 | 15 3/4 | HA VO, PO, mild truncal ataxia, vertical nystagmus, disturbed saccades, anorexia, mutism | mild hemi R, dysmetria R | 1/0 |
| 16 | 14 | 16 | HA, VO, PO, dysmetria R | dysdiadocho R | 3/1 |
| 17 | 10 1/3 | 17 2/3 | HA, VO, PO, truncal ataxia | normal | 1/1 |
| 18 | 9 1/2 | 18 1/4 | HA, VO, PO, diplopia, temper tantrums | temper tantrums, ataxia L | 2/1 |
| 19 | 8 1/3 | 18 1/4 | HA, VO, PO, diplopia | increased processing time | – |
| 20 | 7 | 20 1/4 | HA, VO, PO, mild truncal ataxia and bilateral tremor | rotatory nystagmus, minimal R-ataxia | 3/3 |
| 21 | 5 3/4 | 22 | activity ↓, mild ataxia and possible Babinkipo: confusions + seizure | no exact information | 0/0 |
| 22 | 4 1/4 | 22 1/2 | HA, VO, HT, PO, minimal ataxia | no exact information | 0/0 |
| 23 | 10 3/4 | 25 | HA, dysdiadocho | dysdiadocho | 1/0 |
| 24 | 15 1/2 | 26 1/2 | HA, VO, weight loss | normal | 0/0 |

ADHD = attention deficit hyperactivity disorder; bil = bilateral; dysdiadocho = dysdiadochokinesis; FM FU = Finemotor follow-up, standard deviations from norm for dominant hand (two tests); HA = headache; hemi = hemisindrome with pyramidal signs; HT = head tilt; L = left-sided; PO = papilloedema; po = post-operative; predom = predominant; R = right-sided; VO = vomiting.

Neuropsychological tests

All tests administered are summarized in Table 3, together with normal values and references. Chosen tests were, on the whole, identical to tests we administered in a previous study for evaluation of cognitive impairments in patients with non-progressive congenital ataxia (Steinlin *et al.*, 1999).

Verbal and performance IQ was tested by HAWIK-R and HAWIE-R [Hamburg–Wechsler intelligence scales for children (revision 1983) and adults (revision 1991)], respectively. These are the German versions of the Wechsler intelligence scales (Tewes, 1983, 1994, respectively). Attention was assessed by the TAP test (Testbatterie zur Aufmerksamkeitsprüfung)—three tests of a computer-supported test series by Zimmermann and Fimm (1973): (i) alertness by the reaction to visual stimuli with and without acoustic warning; (ii) selective attention by selective reaction to predetermined stimuli mixed in a series of irrelevant stimuli; and (iii) sustained visual attention (10 min), which was tested at the end of the half day by marking irregular optic stimuli in a series of regular optic stimuli.

Learning, memory and executive functions were tested as summarized in Table 3. Normal values were given only for

ages >18 years for the block board test (a test of visual and spatial memory). For younger patients <5 years, correct tappings were considered abnormal (Schellig, 1997). For verbal fluency, generating words beginning with the letters F/S or FBL, or animal naming was utilized depending upon the age of patients. For the Five Point test, normal values for divergent thinking were only available for ages <14 years. For older patients, we administered the highest given normal values (Regard *et al.*, 1982). For perseveration (repeated figures compared with number of total figures), a score <10 is considered to be normal for all ages. Testing habitual response in favour of an unusual one by the Stroop test (Osterrieth, 1944) was only possible in patients who were able to read.

Statistical analyses

We calculated for mean values of the group and SDs and used the *t*-test and ANOVA (analysis of variance) for analyses of significance in parametric groups. The Mann–Whitney *U* test and Kruskal–Wallis test were used to analyse data that did not fulfil the requirements of

