Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions

D. Restuccia,1 M. Valeriani,1,2 C. Barba,1 D. Le Pera,1 M. Capecci,3 V. Filippini3 and M. Molinari3

Summary
Although cerebellar lesions do not cause evident sensory deficits, it has been suggested recently that the cerebellum might play a role in sensory acquisition and discrimination. To determine whether the cerebellum influences the early phases of cortical somatosensory processing, we recorded cortical somatosensory evoked potentials after median nerve stimulation in five patients with unilateral cerebellar damage. We also performed a dipolar source analysis of traces by means of brain electrical source analysis. In all patients, the amplitude of the frontal N24 and parietal P24 components, as well as the strength of the corresponding dipolar sources, were significantly smaller after stimulation of the symptomatic side. These neurophysiological findings indicate that the primary somatosensory cortical processing is altered after contralateral cerebellar damage. They represent the first indication of a possible substrate for the reduction in cerebral blood flow observed in the parietal cortex after cerebellar lesion. Furthermore, the present data allow characterization of the functional influence of the cerebellar input to the primary somatosensory cortex as specifically acting over the inhibitory components of somatosensory processing.

Keywords: cerebellum; evoked potentials; somatosensory

Abbreviations: BESA = brain electric source analysis; RV = residual variance; SEP somatosensory evoked potentials; SI = primary somatosensory cortex

Introduction
Although the cerebellum receives massive inputs from every sensory system, its lesions cause uncoordinated movements but not gross sensory deficits (Holmes, 1939). This discrepancy between high sensory input and lack of sensory deficit after a lesion is classically interpreted by hypothesizing that cerebellar sensory processing is only devoted to the precise tuning of motor control and has no relevance in the cortical processing of sensory information. This interpretation has been challenged by recent functional neuroimaging reports that demonstrate cerebellar activation in pure sensory tasks, such as cutaneous discrimination (Gao et al., 1996) and in auditory and visual non-motor tasks (Jeuptner et al., 1995; Allen et al., 1997). On the basis of these observations, reports of sensory deficits in patients with cerebellar damage, such as difficulty in weight perception (Holmes, 1917) and disturbances of kinaesthesia (Grill et al., 1994), can be reconsidered. Taking into account the widespread cortico-cerebellar interconnections with multifarious sensory and associative cortical areas (Schmahmann, 1996), it can be hypothesized that cerebellar processing plays a role in influencing functional activity not only in motor-related areas but also in sensory and associative ones. This hypothesis is in line with the proposed function of the cerebellum as a general sensory acquisition controller (Bower, 1995). In spite of growing evidence of the importance of the cerebellum for cortical sensory processing, at present, while clear neurophysiological findings demonstrate the cerebellar influence on the cortical motor area (Ugawa et al., 1991; Di Lazzaro et al., 1994), no data are available about cerebellar effects on the early cortical somatosensory processing.

Somatosensory evoked potentials (SEPs) offer a non-invasive method for assessing the functions of the somatosensory pathways. Subcortical somatosensory pathway assessment is routinely made by evaluating either the cortical N20 deflection, which probably represents the arrival of the afferent volley to the middle layers of the primary somatosensory cortex (Allison et al., 1991a, b), or the potentials generated in subcortical structures and recorded as
In contrast, SEPs occurring later than the cortical (Mauguier et al., 1986). In contrast, SEPs occurring later than the cortical areas, are usually ignored in clinical practice because they are too variable. However, several investigators were able to draw reliable conclusions about cortical SEPs in cerebral lesions in studies in which the unaffected hemisphere of the patient served as a control. Moreover, in order to separate contralateral somatosensory primary cortex. To avoid possible artefacts due to the large variability of cortical SEPs, only patients suffering from strictly unilateral lesions were enrolled in the study. This selection permitted us to evaluate changes in SEP unambiguously by using contralateral responses of the same subject as a control. Moreover, in order to separate the different SEP components, we performed dipolar source modelling of SEPs, which has proved useful in separating the activities of neighbouring cerebral structures (Scherg, 1990; Scherg et al., 1989; Franssen et al., 1992; Buchner et al., 1995).

