Children and Adolescents With Chronic Cerebellar Lesions Show No Clinically Relevant Signs of Aphasia or Neglect

S. Richter,1,5 B. Schoch,2 O. Kaiser,1 H. Groetschel,1 C. Hein-Kropp,1 M. Maschke,1 A. Dimitrova,1 E. Gizewski,3 W. Ziegler,4 H.-O. Karnath,5 and D. Timmann1
1Departments of Neurology, 2Neurosurgery, and 3Neuroradiology, University of Duisburg-Essen; 4Entwicklungsgruppe Klinische Neuropsychologie–Clinical Neuropsychology Research Group, Department of Neuropsychology, City Hospital Bogenhausen, Munich; and 5Center of Neurology, Hertie-Institute for Clinical Brain Research, University of Tuebingen, Tuebingen, Germany

Submitted 13 June 2005; accepted in final form 15 July 2005

Richter, S., B. Schoch, O. Kaiser, H. Groetschel, C. Hein-Kropp, M. Maschke, A. Dimitrova, E. Gizewski, W. Ziegler, H.-O. Karnath, and D. Timmann. Children and adolescents with chronic cerebellar lesions show no clinically relevant signs of aphasia or neglect. J Neurophysiol 94: 4108 – 4120, 2005. First published July 20, 2005; doi:10.1152/jn.00611.2005. We studied language and visuospatial functions of 12 children and adolescents who had undergone surgery for cerebellar astrocytoma without subsequent radiation or chemotherapy and compared them with 27 age-, gender-, and education-matched healthy control subjects. To study possible lateralization of the functions of the left and right cerebellar hemispheres, subjects performed several language tasks including a verb-generation task as well as standard neglect and extinction tests. Three-dimensional-MR images confirmed that lesions affected cerebellar hemispheres in all children but one who had a pure vermal lesion. The right cerebellar hemisphere was affected in six, the left hemisphere in four children, and both hemispheres in one child. There were no signs of aphasia in the children or adolescents with cerebellar lesions. Language abilities did not differ between cerebellar patients and control subjects except for small increases in reaction times in verb generation in patients with left-sided lesions. Visuospatial functions were also intact in cerebellar subjects except for minor group differences in neglect tasks. In sum, chronic focal cerebellar lesions acquired in childhood or youth do not result in persistent language disorders or clinically significant signs of spatial neglect or extinction.

INTRODUCTION

The cerebellum is alleged to be involved in nonmotor functions (Schmahmann 1997; Thach 1998). According to the “cerebellar cognitive affective syndrome” introduced by Schmahmann and Sherman (1998), the vermis takes the role of the cerebellar limbic system, whereas the lateral hemispheres are said to be associated with executive functions, visuospatial processing, and language.

The cerebellum is massively connected to the contralateral cerebral cortex (Middleton and Strick 2001). The right cerebellar hemisphere has been associated with language functions in brain imaging (Ackermann et al. 2004; Petersen et al. 1989; Raichle et al. 1994) and human lesion studies (Fiez et al. 1992; Silveri et al. 1994). As far as verb-generation tasks are concerned, findings are inconsistent. Some studies showed that patients with right-sided cerebellar lesions were unable to reduce their reaction times over blocks of trials and/or produced incorrect answers (Fiez et al. 1992; Gebhart et al. 2000), whereas no impairments were found in other studies (Helmuth et al. 1997; Richter et al. 2004).

Visuospatial functions are alleged to be associated with the left cerebellar hemisphere according to brain-imaging studies in healthy adults (Fink et al. 2000, 2001) and patient studies (Riva and Giorgi 2000). There is also evidence for nonlateralized visuospatial deficits in cerebellar patients (Malm et al. 1998; Molinari et al. 2004; Neau et al. 2000; Schmahmann and Sherman 1998), but impairments of visuospatial functions were not confirmed in other studies (Dimitrov et al. 1996; Gomez Beldarrain et al. 1997).

Spatial neglect occurs mainly after right-sided cerebal lesions and is characterized by an inability to explore and react to stimuli within the contra-lesional hemifield (Karnath et al. 2001, 2003; Mesulam 2002). Based on the contralateral projections from the cerebellum to the cerebral cortex, one would expect ipsilateral neglect in cerebellar patients with left-sided lesions. Neglect has only rarely been assessed in cerebellar patients. Previous results are inconsistent. Neglect to the right was found to be associated with both right and left cerebellar lesions (Aarsen et al. 2004; Hildebrandt et al. 2002; Silveri et al. 2001).

Studies by Riva and Giorgi (2000) and Scott et al. (2001) in children after cerebellar tumor surgery suggest a lateralization of cognitive functions in the cerebellar hemispheres in childhood. Results of the studies by Levisohn et al. (2000), Steinlin et al. (2003), and Aarsen et al. (2004), however, found no evidence to support this conclusion. Finally, whereas deficits in the Riva and Giorgi study seem to be of transient nature, cognitive deficits were found to be more permanent in other studies (Aarsen et al. 2004; Levisohn et al. 2000; Scott et al. 2001; Steinlin et al. 2003).

The aim of the present study was to further investigate if language functions are associated with the right cerebellar hemisphere and visuospatial functions with the left cerebellar hemisphere in children. Children who had previously received surgery for cerebellar astrocytoma performed several language tasks and a series of standard tests for spatial neglect and extinction. Impairments were studied in relation to the site and extent of cerebellar lesion as assessed by means of individual 3D-MRI-scans.
METHODS

Subjects

Twelve children who had previously received surgery to remove a cerebellar astrocytoma at the Department of Neurosurgery, University of Duisburg-Essen, Germany, participated in the study [7 female, 5 male; mean age 14.6 ± 2.8 (SD) yr, range: 9–19 yr]. Three of these (Cb1, Cb5, Cb10) had taken part in a previous study of our group on speech motor deficits in children with acute cerebellar lesions (Richter et al. 2005). Twenty-seven healthy children, 12 girls and 15 boys, served as control subjects. Mean age was 14.4 ± 2.8 yr in the healthy control group (range: 8–19 yr). Patients and control subjects were matched for educational level. One patient (Cb1) was left-handed, another patient (Cb6) was right-handed but preferred to use the left hand after the operation. Two control subjects (Con10, Con27) were left-handed, all other control subjects were right-handed. Healthy control subjects revealed no neurological or psychiatric diseases according to clinical history and neurological examination.