Table 2 Summary of histology and MRI/CT findings

| Patient | Histology | Tumour localization/size | SL* | Hydropre-operative | Vermis post-operative | Hemispheres post-operative |
|---------|-----------|--------------------------|-----|--------------------|--------------------------|----------------------------|
| 1 | PA | R/5 × 4 cm | 1 | + | normal | small resection R median |
| 2 | PA | R | 2 | 0 | atrophy | resection R 1/3 |
| 3 | PA | ML/7.5 cm | 2 | 0 | median resection | resection R 2/3 |
| 4 | PA | ML→L/4 cm | 3 | + | atrophy | resection L 1/4 |
| 5 | PA | ML→L/5 × 5 cm | 4 | +++ | median resection | atrophy |
| 6 | PA | ML/4 × 5 cm | 3 | +++ | superior resection | resection L 1/4 |
| 7 | PA | L/5 cm | 3 | ++ | atrophy | resection L 1/6 |
| 8 | PA | No information | 3 | | median resection | resection L |
| 9 | GC | ML→R/6 × 4 cm | 4 | 0 | resection lower parts | resection ML |
| 10 | PA | ML→R/5 cm | 2 | +++ | resection superior parts | resection ML-R 1/8 |
| 11 | PP | ML/4 cm | 4 | +++ | superior atrophy | normal |
| 12 | PA | R/6 cm | 1 | + | normal | resection R >3/4 |
| 13 | PA | ML→L/4 × 5 cm | 3** | 0 | no information | no information |
| 14 | PA | ML→L/5 cm | 3** | 0 | no information | no information |
| 15 | PA | R→ML/5 × 3.5 cm | 2 | +++ | atrophy | resection R |
| 16 | HB | R/6 × 4 × 5 cm | 2 | 0 | atrophy | resection R 1/3 |
| 17 | PA | R/3 × 7.5 | 1** | + | no information | no information |
| 18 | PA | L→ML/5 × 4 cm | 3 | +++ | atrophy | resection L 1/8 |
| 19 | PA | R/7 × 7 cm | 3 | ++ | atrophy | resection L 2/3 |
| 20 | PA | ML/7 × 7 cm | 2 | 0 | median resection | resection R 3/4 |
| 21 | PP | R/4 × 3 cm | 4 | 0 | atrophy superior parts | atrophy |
| 22 | PA | R/4 cm | 1 | +++ | normal | resection R minimal |
| 23 | PA | R→ML/7.5 × 5 cm | 2 | + | resection lower parts | resection R 3/4 |
| 24 | Astro II | R/big | 1** | + | no information | no information |

**Localization by pre-operative findings. SL* = subgroups of localization: 1 = right sided lesion; 2 = right sided and vermal lesion; 3 = left sided and vermal lesion; 4 = vermis atrophy or resection. + = mild; ++ = significant; +++ = with periventricular CSF leak; ++++ = severe with herniation. Astro = astrocytoma; GC = gangliocytoma; HB = haemangioblastoma; L = left-sided; ML = midline; PA = pilocytic astrocytoma; PP = plexus papilloma; R = right-sided.

parametric testing. Only parametric results are reported if there was no difference between the parametric and nonparametric analyses. The Kolmogorov–Smirnov test was used to control for normal distribution. The χ^2 -test (Bortz, 1993) was used to compare variance of the patient group with the normal population. Finally, we correlated subtest results to see whether any correlation existed between any of the neuropsychological functions.

Results

Intelligence

Mean full scale IQ together with verbal intelligence quotient (VIQ) and performance intelligence quotient (PIQ) are summarized in Table 4. Only three patients had full-scale IQ values below 85 (two patients of 68 and one of 72). Mean values for all subtests of HAWIK are shown in Fig. 3, revealing lower than normal values for subtests of verbal performance, significantly abnormal for digit span ($t = -1.91$ and $P < 0.05$) and vocabulary ($t = -2.38$ and $P < 0.025$). Out of the 21 patients with full-scale IQ values >85 , only seven had no subtests with <7 points and seven patients had 3–5 subtests with <7 points.

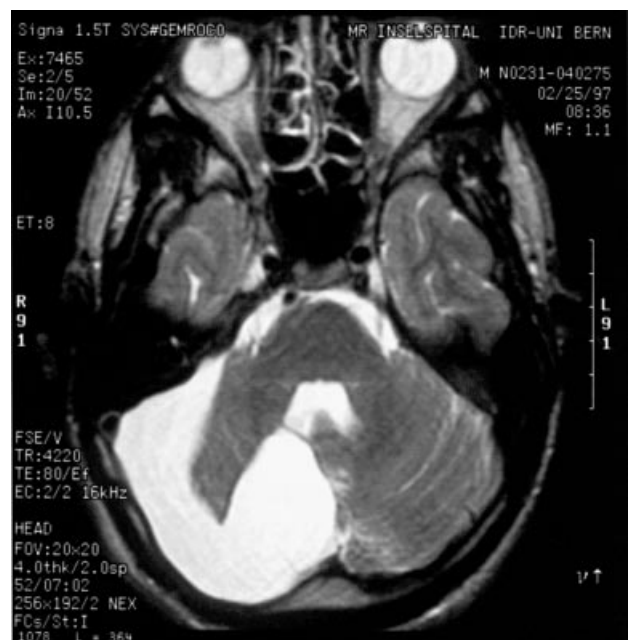


Fig. 1 Axial T₂ weighted image at the level of the posterior fossa [4 mm thick slice; TR (transition time) = 4220 ms; TE (echo time) = 80 ms; FOV (field of view) = 200 mm], demonstrating a partial resection of the right sided cerebellar hemisphere including a significant lesion of the midline (Patient 23).