Table 1  Clinical motor rating scale (Appollonio et al., 1993) in cerebellar patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Total score (0–42)</th>
<th>Dysarthria (0–4)</th>
<th>Ocular movements (0–4)</th>
<th>Muscular tone (0–2)</th>
<th>Postural tremor (0–8)</th>
<th>Upper limb ataxia (0–8)</th>
<th>Lower limb ataxia (0–4)</th>
<th>Standing balance (0–4)</th>
<th>Gait ataxia (0–4)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>0</td>
<td>1</td>
<td>0</td>
<td>0.5</td>
<td>0.5</td>
<td>0</td>
<td>2</td>
<td>1</td>
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<tr>
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<td>0</td>
<td>1</td>
<td>0</td>
<td>0.25</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0.75</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>4</td>
<td>3.75</td>
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<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>7.5</td>
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<td>0.5</td>
<td>0.5</td>
<td>2</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

Figures in parentheses are the ranges of possible scores.

‘far-field’ responses by scalp electrodes (Yamada et al., 1986). In contrast, SEPs occurring later than the cortical N20, which should reflect the initial processing of the somatosensory input in cortical areas, are usually ignored in clinical practice because they are too variable. However, several investigators were able to draw reliable conclusions about cortical SEPs in cerebral lesions in studies in which the unaffected hemisphere of the patient served as a control (Mauguier et al., 1983; Yamada et al., 1984).

The aim of this study was to investigate whether cerebellar lesions can cause electrophysiological modifications in the contralateral somatosensory primary cortex. To avoid possible artefacts due to the large variability of cortical SEPs, only patients suffering from strictly unilateral lesions were enrolled in the study. This selection permitted us to evaluate changes in SEP unambiguously by using contralateral responses of the same subject as a control. Moreover, in order to separate the different SEP components, we performed dipolar source modelling of SEPs, which has proved useful in separating the activities of neighbouring cerebral structures (Scherg, 1990; Scherg et al., 1989; Franssen et al., 1992; Buchner et al., 1995).

Material and methods

Subjects and SEP recording

We recorded scalp SEPs from five subjects (aged 25–64 years, mean 43.8 years; four male) with clinical and radiological evidence of strictly unilateral hemispheric focal lesion of the cerebellum, which did not involve brainstem structures. In particular, one of them had previously undergone left hemicerebellar resection for a large cerebellar hemangioma, two of them suffered from left cerebellar ischaemia in the PICA (postero-inferior cerebellar artery) territory, one had had a left cerebellar haemorrhage, and one showed a large left cerebellar hependymoma. Cerebellar impairment was quantified using a modified version of the motor deficit scale proposed by Appollonio and colleagues, which ranges from zero (absence of any deficit) to 42 (presence of all deficits to the highest degree) (Appollonio et al., 1993); motor impairment scores are illustrated in Table 1. The clinical examination did not reveal any sign of cranial nerve, pyramidal and extrapyramidal tracts or peripheral nerve involvement in any subject. Somatosensory functioning was analysed by testing: (i) non-painful pinprick sensation and touch sensation, the latter quantified by two-point discrimination; (ii) joint position sense, i.e. the ability to identify with eyes closed flexion and extension of the fingers and toes at different angular velocities and to reproduce passive joint movements with the control limb; (iii) sensitivity to painful pinprick; and (iv) thermal sensitivity to heat and cold. Brain MRI was performed in all patients with a superconducting 0.5 tesla unit, using multiplanar SE (spin-echo), FSE (fast spin-echo) and IR (inversion recovery) sequences. None of the patients showed sensation deficits. Experimental procedures were approved by the ethics committee of our university; written consent was obtained from each subject according to the Declaration of Helsinki.

For SEP recording, subjects lay on a couch in a warm and darkened room. Symptomatic and asymptomatic sides were explored in each subject. Stimuli were delivered on the median nerve at the wrist, with duration of 0.2 ms, a rate of 1.5 Hz and motor threshold intensity. Disk recording electrodes (impedance <5 kΩ) were placed at 19 locations of the 10–20 system (excluding Fpz and Oz). The reference electrode was at the lobe of the ipsilateral ear (Tomberg et al., 1990) and the ground at Fpz. The analysis time was 64 ms, which included 5 ms of preanalysis, with a bin width of 250 µs. The amplifier bandpass was 1–3000 Hz (12 dB roll-off). An automatic artefact rejection system excluded from the average all runs containing transients exceeding ±65 µV for any recording channel. In order to ensure baseline stabilization, SEPs were digitally filtered off-line by means of a filter with a bandpass of 19–1900 Hz. Two averages of 1500 trials each were obtained and printed with an inkjet printer. Frozen maps showing the distribution of the responses over the scalp were obtained by linear interpolation from the four nearest electrodes.