Children were included in the language analysis, if they were German native speakers, ≥8 yr old and at least in the third grade. The latter criterion was chosen to assure some basic level of orthographic knowledge. Results of the language tests of one patient (Cb6) were excluded from analysis because she was not a German native speaker. One control subject (Con21) was in the second grade only. Results of the language tests of this child were also excluded.

The cerebellar operation had been performed at least one year ago (mean: 5.7 ± 3.4 yr, range: 1–13.4 yr). All patients had presented with astrocytoma. One child revealed an astrocytoma grade II, the others astrocytomas grade I. None of the children had received radiation and/or chemotherapy or was taking centrally acting medication at the time of testing. The cerebellar patients showed no evidence of extra-cerebellar lesions based on clinical examination and MRI data.

Subjects underwent a standard neurological examination according to the International Cooperative Ataxia Rating Scale (ICARS) (Trouillas et al. 1997). Total ICARS-score ranges from 0 (no ataxia) to 100 (most severe ataxia). Mean total ICARS-score was 3.8 ± 5.0, ranging from 0 to 14.5.

Written informed consent was obtained from all children and parents, who were recompensed for their travel expenses. The local committee of research ethics approved the study. Basic characteristics of patients with cerebellar lesions are summarized in Table 1.

### TABLE 1. Patient data and pre- and postoperative clinical signs

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Age</th>
<th>Handedness</th>
<th>Diagnosis</th>
<th>Lesion Site</th>
<th>Evans</th>
<th>Time Since Surgery mo</th>
<th>PG</th>
<th>Upper limb</th>
<th>Lower limb</th>
<th>SP</th>
<th>OC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cb1</td>
<td>f</td>
<td>11</td>
<td>Left</td>
<td>Astro I</td>
<td>Right</td>
<td>0.1</td>
<td>20</td>
<td>41</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Cb2</td>
<td>f</td>
<td>12</td>
<td>Right</td>
<td>Astro I</td>
<td>Right</td>
<td>2.0</td>
<td>31</td>
<td>75</td>
<td>0.0</td>
<td>0.5</td>
<td>0.0</td>
<td>0.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Cb3</td>
<td>f</td>
<td>17</td>
<td>Right</td>
<td>Astro I</td>
<td>Right</td>
<td>0.26</td>
<td>35</td>
<td>97</td>
<td>1.5</td>
<td>7.5</td>
<td>1.0</td>
<td>0.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Cb4</td>
<td>m</td>
<td>16</td>
<td>Right</td>
<td>Astro I</td>
<td>Right</td>
<td>0.25</td>
<td>38</td>
<td>97</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Cb5</td>
<td>m</td>
<td>19</td>
<td>Right</td>
<td>Astro II</td>
<td>Right</td>
<td>2.0</td>
<td>28</td>
<td>55</td>
<td>3.0</td>
<td>0.0</td>
<td>0.0</td>
<td>3.0</td>
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</tr>
<tr>
<td>Cb6</td>
<td>f</td>
<td>17</td>
<td>Right¹</td>
<td>Astro I</td>
<td>Right</td>
<td>0.18</td>
<td>36</td>
<td>39</td>
<td>2.5</td>
<td>7.0</td>
<td>1.0</td>
<td>0.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Cb7</td>
<td>f</td>
<td>16</td>
<td>Right</td>
<td>Astro I</td>
<td>Left</td>
<td>0.10</td>
<td>30</td>
<td>18</td>
<td>0.0</td>
<td>1.0</td>
<td>0.0</td>
<td>1.0</td>
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</tr>
<tr>
<td>Cb8</td>
<td>m</td>
<td>16</td>
<td>Right</td>
<td>Astro I</td>
<td>Left</td>
<td>0.18</td>
<td>29</td>
<td>161</td>
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<td>0.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Cb9</td>
<td>m</td>
<td>9</td>
<td>Right</td>
<td>Astro I</td>
<td>Left</td>
<td>0.10</td>
<td>16</td>
<td>12</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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</tr>
<tr>
<td>Cb10</td>
<td>f</td>
<td>14</td>
<td>Right</td>
<td>Astro I</td>
<td>Left</td>
<td>0.04</td>
<td>23</td>
<td>52</td>
<td>1.0</td>
<td>3.0</td>
<td>0.0</td>
<td>2.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Cb11</td>
<td>m</td>
<td>14</td>
<td>Right</td>
<td>Astro I</td>
<td>Bilateral</td>
<td>0.15</td>
<td>32</td>
<td>78</td>
<td>0.0</td>
<td>3.0</td>
<td>0.0</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Cb12</td>
<td>f</td>
<td>14</td>
<td>Right</td>
<td>Vermis</td>
<td></td>
<td>88</td>
<td>0.0</td>
<td>88</td>
<td>0.5</td>
<td>1.0</td>
<td>0.0</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Ch. cerebellar; f, female; m, male; astro I/II, astrocytoma grade I/II; BI, bicaudate index; Evans, Evans index; pathological values are marked in bold; ICARS score (Trouillas et al. 1997), total score: maximum = 100. Subscores: PG: posture and gait (maximum = 34), KF: kinetic function (maximum lower limb = 16, upper limb = 36), SP: speech (maximum = 8), OC: oculomotor (maximum = 6). ¹Cb6 was right-handed, but preferred to use the left hand after the operation due to remaining ataxia.

Experimental procedure

The investigation consisted of three main parts, assessment of language, visuospatial functions, and localization of the cerebellar lesion on the basis of individual three-dimensional (3D)-MRI scans.