Attention and processing speed

In the test for phasic alertness, the patients showed a mean z-value of -0.27 (SD 0.84). In selective attention (Go/No Go test) and in divided attention, mean z-values were -0.561 (SD 0.96) and -0.591 (SD 0.97) respectively. Processing speed in the whole group revealed a z-value of 0.57 (SD 1.03). There was a significant deviation from the norm for selective



Fig. 2 Sagittal T₁ weighted image (5 mm thick slice; TR = 440 ms; TE = 19 ms; FOV = 220 mm) demonstrating partial resection of the vermis (Patient 20).

attention and processing speed ($P < 0.01$) and for divided attention ($P < 0.005$), with a trend of significance ($P < 0.1$) for phasic alertness.

Memory and learning

Immediate recall (block board test and digit span) showed mean z-values of -0.19 (SD 1.17) and mean subtest values of 8.8 (SD 2.28). There was significant deviation from the norm for digit span, with $P < 0.05$. The block board test was difficult to evaluate. Patients >18 years all gave normal z-values. Six out of 13 of the younger patients (<16 years) had abnormal results. Four of the five patients <10 years showed abnormal values, although the validity of reference values for younger patients might not be adequate.

Subtest results of semantic memory (information, vocabulary and picture completion) revealed mean values of 9.0 (SD 3.08), 8.5 (SD 2.73) and 10.2 (SD 3.48), respectively, with significance of abnormality only for vocabulary ($P < 0.05$).

Verbal free recall, recognition and learning [verbal learning memory test (VLMT)] in all except three patients were

Table 4 Summary of full-scale, verbal and performance IQ of all patients

| | Mean value (SD) | t-test | Abnormal n (percentage) |
|----------------|-----------------|--------|-------------------------|
| Full scale IQ | 99.1 (15.38) | -0.28 | 3 (12.5) |
| Verbal IQ | 96.8 (16.14) | -1.05 | 6 (25) |
| Performance IQ | 101.3 (16.53) | 0.44 | 3 (12.5) |

Table 3 Tests performed, their normal values and literature references

| Test | Function tested | Name of test | Normal values | References |
|----------------------------|-----------------------------|---|-----------------|---|
| FS IQ | VIQ and PIQ | HAWIK-R (1983)/HAWIE-R (1991) | 100 ± 15 | Tewes, 1983, 1994 |
| Executive functions | Verbal fluency/roduction | Words with F/S/FBL and animals | 0 ± 1 | Földeny, 1987 |
| | Suppression of interference | Stroop test | 0 ± 1 | Osterrieth, 1944; Wehrli, 1980 |
| | Design fluency | Five-point test | 0 ± 1/<10 | Regard <i>et al.</i> , 1998 |
| Memory | Similarities | HAWIK-R/HAWIE-R | 10 ± 3 | Tewes, 1983, 1994 |
| | Vocabulary | HAWIK-R/HAWIE-R | 10 ± 3 | Tewes, 1983, 1994 |
| | General | HAWIK-R/HAWIE-R | 10 ± 3 | Tewes, 1983, 1994 |
| | Verbal learning and memory | Verbal learning memory test (VLMT) | 0 ± 1 | Schweissthal, 1997 |
| | Visual learning and memory | Rey visual design learning test (RVDLT) | 0 ± 1 | Rey, 1964 |
| | Recall complex figure data | Rey-Osterrieth complex figure test | 0 ± 1 | Spreen, 1991; Osterrieth, 1944 |
| Attention/processing speed | Digit span | HAWIK-R/HAWIE-R | 10 ± 3 | Tewes, 1994 |
| | Visual and spatial memory | Block board test | >4/0 ± 1 | Schellig, 1997 |
| | Alertness | Computer-supported test series by Zimmermann and Fimm (TAP) | 0 ± 1 | Zimmermann and Fimm, 1973; Kunert, 1996 |
| | Selective attention | | | |
| Other tests | Sustained attention | | | |
| | Processing speed | Number connection test | 0 ± 1 | Oswald and Roth, 1978 |
| | Naming | Token test | 0 (n of errors) | De Renzi <i>et al.</i> , 1962; Gutbrod and Michel, 1986 |
| | Copying | Rey-Osterrieth complex figure test | 0 ± 1 | Wehrli, 1980 |

within normal limits with mean *z*-values of 0.8 (SD 0.71), 0.4 (SD 0.63) and 3.3 (SD 0.71), respectively. However, all three patients with *z*-values <0 were tested in a language other than their mother tongue, which might have influenced their results. Visual free recall and recognition [Rey visual design learning test (RVDLT)] was normal with mean *z*-values of 1.16 (SD 0.68) and 1.43 (SD 0.87).