Data analysis

SEPs were identified on the basis of latency, polarity and scalp distribution. Amplitudes and peak latencies were measured on the average of the two runs. Amplitudes were measured from the baseline. We evaluated the principal scalp components, labelled as in earlier reports (Arezzo et al., 1981; Desmedt et al., 1987; Allison et al., 1991a, b; Garcia Larrea et al., 1992; Valeriani et al., 1997b, 1998; Restuccia et al., 1999),
i.e. parietal N20 wave, frontal P20, central P22, frontal N24, parietal P24 and frontocentral N30 waves. In each patient, for each SEP component we compared differences of latency values between the symptomatic and asymptomatic sides by paired t-tests. Because the distribution of amplitude values was not Gaussian, side differences in amplitude values were compared by Wilcoxon’s test.

In patients, both peak and amplitude values were compared with those obtained in a population of 10 healthy subjects matched for age and sex (six men, four women; mean age
Fig. 2 SEPs to median nerve stimulation in two of the five cerebellar patients. SEPs obtained after symptomatic side stimulation (thick traces) are superimposed over those obtained after asymptomatic side stimulation (thin traces). N20/P20, P22 and N30 components do not show any difference between asymptomatic side and symptomatic side stimulation, whereas both frontal N24 and parietal P24 components are clearly smaller after stimulation of the symptomatic side. After symptomatic side stimulation, the N30 response seems to be reduced at the frontal location, while it remains substantially unchanged in central traces. Because the overall frontal negativity is an amalgam of the N24 and N30 activities in normal conditions, this finding is probably caused by the amplitude reduction of the frontal N24 after stimulation of the symptomatic side. Traces from both patients also show changes in other SEP components, which are, however, inconstant; for instance, the later positive peak in parietal traces from Subject 2, which should probably be considered as a P45 response, seems to be markedly decreased after stimulation of the symptomatic side; on the other hand, the same peak was greatly increased in three asymptomatic sides and reduced in the remaining two, so that its modifications seem independent of the cerebellar lesion.

Fig. 3 Histogram showing the average strength of each dipole (Dip.) in normal subjects after stimulation of the right median nerve (black columns) and left median nerve (open columns). Bars above each column represent standard deviations. Dipole strengths do not show any significant difference between left and right stimulation.

46 ± 7 years), from whom SEPs were recorded after stimulation of the right and left median nerves at the wrist.

To assess the distribution of responses in controls and patients, their amplitudes were submitted to Friedman’s test, considering scalp locations as the source of variation. When statistical significance was reached, a post hoc analysis was carried out with the Wilcoxon test.

In patients and controls, we also evaluated the interside
asymmetry of amplitude for each SEP component, by calculating the \((ampl\ max – ampl\ min)/ampl\ max\) ratio as a percentage, where \(ampl\ max\) and \(ampl\ min\) represent the larger and the smaller amplitude value of each component, respectively, obtained in an individual after stimulation of the right or left median nerve. Interside asymmetry values obtained in controls were compared with those obtained in patients by means of the Mann–Whitney U-test.

Two grand averages were also obtained from SEPs of the asymptomatic and symptomatic sides. Before calculating the grand average, all traces were made coincident at the latency of the N20 potential. We performed this normalization of latencies to prevent artificial smoothing due to different latencies of the responses between subjects.

**Brain electric source analysis (BESA)**

A detailed description of BESA is given elsewhere (Scherg, 1990). The BESA program calculates potential distributions over the scalp from preset voltage dipoles within a three-shell model of the head. It also evaluates the fit between the recorded and calculated field distributions. The percentage of data that cannot be explained by the calculated field distribution is expressed as residual variance (RV). The lower the RV the better the dipolar model and, in an ideal case, the RV should be due only to the recorded noise. In general, RV values lower than 10% are considered acceptable, particularly when obtained from individual recordings. However, it should also be clear that even zero RV does not prove the model to be correct, because of the infinite number of solutions to the inverse problem of deriving intracranial sources from the extracranial potential field. BESA uses a spherical three-shell model with an 85 mm radius and assumes that the brain surface is 70 mm from the centre of the sphere. The spatial position of each dipole is described on the basis of three axes: (i) the line through T3 and T4 (x-axis); (ii) the line through Fpz and Oz (y-axis); and (iii) the line through Cz (z-axis). The three axes intersect at the centre of the sphere. The spatial orientation of the dipoles is described by two angles: (i) \(\phi\) is the angle in the \(x-y\) plane measured anticlockwise from the nearest \(x\)-axis; (ii) \(\theta\) is the vertical angle that is measured from the \(z\)-axis and is positive for the right hemisphere. The strength is given in \(\mu V_{eff}\), 1 \(\mu V_{eff}\) being the strength of a horizontal dipole, located at \(y = 50\) mm, which produces a voltage difference of 0.5 \(\mu V\) between C3 and C4.