Language

VERB GENERATION. Subjects sat comfortably in a chair and looked at a central fixation cross on a computer monitor in front of them. Colored photographs of real objects (e.g., a car) were presented for 4 s with an interval of 3 s. Two different types of responses were tested. In one, the naming condition, subjects were asked to name the pictured object (e.g., “car”). In the verb-generation condition, they were instructed to say what one can do with the object, i.e., to produce the corresponding verb (“drive”). There were two naming blocks and four verb-generation blocks. The order of testing was: naming block 1, verb-generation blocks 1–4, naming block 2. There was a training block of five trials before the first naming block and a training block of nine trials before the first verb-generation block using objects that differed from those used in the actual experiment. The objects shown (see Table 4) were the same in both conditions, and the sequence of objects was varied between blocks.

The time between the object presentation and verbal responses (i.e., vocal reaction times) was measured. To this end, the responses were segmented semi-automatically with the help of a MATLAB routine based on loudness functions (Merk 2002; Ruske and Beham 1992). For further details of the verb-generation task and segmentation routine, see Richter et al. (2004).

We analyzed for each presented object the answers given by the subjects based on a thesaurus of the German language (http://wortschatz.umi-leipzig.de; Table 4). In addition to giving synonyms for nouns and verbs, the thesaurus also indicated which verbs are typically associated with specific objects.

Verbal response onsets were excluded from statistical analysis, when answers were wrong (inappropriate verb or noun, inappropriate word category), no answer was given, or the answer was inappropriate only after a correction of the subject. The latter answers were not considered “wrong” based on the quality of responses.

Only a very few answers were excluded from the statistical analysis. Across the total of 1,152 trials in the patient group (11×96), 7 trials were excluded due to self-correction (0.6%). In the 2,496 trials of the control group (26×96), a total of 18 trials (0.7%) were excluded due to remaining ataxia.
excluded (self-correction: 4 trials, noun instead of verb: 7 trials, verb instead of noun: 1 trial; no answer: 4 trials, inappropriate verb: 2 trials).

APHASIA TEST. The Aachener Aphasiestest (AAT) is a standardized aphasia test widely used in German speaking countries which has been validated in a large group of aphasic patients ($n = 376$). The combination of two subtests of the AAT, the token test and the written language subtest, has been shown to detect aphasic symptoms with a high sensitivity (Huber et al. 1983). In the token test, the subject is asked to point to different tokens, touch them or pick them up according to instructions of increasing complexity. The written language subtest includes word reading, spelling, and writing to dictation. Additionally, an experienced speech therapist (C. H.-K.) evaluated recordings of spontaneous speech regarding signs of aphasia or delays in speech development based on AAT rating scales.

DEVELOPMENTAL LANGUAGE TEST. The Heidelberger Sprachentwicklungstest (HSET) is a German developmental language test for children aged 3–9 yr, validated in 791 healthy children (Grimm and Schöler 1978, 1991). It is explicitly stated by the developers of the test that the HSET might be readily applied also in older children. In the sentence-construction subtest, a sentence has to be constructed from two or three words (e.g., girl, play, doll). In the plural-singular formation subtest, the task is to generate the plural form from the singular form or vice versa of real (sparrow–sparrows) or artificial formation subtest, the task is to generate the plural form from the singular form or vice versa of real (sparrow–sparrows) or artificial words (“Mattau”–“Mattaus”; “Plabeln”–“Plabel”).

Quantitative and qualitative speech analysis

To assess speech motor deficits that might influence the preceding measures of language function, a quantitative and qualitative analysis of dysarthric speech symptoms was performed.

In a syllable-repetition task, subjects were asked to repeat six different consonant-vowel syllables involving (co-)articulations of major articulatory organs. Subjects were advised to produce syllable chains as fast and as regularly as possible for $\sim 5$ s after a brief demonstration by the experimenter. In a sentence-production task, subjects had to repeat 12 test sentences that differed only with respect to a target word belonging to one of three categories. There were two-syllabic words of a simple consonant-vowel-structure, two-syllabic words containing consonant clusters and three-syllabic words. The sentences were read aloud by the experimenter and repeated by the subject.

Measurement of syllable durations in target words and repeated syllables was based on a syllable-segmentation algorithm operating on loudness contours of the speech signal (see Merk and Ziegler 1999).

For the qualitative speech analysis, the speech therapist (C. H.-K.) rated dysarthria symptoms in recordings of spontaneous speech on a four-point-scale according to Kluin et al. (1988) and Darley et al. (1969a,b). For more detailed information on the quantitative and qualitative speech analysis, see Merk and Ziegler (1999) and Richter et al. (2005).

Visuospatial functions

LETTER-CANCELLATION TEST. In the letter-cancellation test by Weintraub and Mesulam (1985), 30 target letters “A” are distributed amid distractors both on the left and right half of a horizontally oriented sheet of paper. Patients were asked to cancel all of the targets. The test was finished when subjects indicated twice that they believed they had cancelled all target stimuli. Results are presented as percentage omissions on the left and right side separately with reference to the total number of target stimuli. In adults, omissions of more than five left-sided targets (i.e., $>17\%$) are taken to diagnose spatial neglect (Weintraub and Mesulam 1985).

LINE BISECTION. Six sheets of paper with one line each (length: 24.1 cm, width: 0.03 cm) were presented one after the other, and the subject was asked to mark with a pen the middle of the line. The line was not positioned exactly in the middle of the sheet so that subjects could not use the edges of the paper to orient their response. The side with the smaller margin was presented three times each on the left and on the right to prevent adaptation. For each trial, the difference between the subject’s estimation of the line’s middle and the actual central point was calculated, both as absolute and signed values. Deviations to the right were arbitrarily assigned a positive sign, those to the left a negative one. Differences were expressed as percentage of half the length of the line and averaged across the six trials.

EXTINCTION. Patients with visual extinction may react normally to stimuli when presented on one side of the visual field. However, if two stimuli are presented simultaneously, the stimulus on the side contralateral to the cerebral lesion may not be noticed (e.g., Heilman et al. 1997). In adults, visual extinction is diagnosed if a subject fails to perceive the left stimulus during bilateral presentation in $>50\%$ of the trials, although the same stimuli are reported $\approx90\%$ correctly with unilateral stimulation presentation (Karnath et al. 2003).