Recall of the Rey figure was abnormal in six patients; the mean *z*-value was -0.66 (SD 1.19). See below for comparison of copying and recall of the Rey figure.

Executive functions

Verbal fluency assessed by the F/S and FBL-test showed a mean *z*-value of -0.81 with a large SD of 1.46. There was a significant deviation from the normal population with *P* < 0.001. Design fluency was normal for all but two patients with *z*-values of -1.3 and -2.0. The mean *z*-value was 0.67 (*P* > 0.05); however, for this test there was a significant SD of

1.26 (*P* < 0.05). Perseveration for this test was abnormal in six out of 24 patients (25%). Test for interference (Stroop test) was abnormal for all three subtests: reading of coloured words showed a mean *z*-value of -1.25 (SD 1.1), reading of coloured lines -1.37 (SD 1.08) and interference -1.19 (SD 1.4). All three subtests were abnormal with *P* < 0.001. Large standard deviations for all three subtests reveal the increased scattering of the group. Results for similarities are shown in Fig. 3.

Further testing

Naming by the Token test showed these patients to have no problems; *z*-values were all within the norm.

Copying of the Rey figure was the most affected function for these patients. The mean *z*-value for copying was -1.92 (SD 1.21), this being significantly worse than mean *z*-value for later recall of the figure (*P* < 0.001 versus *P* < 0.01).

Summary of test results

A summary of all results with statistically significant deviations from the norm in different subtests is given in Table 5. This reveals that memory, attention, visual-spatial abilities and interference are especially affected. Although most patients had normal values for full-scale IQ and needed no special schooling, these partial neuropsychological deficits were not without importance in the daily life of these patients. Many parents report additional school problems for these children compared with their siblings and adult patients complain about these mild deficits.

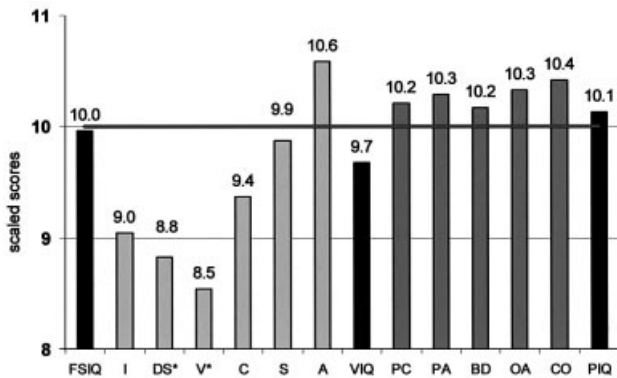


Fig. 3 Mean values of subtest in HAWIK-R or HAWIE-R in all patients. Bold horizontal line represents the normal values. A = arithmetic; BD = block design; DS = digit span; I = information; PA = picture arrangement; PC = pictures completion; S = similarities; OA = object assembling; SS = symbol search; V = vocabulary.

Age

Figure 4 shows the comparison of subtest values of HAWIK-R or HAWIE-R for the following three age groups: age at diagnosis/operation for group 1, the preschool group, was 3.5–6.5 years (*n* = 10); for group 2, the early school age

Table 5 Overview on statistically significant abnormal results of different cognitive functions of all patients

| Cognitive function | Test | <i>t</i> -test | Level of significance |
|----------------------|--------------------------------|----------------|-----------------------|
| Immediate memory | Digit span (DS) | -1.91 | <i>P</i> < 0.05 |
| Semantic memory | Vocabulary (V) | -2.38 | <i>P</i> < 0.05 |
| Free recall (visual) | RVDLT* | 3.67* | <i>P</i> < 0.01 |
| Recognition (visual) | RVDLT* | 5.72* | <i>P</i> < 0.001 |
| Visual memory | Rey-Osterrieth figure (recall) | -3.29 | <i>P</i> < 0.005 |
| Selective attention | TAP (Go/Nogo) | -2.69 | <i>P</i> < 0.01 |
| Divided attention | TAP (divided attention) | -3.34 | <i>P</i> < 0.005 |
| Processing speed | Number connection test | -2.79 | <i>P</i> < 0.01 |
| Visuo-constructive | Rey-Osterrieth figure (copy) | -9.39 | <i>P</i> < 0.001 |
| Verbal | F-test, FBL-test | -3.88 | <i>P</i> < 0.001 |
| Interference | Stroop test | -4.91 | <i>P</i> < 0.001 |