Four geometrical figures (square, circle, triangle, diamond), each $\sim0.7\text{ in}$ in size, were presented for 180 ms in random order 4° left and/or right of a central fixation point with the help of the computer program “Mel” (Psychology Software Tools). There were 10 trials with bilateral and 20 trials with unilateral presentations. We observed whether subjects perceived the stimuli and also if they recognized their form. Results are presented as percentage of stimuli perceived/recognized on the left and right side in bilateral compared with unilateral presentations.

MRI analysis

In cerebellar patients, extent of surgical lesions was defined based on individual 3D-MRI data sets. First, a 3D sagittal volume of the entire brain was acquired using a T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (FOV = 256 mm, number of partitions = 160, voxel size = $1 \times 1 \times 1$ mm³, TR/TE = 2400/4.38 ms, flip angle = $8\text{°}$) on a Siemens Sonata 1.5 Tesla MR. In addition, axial and sagittal 2D-T2 weighted images of the entire brain were acquired. 3D-MPRAGE and 2D-T2 weighted images were visually examined to reveal possible extracerebellar pathology.

Surgical lesions were manually traced on axial and sagittal slices of the nonnormalized 3D-MRI data set and saved as region of interest using MRIcon (http://www.mricon.com) (Rorden and Brett 2000). The same software was used to calculate individual lesion volumes from nonnormalized ROI.

Individual volume of the lesion and the complete 3D-MRI data set were then spatially normalized into a standard proportional stereotaxic space (the MNI 152-space) using SPM99 (http://www.fil.ion.ucl.ac.uk/spm/; Wellcome Department of Cognitive Neurology, London, UK). The MPRAGE volume was registered and resampled to $2 \times 2 \times 2$ mm³ voxel size. Because MRI atlases of the cerebellum are available for adult brains only, lesions of all subjects regardless of age were normalized to the adult MNI 152 brain average template.

The MNI coordinates of cerebellar lesions were determined in the horizontal ($x$), sagittal ($y$), and vertical ($z$) directions. Based on these coordinates, the corresponding cerebellar lobules (Schmahmann et al. 2000) and affected cerebellar nuclei were defined (Dimitrova et al. 2002). Sagittal divisions were defined according to Luft et al. (1998). Both lesions of the paravermis ($-24$ mm $\leq x \leq -10$ mm, $+10$ mm $\leq x \leq +24$ mm) and lateral hemispheres ($x \leq -24$ mm, $x \geq +24$ mm) were considered hemisphere lesions.

The process of spatial normalization is likely to introduce some errors in individual anatomy. Extent of individual normalized lesions were manually adjusted based on nonnormalized data using characteristic anatomical landmarks by an experimenter (B.S.) blinded for behavioral data.
Degree of preoperative hydrocephalus was assessed based on diagnostic 2D-MRI scans using the bicaudate index (Aarsen et al. 2004) and the Evans score (Evans 1942). The bicaudate index is equal to the width of the lateral ventricles on the level of the caudate nuclei, divided by the width of the brain on the same level. A value $>0.16$ is considered pathological up to the age of 30 yr (van Gijn et al. 1985). The Evans score equals the maximum distance between the frontal horns of the lateral ventricles as percentage of the maximum diameter of the parietal lobes. A percentage $>30$ is considered pathological.

Six patients revealed a preoperative hydrocephalus according to both indices ($Cb2$, $Cb3$, $Cb4$, $Cb6$) or according to the bicaudate index ($Cb8$) or Evans score ($Cb11$) alone. In two patients, preoperative hydrocephalus could not be assessed because diagnostic 2D-MRI scans were not available ($Cb5$, $Cb12$). At the time of testing, none of the cerebellar patients revealed a hydrocephalus.

The cerebellar lesion sites according to MRI analysis are summarized in Table 2 and illustrated in Fig. 1. Cerebellar children were assigned to groups based on the affected hemisphere. There were six children with right-sided lesions ($Cb1$–$Cb6$), three of them involving the right dentate ($Cb3$, $Cb5$, $Cb6$). Four patients presented with a left-sided lesion ($Cb7$–$Cb10$), involving the left dentate in one case ($Cb10$). Two children ($Cb4$ and $Cb10$) showed small extensions of the lesion to the contralateral side that were not further considered. One child revealed a lesion of both hemispheres involving the right dentate nucleus ($Cb11$). $Cb12$ was the only child with a pure vermian lesion; lesions in another eight cases included the vermis ($Cb2$–$Cb6$, $Cb9$–$Cb11$). In cases in which the dentate was included, it was typically the posterior region of the nucleus that was affected.

**Table 2. Cerebellar lesion site according to MRI analysis**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Vermis</th>
<th>Paravermis</th>
<th>Hemisphere</th>
<th>White Matter</th>
<th>Nuclei</th>
<th>Volume, cc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right-sided lesions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$Cb1$</td>
<td>III, IV, V, VI, VIIA, VIIB, VIIIA, VIIIB, IX, X</td>
<td>r: CRI, CRII, VIIB, VIIIA</td>
<td>r: VI</td>
<td>V 1.2, 3 (r: PV 2)</td>
<td>(NF b) (NI b)</td>
<td>1.2</td>
</tr>
<tr>
<td>$Cb2$</td>
<td>IX, X,</td>
<td>r: VIIA, VIIIA, VIIIB, X</td>
<td></td>
<td></td>
<td></td>
<td>26.2</td>
</tr>
<tr>
<td>$Cb3$</td>
<td>VI, VIIA, VIIb, VIIIA</td>
<td></td>
<td>r: VI, CRI, CRII</td>
<td>V 1.2, 3 (r: PV 2)</td>
<td>NF b r ND</td>
<td>12.0</td>
</tr>
<tr>
<td>$Cb4$</td>
<td>V, VI, VIIA, VIIIB</td>
<td>r: VI, (CRI, IX)</td>
<td></td>
<td>V 1.2 (r: PV 2)</td>
<td>NF b (NI r)</td>
<td>9.6</td>
</tr>
<tr>
<td>$Cb5$</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>8.4</td>
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<tr>
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<td>III, VIIA, VIIb, VIIIA, VIIIB, IX</td>
<td></td>
<td></td>
<td></td>
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<td>10.8</td>
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<td>$Cb9$</td>
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<td></td>
<td>8.0</td>
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<td>$Cb10$</td>
<td>IX, X</td>
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<td></td>
<td></td>
<td></td>
<td>9.0</td>
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<tr>
<td><strong>Bilateral and pure vermian lesions</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>$Cb11$</td>
<td>III, IV, V, VI, VIIA, VIIB, VIIIA, VIIIB, IX, X</td>
<td>r: (V, VI, VIIA, IX)</td>
<td></td>
<td>V 1.2, 3 (r: PV 2)</td>
<td>(NF b) (NI b)</td>
<td>15.5</td>
</tr>
<tr>
<td>$Cb12$</td>
<td>(I, II, III), VIIa, VIIB, VIIIA, VIIIB, IX, X</td>
<td>r: (VIIA, VIIIB, VIIIA)</td>
<td></td>
<td>V 1.2, 3 (r: PV 2)</td>
<td>(NF b) (NI b)</td>
<td>8.6</td>
</tr>
</tbody>
</table>

r, right side; l, left side; b, both sides; subdivisions of white matter according to Luft et al. (1998), with V1–3, vermis 1–3; PV1–3, paravermis 1–3; MH1–3, medial hemisphere; and LH 1–3, lateral hemisphere 1–3. NF, fastigial nuclei; NI, interposed nuclei; ND, dentate nuclei; p, posterior; a, anterior; cc, cubic centimeters; affected regions in brackets mark those regions marginally affected.
COMPARISON OF NAMING AND VERB GENERATION. Reaction times were averaged in the two naming and four verb-generation blocks. ANOVA with group as between-subjects factor and block as within-subject factor revealed neither a main effect of group (P = 0.787) nor a block effect (P = 0.632) or block by group interaction (P = 0.714). In the post hoc analyses, similar results were obtained (Table 3).

QUALITY OF RESPONSES. In the naming condition, all answers were correct both in patients and control subjects except for one wrong answer in a control subject, who gave a verb instead of a noun (sweep instead of broom). In the verb-generation condition, patients gave no wrong answers. In the control subjects, a noun was given instead of a verb in seven cases [children’s drum – music (4 trials), pocket lamp – light (2 trials), doll – game] and an inappropriate verb was given in two cases [cooking pot – eat (2 trials)].

The most frequent answer for each object was the same for both the patients’ subgroups and control subjects (Table 4). One single verb was generated in response to an object by a control subject. The results were the same for the patients’ subgroups

The most frequent answer for each object was the same for both the patients’ subgroups and control subjects (Table 4). One single verb was generated in response to an object by a control subject. The results were the same for the patients’ subgroups.
data. In Table 5, individual values are marked in bold that fall below the normal range. In the token test, none of the cerebellar patients and one control subject (Con20, 3.7%) fell below the normal range. In the written language test, none of the cerebellar patients and two of the control subjects (Con20, Con25, 7.4%) fell below the normal range. Compared with German norms for the token test acquired in children aged 8–14, and none of the children >14 yr revealed pathological results, except one control child (Con20).

According to Huber et al. (1983) the relation between the results of the token test and the test of written language sheds light on the presence of aphasia. Three control subjects (Con5, Con20, Con25) revealed such a critical constellation of results in the two tests. However, one of these was very young (Con5: 8 yr).

Finally, none of the cerebellar or control children revealed perceptible signs of aphasia. No problems with word finding.

![Image](http://jn.physiology.org/)

**FIG. 2.** A: means ± SD of the reaction times (s) across the 16 trials in the 6 subsequent blocks for the cerebellar subgroups with right- and left-hemisphere lesions and control subjects. B: means of the reaction times (s) across the 16 trials in the 6 subsequent blocks for the group of all cerebellar patients and control subjects. The 1st and the last block are naming blocks (nam1, nam2), the 2nd to 5th blocks are verb-generation blocks (vg1–vg4).

paraphasia, neologism, aggrammatism, jargon, or verbal stereotypes were observed in spontaneous speech samples.

**DEVELOPMENTAL LANGUAGE TEST**. Performance in our patients and control subjects was referred to the data of the oldest norm group (8–9.9 yr; n = 92) (Grimm and Schöler 1978). In general, the definition of a percentile rank as “average” is based on stanine scores. A percentile rank <22 reflects “below average” (stanine 1–3), between 23 and 76 “average” (stanine 4–6), and ≥76 “above average” performance (stanine 7–9). In the present study, a further differentiation in low (PR 4–10, stanine 2), below average (PR 11–22, stanine 3), low average (PR 23–39, stanine 4), and average (PR 40–59, stanine 5) was applied.

In the plural-singular formation task, mean percentile rank was somewhat smaller in the patients with left-sided lesions (45.0 ± 35.8) and in the control subjects (48.4 ± 29.2) than in the children with right-hemisphere lesions (58.4 ± 37.1). A univariate ANOVA with group (right-sided lesions vs. left sided-lesions vs. control subjects) as between-subjects factor revealed a nonsignificant effect (P = 0.769).

Three of 11 cerebellar children (27.3%) revealed a percentile rank of 14, which was below average. Two children had left-hemisphere lesions (Cb8, Cb10; 50%) and one a right-hemisphere lesion (Cb3; 16.7%). In the control group, there were four subjects with a low (15.4%), three children with a below average (11.5%), and two children with a low average percentile rank (7.7%).