*Performance compared with normal population superior; all other tests show inferior performance.

group, it was 7–9.5 years ($n = 7$); and for group 3, it was 10–15.5 years ($n = 7$). Figure 4 reveals that group 2 was most affected for almost all subtest functions, but most pronounced for subtests of verbal performance. In addition, group 2 was also slightly more disturbed for memory and learning as seen in verbal free recall and recognition. However, a significant difference between the three groups was only reached for information, where group 2 with a mean value of 7.57 was significantly more disturbed than group 3 with a mean value of 10.29 ($P < 0.05$). These data were in contrast to the data for alertness, with group 3 being most disturbed (mean z -values of 0.2 for group 1, 0.43 for group 2 and -0.99 for group 3), with $P < 0.05$ for the comparison of group 1 or 2 with group 3.

Localization

The mean full-scale intelligence quotient (FS IQ) of the whole group was 99.1; patients with right-sided tumours

showed a mean FS IQ of 105.8 and those with left-sided tumours a mean FS IQ of 91.9. The mean PIQ was 101.3; in children with right-sided tumours, the mean was 104.2 and, in those with left-sided tumours, it was 97.7. The difference between children with right-sided and left-sided tumours was more pronounced with respect to VIQ (103.9 versus 88.2; overall mean 96.8). Table 6 gives an overview of statistically significant differences of functions with respect to tumour lateralization. FS IQ in respect to subgroups of localization of residual cerebellar lesions showed an effect of lateralization of tumour, but also an important effect of vermis involvement (as shown in Fig. 5 and especially Fig. 6). However, these results only reached statistical significance for influence of localization on subgroups with selective attention ($P = 0.0093$) and a trend of significance for digit span ($P = 0.027$).

A correlation matrix between subtests revealed high correlations ($r > 0.5$) between (i) arithmetic, digit span, block tapping, and (ii) copy and recall of the complex figure

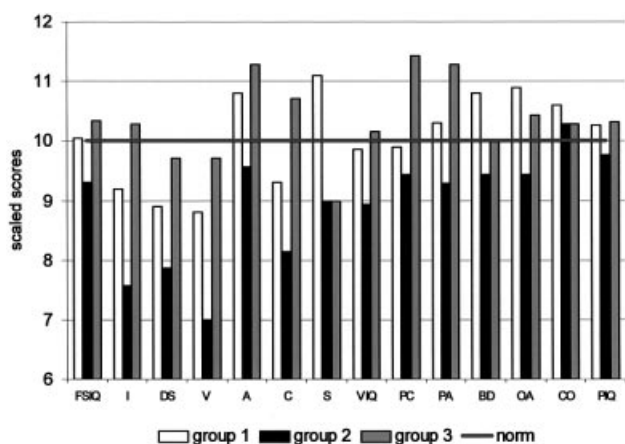


Fig. 4 Comparison of subtest values of HAWIK-R or HAWIE-R in different age groups. A = arithmetic; BD = block design; C = comprehension; CO = codes; DS = digit span; I = information; PA = picture arrangement; PC = pictures completion; S = similarities; OA = object assembling; V = vocabulary; VIQ = verbal intelligence quotient; PIQ = performance intelligence quotient.

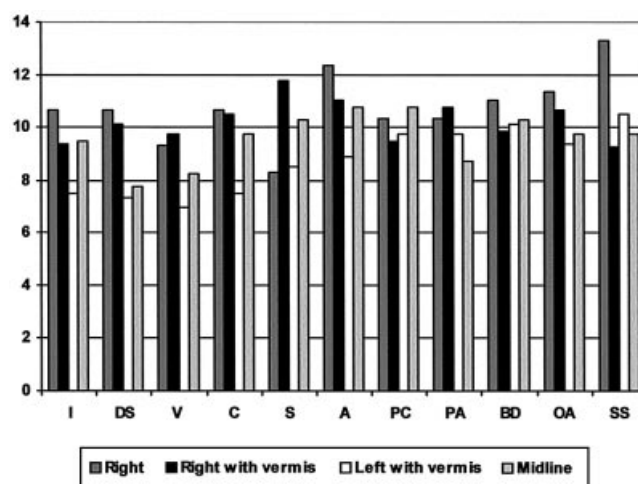


Fig. 5 Mean values for subtests related to localization of tumour. A = arithmetic; BD = block design; C = comprehension; DS = digit span; I = information; PA = picture arrangement; PC = pictures completion; S = similarities; OA = object assembling; SS = symbol search; V = vocabulary.