In sentence construction, the group means were: right cerebellar patients: 75.4 ± 20.71, left cerebellar patients: 44.0 ± 36.56, and control subjects: 70.3 ± 26.4. The lower mean in the left-cerebellar patients was due to the fact that one patient had a low average (Cb9), and two patients had a below average percentile rank (Cb8, Cb10). Two control subjects performed below average (7.7%) and three revealed a low average percentile rank (11.5%). Univariate ANOVA showed a nonsignificant group effect (P = 0.171).

Post hoc comparisons (t-test) for the plural-singular formation and sentence-construction tasks revealed similar results as in the main analysis.

Variability of results was comparatively high in both HSET subtests already in control subjects (Table 5, Fig. 3). This is further demonstrated by calculation of a normal range based on the mean ± 2 SD in the control children. Lower normal range resulted in percentiles <5 in plural-singular formation and <10 in sentence construction. Based on the present findings in control subjects, none of the control and cerebellar subjects revealed abnormal results in the plural-singular and the sentence-construction task (Table 5). Overall HSET subtests did not appear effective to distinguish between control and patient groups.

**QUANTITATIVE AND QUALITATIVE SPEECH ANALYSIS**. Syllable duration was longer in the sentence-production task than in the oral diadochokinesia task in patients and control subjects (main effect of task: P < 0.0001). There was neither a group effect (P = 0.555) nor an interaction between task and group (P = 0.795). The means in the individual groups and tasks were: sentence production, right cerebellar patients: 193.66 ± 25.21 ms, left cerebellar patients: 189.91 ± 38.34 ms, control subjects: 204.43 ± 31.58 ms; syllable repetition, right cerebellar patients: 167.76 ± 16.33 ms, left cerebellar patients: 163.39 ± 25.18 ms, control subjects: 170.21 ± 29.74 ms (main effect of group: P < 0.0001). There was neither a group effect (P = 0.636) nor an interaction between group and task (P = 0.438).
26.20 ms, control subjects: 171.19 ± 16.53 ms. (Post hoc comparisons: task effects, all P values ≤0.0001; group effects, all P values ≥0.361; task by group interactions, all P values ≥0.589.).

None of the cerebellar or control children revealed perceptible signs of cerebellar dysarthria. Specific articulation problems (e.g., sigmatism, nasality) were present in three cerebellar (Cb1, Cb4, and Cb9) and in five control children (Con4, Con10, Con19, Con23, Con24).

**Visuospatial functions**

**CANCELLATION TEST.** None of the subjects showed spatial neglect, i.e., had more than five omissions (17%) on the left side (see Table 6). In patients’ subgroups, average percentage of omissions was 3.3 ± 3.8% on the left and 0.8 ± 1.7% on the right in the group with left-sided lesions. In the subgroup of patients with right-hemisphere lesions, average percentage of omission was 0.6 ± 1.4% on the left and 1.1 ± 1.7% on the right. Control subjects omitted 0.5 ± 2.0% targets on the left and 0.7 ± 1.7% on the right. Average percentage of omissions on the left was larger in the subgroup of patients with left-sided lesions compared with patients with right-sided lesions or control subjects. This was due to Cb8 and Cb9, who missed two A’s on the left each. A Kruskal-Wallis H test comparing the three groups of subjects revealed no significant differences for omissions on the right (P = 0.76) and a difference close to significance on the left (P = 0.06). Nearly significant differences between left-hemisphere patients and the other groups for omissions on the left were also found in post hoc compar-
signed, but not for absolute deviations (absolute lesions and control subjects were close to significance for significance ($P_{H11005}$/ANOVA with group as between subjects factor missed significance ($P_{H11006}$)).

Patients with left-sided lesions did not significantly differ from control subjects ($P_{H11006}$). The remaining tests were not significant (see Table 3).

The mean ± 2 SD was calculated for the control children to define a normal range of performance. In the letter-cancellation task, three of the cerebellar patients (25%) and one of the control subjects (3.8%) fell below the normal range (Table 6). Two patients had a left-sided (50%) and one patient a vermal lesion (8.3%).

LINE BISECTION. A univariate ANOVA showed that absolute percentage deviation from the center did not differ between both cerebellar patient groups and control subjects (right-hemisphere lesions: $5.2 \pm 1.7\%$, left-hemisphere lesions: $3.5 \pm 2.0\%$, control subjects: $4.2 \pm 1.8\%$; $P_{H11006}=0.26$).

Regarding signed deviation, Table 6 reveals that both patients with left- and right-sided lesions tended to define the middle of the line leftward from the actual middle (right-hemisphere lesions: $-2.2 \pm 3.2\%$, left-hemisphere lesions: $-0.8 \pm 3.2\%$), while control subjects set the middle of the line rightward from the actual middle ($0.7 \pm 3.0\%$). A univariate ANOVA with group as between subjects factor missed significance ($P_{H11006}=0.07$).

Differences between the group of patients with right-sided lesions and control subjects were close to significance for signed, but not for absolute deviations (absolute $P_{H11006}=0.14$, signed $P_{H11006}=0.03$). The difference between the group of all cerebellar patients (signed: $-1.7 \pm 2.8\%$, absolute: $4.5 \pm 1.8\%$) and the control group was not significant for absolute ($P_{H11006}=0.43$) but significant for signed deviation ($P_{H11006}=0.01$). Patients with left-sided lesions did not significantly differ from control subjects (absolute $P_{H11006}=0.70$, signed $P_{H11006}=0.56$).

In the line-bisection task, one of the cerebellar patients (8.3%) and one of the control subjects (3.7%) fell below the normal range of performance based on the results in the control group (mean ± 2 SD; Table 6). The patient had a right-sided lesion.

EXTINCTION. Detection. All cerebellar and control children perceived all stimuli on either side both in trials with one stimulus and in the critical trials with two stimuli. Thus no patient revealed significant signs of extinction.

Identification. Identification of stimuli was also close to perfect (see Table 6). Percentage of correctly identified items on the left side under unilateral and bilateral stimulus presentation was 100% and 100% correct in children with left-sided lesions, 100% and 96.7 ± 5.2% in children with right-sided lesions, and 100% and 98.1 ± 4.8% in control children. Percentage of correctly identified stimuli on the right side under unilateral and bilateral stimulus presentation was 97.5 ± 5.0% each in children with left-sided lesions, 100% and 95 ± 5.5% in children with right-sided lesions, and 99.6 ± 1.9% and 96.3 ± 7.4% in control children.

The one cerebellar child with a bilateral lesion ($Cb11$) did not identify 3 of 10 presentations of bilateral stimuli on the left as well as on the right side (70% detection on each side).

A Kruskal-Wallis $H$ test comparing the percentage of correctly identified stimuli in bilateral trials in the three groups of subjects revealed no significant differences for both stimuli on the right ($P_{H11006}=0.60$) and left ($P_{H11006}=0.39$). Moreover, post hoc tests comparing each patients’ subgroup and the group of all cerebellar patients to control subjects were nonsignificant (see Table 3).

One of the cerebellar patients (8.7%) and one of the control subjects (3.8%) fell below the normal range of performance in control children (mean ± 2 SD; Table 6). The patient had a bilateral lesion ($Cb11$).

DISCUSSION

Children and adolescents with chronic focal cerebellar lesions did not show clinically relevant signs of aphasia, spatial neglect, or visual extinction. There were minor group differences in verb-generation and neglect tasks. No clear evidence was found for the assumption of a lateralization of language functions to the right cerebellar hemisphere and visuospatial...
functions to the left cerebellar hemisphere. Whereas minor differences in verb generation and letter cancellation were present in patients with left-sided lesions compared with control subjects, patients with right-sided lesions tended to be impaired in line bisection. The present results suggest that no clinically significant disorders in language and visuospatial functions are present in children and adolescents with chronic focal cerebellar lesions.

**Verb generation**

In the verb-generation task, there were no differences between patients and control subjects concerning quality of responses and reduction of verbal reaction times (learning). The results are in accordance with previous studies in adult cerebellar patients (Helmuth et al. 1997; Richter et al. 2004). Preserved learning and correct answers contradict other studies where learning and/or quality of answers were impaired in adult cerebellar subjects (Fabbro et al. 2000; Fiez et al. 1992; Gebhart et al. 2000).

The results of the Fiez and Gebhart studies may differ from the present findings for several reasons. First, the Fiez patient had an acute infarction, whereas our patients revealed a chronic disease. However, the authors report that there were no marked changes in the patient’s performance over a period of 10 mo.
Second, neither Fiez et al. \((n = 1)\) nor Gebhart et al. \((n = 4)\) based their findings on a larger group of cerebellar patients. Finally, pictures of objects were used in the present study and written nouns in previous experiments. The association between pictures of objects and appropriate verbs may be stronger than between written nouns and appropriate verbs. Therefore, patients may be less impaired in the present study. However, Helmut et al. \((1997)\) used written nouns and showed no impairment in verb generation in adult cerebellar patients.

In our previous study of adult cerebellar patients, there was a tendency of reaction times in the verb-generation condition to be proportionately more prolonged relative to naming in the cerebellar patients compared with control subjects. The same tendency was found in the present study in cerebellar children with left-sided lesions. It cannot be excluded that the effect reflects inherent difficulties in verb processing, i.e., grammatical or semantic deficits \((Cappa et al. 1998; Peran et al. 2003)\).

Apart from linguistic deficits, dysarthria-related problems with the motor parts of the verb-generation task have to be considered. First, the lexical semantic representation of actions is expected to be accomplished in motor regions \((Cappa et al. 2002)\). Next, movement imagination has generally been shown to activate similar cerebellar regions as actual movements in brain imaging studies \((Hanakawa et al. 2003)\). Moreover, inner speech has been found to activate cerebellar regions \((Ackermann et al. 1998, 2004)\). These motor processes might play a greater role in verb generation than in naming, e.g., when subjects think about what one can do with the object or silently search for the correct verb association. They may be the reason for the increase in reaction times in verb generation compared with naming in patients with left-sided lesions.

This interpretation is supported by the fact that increases of verbal reaction times were generally more pronounced in the patients with left-sided lesions. Cerebellar dysarthria has been related to left-sided cerebellar lesions by Lechtenberg and Gilman \((1978)\). It has to be noted, however, that increased mean reaction time in the group of left-sided cerebellar patients was mainly due to findings in one child \((Cb9\), mean verbal reaction time: \(1,200\) ms), who showed also comparatively long syllable durations in the syllable-repetition \((mean: 201\) ms) and sentence-production tasks \((242\) ms). \(Cb9\) was the youngest child in the cerebellar group and age effects have to be considered too.

**Aphasia**

The token test and the written language subtest of the AAT were used because performance in these two tests is especially sensitive to the effects of aphasia \((Huber et al. 1983)\). However, neither these tests nor a perceptual analysis of spontaneous speech revealed signs of aphasia in the cerebellar group. Preserved performance of cerebellar children in the token test is in accordance with the results of Steinlin et al. \((2003)\) in chronic patients after astrocytoma surgery. In contrast, deficits were found in the token test in children with acute right cerebellar affection due to astrocytoma surgery by Riva and Giorgi \((2000)\). Results agree with their hypothesis that language deficits might be of transient nature.

More specific grammatical functions were examined in two subtests of a developmental language test \((HSET)\). No significant group differences were found, but there was a tendency of children with left-sided lesions to perform worse in the sentence-construction task. Although language dysfunctions were expected in patients with right-sided lesions, abnormalities in patients with left-sided lesions do not exclude a role of the cerebellum in language. Only in the lesion studies of Riva and Giorgi \((2000)\) and Scott et al. \((2001)\) language impairments were related to right-hemisphere lesions. In the latter, however, all children but one received cranial radiation. In the Riva and Giorgi study, children with acute cerebellar lesions were investigated.

It has to be noted, however, that specificity of individual findings in the HSET subtests is limited. Both in the plural-singular formation and sentence-construction task variability was high already in control subjects. Moreover, in the plural singular-formation task, \(10\) \(\left(38.5\%\right)\) of the control children performed below the normal test range or presented with a low percentile rank compared with \(3\) \(\left(27.3\%\right)\) of the group of all cerebellar patients. Especially the building of the plural form of artificial words appears to be difficult for both patients and control children likely due to its abstract nature.