Table 6 Overview of statistically significant differences in tests comparing results in patient with right- and left-sided lesions

| | Right-sided lesion Mean (\pm SD) | Left-sided lesion Mean (\pm SD) | t -test | U -test |
|----------------------------|--|---------------------------------------|-----------|-----------|
| Full scale IQ ¹ | 105.8 (10.26) | 91.9 (16.7) | -2.35* | |
| Verbal IQ ¹ | 103.9 (8.93) | 88.2 (19.34) | | 25.50+ |
| Information ² | 10.0 (2.83) | 7.7 (2.55) | -1.92+ | |
| Vocabulary ² | 9.9 (2.02) | 7.0 (3.80) | -2.19* | |
| Digit span ² | 10.2 (2.18) | 7.7 (1.58) | -2.89** | |
| Figures ² | 11.5 (1.86) | 9.11 (2.42) | -2.54* | |
| Stroop B ³ | -0.89 (0.74) | -1.93 (1.176) | -2.01+ | |
| Stroop C ³ | -0.39 (0.65) | -1.86 (15.10) | | 13.00+ |

¹Value in IQ points, norm 100 ± 15 ; ²Values in subtest scaled scores, norm 10 ± 3 ; ³ z -values, norm 0 ± 1 ; * $P < 0.05$; ** $P < 0.001$; + = trend to significance.

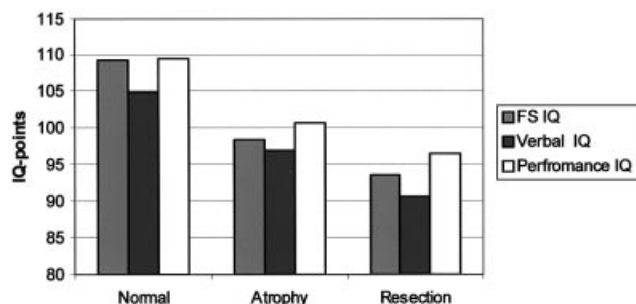


Fig. 6 FS IQ, verbal IQ and performance IQ related to residual vermis findings, showing normal vermis, atrophic vermis and resected vermis.

of Rey. For both subgroups of the tests, the scores were summarized to a combined score—the first group representing executive function tests and the second subgroup visual constructive function tests. Further statistical analyses by parametric ANOVA and non-parametric Kruskal–Wallis testing revealed the side location of the lesion in different test subgroups to be significant for executive function tests ($P = 0.011$ for ANOVA testing and $P = 0.021$ for Kruskal–Wallis testing), while lesion of the vermis showed a trend to significance for the visual–constructive function tests ($P = 0.056$ for ANOVA testing and $P = 0.075$ for Kruskal–Wallis test).

Psychopathology

Although no formal testing of behaviour was performed, eight out of 24 patients were diagnosed with special behaviour problems. These behaviour problems were evident during testing and/or from the patient's history. They were confirmed by previous psychological assessments or the patients received psychiatric treatment for these problems. Three children suffered from severe problems of attention deficit, which interfered significantly with their school performances. The other five patients had one of the following: selective mutism, phobia, anorexia, addiction to gambling or uncontrolled temper tantrums. It is possible, that with more extensive psychiatric exploration, even more patients would have been detected. It seems worth mentioning that all but one patient with behavioural or psychiatric problems had vermal lesions.

Discussion

Although FS IQ as well as VIQ and PIQ for the whole group show mean values within normal limits (100/97/101) and only five and three out of 24 children showed VIQ and PIQ values, respectively, below the normal, analyses of subtests and further tests reveal significant neuropsychological sequelae in children after resection of posterior fossa tumours. Analyses of subtests show two-thirds of our patients have deficits in selected domains of cognitive processing.

Thirty-six partial neuropsychological deficits were detected in 21 patients with normal full-scale IQ. This is significantly above the frequency of the general healthy population, where 4–7% of all children have partial neuropsychological deficits (Remschmidt, 1997). The fact that these children have a typical pattern of neuropsychological deficit rather than a diffuse dysfunction supports the idea that these problems are related to cerebellar lesion rather than a potential impact on intellectual and emotional development by psychological trauma induced by a major medical or neurosurgical disease. This assumption is further supported by the study of Karatekin *et al.* (2000), which showed that neuropsychological deficits of children after a cerebellar tumour differ from those seen in children after temporal tumours. The similarity of the pattern of abnormalities to those described by Schmahmann and Sherman (1998), as the cerebellar cognitive affective syndrome in adults, and to those demonstrated in similar studies in children after cerebellar tumours (Levisohn *et al.*, 2000; Riva and Giorgi, 2000) are additional points in favour of the existence of a cerebellar cognitive syndrome.