The observation of mainly preserved language functions seems at variance with previous findings in children after cerebellar surgery. One reason might be that in these studies, different language tests were used, e.g., the verbal subtests of the Wechsler intelligence scale \((e.g., vocabulary, comprehension)\) \((Leissohn et al. 2000; Scott et al. 2001; Steinlin et al. 2003)\). Differences in pathology as well as lesion size and localization have also to be taken into account. Whereas the present and two previous studies \((Aarsen et al. 2004; Steinlin et al. 2003)\) included children with astrocytoma only, other studies examined patients with both astrocytoma and medulloblastoma \((Leissohn 2000; Riva and Giorgi 2000; Scott et al. 2001)\). Direct comparison of lesion localization is difficult because 3D MR data sets were available in the present study only. In the present study, however, patients were included with lesions affecting primarily the posterior cerebellar lobe which is supposed to be involved in nonmotor functions \((Schmahmann and Sherman 1998)\). Furthermore, the results of all previous studies in children were not compared with control groups but to test norms found in the literature. Norms acquired in a larger group of children have the advantage that the interindividual variability is small. However, norms are often not available for each investigated age group and language, and it is not clear if they are applicable if a test is performed as part of a 2- to 4-h test battery.

In sum, no significant signs of aphasia were observed in the present group of children and adolescents with chronic cerebellar lesions. It cannot be excluded, however, that more subtle language deficits may be revealed in a larger group of children with chronic cerebellar lesions in more challenging tasks. Specific problems in grammar function, verbal working memory, temporal aspects of both speech production and perception have been shown in adult cerebellar patients \((Ackermann et al. 2004; Desmond et al. 1997; Gasparini et al. 1999; Justus 2004; Marien et al. 1996, 2000; Zettin et al. 1997)\).

**Visuospatial functions**

None of the cerebellar patients showed clinically relevant signs of spatial neglect in the letter-cancellation and line-bisection tasks or any signs of visual extinction as they are
typically observed after cerebral lesions in the right hemisphere.

In the letter-cancellation task, the absolute number of missed targets was small in the patients. Not a single patient missed more than two left-sided targets. The percentage of children missing left-sided targets, however, was larger in the group of patients with left-sided lesions (2/4) than in the patients with right-sided lesions (2/6) and group differences were close to significance. The result is in agreement with the assumption of visuospatial functions lateralized to the left cerebellum. Findings, however, need to be confirmed in a larger group of patients with left-sided lesions.

Left-sided targets were also missed by the patient with a pure vermal lesion (Ch12) and the two youngest control children (Con5, Con21). One of the patients with left-sided lesions was only 9 years old. Age effects cannot be excluded.

Deviations in the line-bisection task were small in cerebellar patients. There were no significant differences in the absolute deviations comparing control subjects and patients with left- or right-sided lesions. Patients with right cerebral lesions bisect horizontal lines significantly to the right of the veridical center (Ferber and Karnath 2001; Heilman et al. 1997). A similar finding was expected in chronic cerebellar patients with left-sided lesions. Although this assumption was not confirmed, subtle impairments could not be excluded in line bisection irrespective of lesion side. There was a tendency of cerebellar patients, in particular patients with right-sided lesions, to define the middle of the line more to the left, whereas control subjects defined the middle of the line more to the right. While neglect of the right hemispace after right-sided cerebellar lesions contradicts the assumption of a left-cerebellar involvement in visuospatial functions, it is in agreement with the results of previous studies (Silveri et al. 2001).

Finally, cerebellar children perceived all stimuli in the extinction task. In the present study, it was also assessed if subjects were able to identify the stimuli. Few errors were observed in bilateral trials with no significant group differences. Errors were not confined to the ipsilateral space, i.e., children with right-hemisphere lesions did not preferentially misperceive targets on the right, and children with left-hemisphere lesions did not misperceive more targets on the left. Performance was worst in the one patient with a bilateral lesion (Ch11), who misperceived stimuli on the left and right side in three bilateral trials. Ch11 presented with preoperative hydrocephalus, which may explain part of the findings.

Former group studies in children after cerebellar surgery assessed visuospatial functions by means of several subtests of the Wechsler intelligence scale (block design, object assembly) or copying and recall of the Rey-Osterrieth complex figure. Only in the Aarsen study (Aarsen et al. 2004) line bisection was applied. In all of these studies, deficits in visuospatial functions were found. Although two of the four studies could associate deficits with left-hemisphere lesions (Riva and Giorgi 2000; Scott et al. 2001), in the study of Steinlin et al. (2003), they were associated with vermial affection.

Interestingly, in the study of Aarsen et al. (2004), visuospatial deficits were associated with preoperative hydrocephalus. In the present study, no significant correlations could be observed. However, the number of children was small, preoperative MRI scans were not available in 2 of the 12 children and overall deficits were weak. Finally, effects of disordered eye movement cannot be excluded. Although there was no significant relation to oculomotor signs in clinical testing, eye movements have not been quantified during testing.

In sum, minor group differences in visuospatial functions were observed. While mild differences in the letter-cancellation task were found in left-sided lesions, deviations in line bisection were more pronounced in right-sided lesions.

Conclusion

In conclusion, children and adolescents with chronic focal cerebellar lesions did not show clinically relevant signs of aphasia, spatial neglect, or visual extinction. Minor group differences were present in verb-generation and neglect tasks. Findings were not consistent with a lateralization of language functions within the right cerebellum and visuospatial functions within the left cerebellum. Lack of clinically significant findings need to be confirmed in a larger group of children with chronic cerebellar lesions and in children with acute cerebellar lesions.

Acknowledgments

We thank the participating patients and control subjects for their time and effort.

Grants

The study was supported by Deutsche Forschungsgemeinschaft Grants DFG Ti 239/5–1 and Ti 239/5–2.

References