The most prominent problems within general intelligence tests were an impairment in the performance of digit span and vocabulary, which are subtests for short-term memory and semantic memory, respectively. Short-term memory was more frequently disturbed with an auditory verbal test (digit span) and less in a visual-spatial test (Black board test). These results confirm the findings of Riva and Giorgi (2000) and those of Levisohn *et al.* (2000). Short-term memory problems in patients with cerebellar abnormalities might be explained by the theory of Keele and Ivry (1990) that the cerebellum has an important role for timing. Due to aberrations in timing, the capability of encoding and organising the incoming information might be disturbed. The fact that the patients achieved a normal or even high normal performance in learning tests such as VLMT and RVDLT shows that they have normal abilities to learn numbers and figures when correct succession or timing was not mandatory. The difference between auditory–verbal and visual–spatial short-term memory might be explained by the additional influence of (mute) articulation speed for the capacity of remembering the numbers (Baddeley, 1990).

Alertness was normal in our patients during testing for phasic alertness, but there were difficulties noted in selective and, even more notably, for sustained attention. These findings are consistent with the results from Akshoomoff *et al.* (1992). These dysfunctions can also be seen in patients with frontal lesions. Sturm and Zimmermann (2000) showed that alertness in these patients is disturbed by increased interference, but also fixation on an expected result (perseveration). Additional tests in our patients (fluency test and Stroop interference test) led us to assume that alertness in patients with cerebellar disorders is disturbed by the same basic dysfunctions as in patients with frontal lesions. Sustained and selective attention are functions of the working memory, supporting the results of Mandolesi *et al.* (2001),

revealing that working memory is not only disturbed by frontal, but also by cerebellar lesions.

Further hints at frontal dysfunction are problems in organization and planning, as shown by verbal and design fluency. Verbal fluency is more affected than design fluency, possibly due either to the important function of semantic organization strategies in verbal fluency or to the effect of the cerebellum in word generation. Performance in design fluency was relatively low with an additional tendency to perseverate, revealing a deficit of inhibitory alertness and organization strategies. Executive functions of interference were disturbed for all three levels of interference in the Stroop test—a cerebellar dysfunction that was also shown by Fiez *et al.* (1992). Interference is a function of processing time and memory span. Patients with increased interference also show difficulties with attention (especially sustained attention) and vice versa. This illustrates that the difficulties of patients with cerebellar problems for attention, interference and processing time might aggravate each other reciprocally. Our patients confirm the growing evidence that cerebellar dysfunction includes a mild frontal dysfunction, explained by the cerebello-frontal connections (Grafman *et al.*, 1992; Leiner *et al.*, 1995; Schmahmann and Sherman, 1998).

There were significant difficulties in copying and recall of the Rey figure, confirming the results of Levisohn *et al.* (2000). The major difficulties in copying the Rey figure reveal significant planning and organization problems, but less pronounced visual-spatial memory problems. The fact that all but two patients improved significantly for recall compared with copying has to be interpreted as planning of copying the figure being significantly disturbed, which results in difficulty for memorising being due to primary insufficiency of copying. Difficulties in planning and organization tasks for cerebellar patients are largely explained by fronto-cerebellar pathways (Schmahmann and Pandya, 1995, 1997). However, the significantly pronounced difficulties in the planning and organization task of copying the Rey figure compared with other planning and organization tasks (for example, fluency) might be related to an additional dysfunction in the spatial domain. The most likely explanation is a disconnection of pathways from the cerebellum to the posterior parietal regions and vice versa (Brodal, 1978; Schmahmann and Pandya, 1989; Middleton and Strick, 1994).

The number connecting test is known to correlate well with full-scale IQ (Oswald and Roth, 1978). However, our patients demonstrated significant slowing for this function. Mild motor problems might influence this result, but articulation difficulties might also be involved in this dysfunction, as a mute naming of the numbers increases the speed for this test.

Results for semantic memory are a further clue for the importance of the cerebellum in word finding. Semantic memory was normal for pictures, but slightly disturbed for vocabulary and also information. There was a gap for vocabulary in children who suffered the acute episode of tumour treatment between the ages of 5 and 10 years, pointing

to the possibility that the cerebellum has an important impact, during this time, upon vocabulary development, as well as information.

More than 30% of our patients had psychopathological symptoms. This is in concordance with the study of Levisohn *et al.* (2000), where 32% of the children showed deficits in affect regulation. Over the last few years, several studies have pointed to the importance of the vermis in patients with psychopathological problems such as attention deficit hyperactivity disorder (Berquin *et al.*, 1998; Mostofsky *et al.*, 1998) and schizophrenia (Ackermann and Daum, 1995). The majority of our patients with psychopathological problems had an affected vermis—a finding that supports the postulation of Schmahmann and Sherman (1998) of a cerebellar limbic system within the vermis.

Left-sided tumour to right-sided tumour comparison reveals a difference for almost all different functions—the children with left-sided tumours being slightly more affected than those with right-sided tumours (Table 6). Most importantly, there was a difference for FS IQ (91 versus 106), vocabulary, digit span and figures. These data are contrary to the findings of Riva and Georgi (2000), where left-sided tumour led to more pronounced visual-constructive problems and right-sided tumours to more verbal problems. Comparison of our data with those of Riva and Georgi (2000) showed that the lesions of their children seemed to be more localized to one hemisphere, whereas the majority of our patients had significant involvement of the vermis. Figure 6 shows FS IQ, VIQ and PIQ in relation to extent of vermal lesion. Although statistically not significant, there is a tendency for vermal lesion to affect cognitive function. On reanalysing our data, it became obvious that our children with left-sided tumours had, in general, more significant vermal involvement than those with right-sided tumours. Therefore, it might be that, in our study, lateralization of dysfunction was overshadowed by vermal dysfunction.

Statistical analyses of the effect of localizations to specific neuropsychological functions are limited in our study and the results have to be discussed carefully. Adequate extension of residual lesion by MRI and, therefore, allocation to different subgroups was sometimes difficult. In addition, the numbers in the different groups were mostly small. However, there are still some interesting points, which are worth mentioning. The results of our study show that there is a tendency for left-sided lesions and vermal lesions to produce further neuropsychological deficits (Figs 5 and 6). Comparing the subgroup of executive functions to the subgroup of visual-constructive functions reveals left cerebellar hemispheres to be important for the executive functions ($P = 0.01$) and vermis to be more important for visual-constructive functions ($P = 0.06$).

Comparison with our previous data from patients with congenital non-progressive cerebellar ataxia (Steinlin *et al.*, 1999) showed a similar pattern of dysfunction for attention and executive functions. However, this recent study showed more dysfunction for verbal than performance IQ, which is

contrary to the previous study. We suggested in this previous publication that better plasticity of the left cerebral hemisphere compared with the right hemisphere (Woods and Teuber, 1973; Glos and Pavlovkin, 1985) might explain these findings. The recent results suggest that this postulated difference of plasticity disappears later in life. Another explanation for the pronounced verbal difficulties of the patients in this study might be a more pronounced effect of vermal lesion for the patients after cerebellar tumours compared with patients with congenital non-progressive cerebellar ataxia and more generalized affection of cerebellum. The idea from our previous study (Steinlin *et al.*, 1999) that the earlier the damage in life, the more important cognitive problems will be, was not confirmed by this present study. The results of this study are more suggestive for a vulnerable age between 5 to 10 years. An explanation for these findings might be that generalized cerebellar dysfunction leads to the most pronounced cognitive problems. However, more localized lesions of the cerebellum showed an age-dependent effect on later cognitive function with a vulnerable age around early school age.

In conclusion, our study supports previous findings that the cerebellum is important in cognitive functioning. Besides the similarity of frontal impairment of executive functions, there are also additional challenges especially in visual-spatial domains, attention and short-term memory. The pattern of these dysfunctions, involving many different cognitive functions, supports the idea that cerebellar cognitive and affective symptoms can not be explained by one uniform cerebellar dysfunction, but are rather a consequence of the many pathways connecting the cerebellum and the cerebrum in both directions (Schmahmann and Sherman, 1998). It is important to point to the psychopathological problems of these children. Both early and long-term neuropsychological follow-up and specific intervention until integration into professional life seems mandatory for children after posterior fossa tumours, irrespective of further administered therapies such as radiotherapy or chemotherapy.

Acknowledgements

We wish to thank Susan Blaser for her help in preparing this manuscript.

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*Received June 16, 2002. Revised December 2, 2002.
Second revision April 12, 2003. Accepted April 16, 2003*