Dipole parameters in single individuals were compared using Wilcoxon’s test. Strengths of dipole activity obtained from stimulation of the asymptomatic side as well as the symptomatic side were compared by means of paired Student’s \(t\)-test. Strengths of dipole activity in patients were compared with those obtained from controls. Comparisons were performed by means of two-way ANOVA (analysis of variance).

In order to correlate clinical deficits with the neurophysiological abnormalities, we evaluated the interside asymmetry of dipole strengths, by calculating the \((strength\ max – strength\ min)/strength\ max\) ratio as a percentage, where \(strength\ max\) and \(strength\ min\) represent the larger and the smaller strength value respectively of each dipolar activity obtained in an individual after stimulation of the right or left median nerve. Interside asymmetry values obtained in patients were correlated to the total motor impairment score by Spearman’s test.

**Results**

SEP findings in our cerebellar patients are summarized in Table 2. For both sides, latency and amplitude SEP values of cerebellar patients were similar to those obtained in controls. In patients as well as in controls, N20 and P20 responses were readily identifiable in the centroparietal region contralateral to the stimulus and in the frontal traces, respectively. The N20 response was always evident in both C3 and P3 locations. On the basis of our previous results (Valeriani et al., 1997a), we distinguished N20p or N20c depending on whether the recording site was over the parietal or the central region.

In controls, the P20 amplitude reached its maximum value at frontal locations contralateral to the stimulated side (Friedman test, \(P < 0.05\); Wilcoxon test, \(P < 0.05\)). The P22 potential was recorded by the central electrode contralateral to the stimulation site in 17 out of 20 SEPs. Maximal N24 amplitude was reached at frontal locations contralateral to the stimulated side (Friedman test, \(P < 0.05\); Wilcoxon test, \(P < 0.05\)). The N30 response was identifiable in all subjects in the frontocentral region, with a mean amplitude that was significantly higher in the Fz recording (Friedman test, \(P < 0.05\)).

In cerebellar patients, the P20 amplitude reached its maximum value at frontal locations contralateral to the stimulated side (Friedman test, \(P < 0.05\); Wilcoxon test, \(P < 0.05\)). The P22 potential was recorded by the central electrode contralateral to the stimulation site in all 10 SEPs. When identifiable (Table 2), the N24 reached its maximum amplitude at frontal locations contralateral to the stimulated side (Friedman test, \(P < 0.05\); Wilcoxon test, \(P < 0.05\)). The N30 response was identifiable in all subjects in the frontocentral region. Its mean amplitude was significantly higher in the Fz recording (Friedman test, \(P < 0.05\)).

Furthermore, a comparison between sides demonstrated that in the patients there was no significant difference between the latency values of the asymptomatic and symptomatic sides. Conversely, when the amplitude values of the asymptomatic and symptomatic sides of the patients were compared, both frontal N24 and parietal P24 values were significantly smaller after stimulation of the symptomatic side than after asymptomatic side stimulation (N24, Wilcoxon...
### Table 2 SEP values

<table>
<thead>
<tr>
<th>Patient</th>
<th>Amplitude (µV)</th>
<th>Latency (ms)</th>
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</thead>
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<td></td>
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<tr>
<td>Median nerve, asymptomatic side</td>
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<tr>
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</tr>
<tr>
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<tr>
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</tr>
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</tr>
<tr>
<td>5</td>
<td>2.59</td>
<td>1.1</td>
</tr>
<tr>
<td>Median nerve, symptomatic side</td>
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</tr>
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<tr>
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</table>

*P > 0.05
†Ratio not available because of lack of reliable response after left or right side stimulation.

Mann–Whitney test between side differences in control and cerebellar patients. Differences were found either for latency or for amplitude values. When we compared side differences in amplitude between controls and patients, we found that the amplitude asymmetry for the P24 potential was significantly higher in patients than in controls (Mann–Whitney test, P < 0.05) (Table 2). In conclusion, although control subjects did not show any significant side difference, a significant difference in the N24 and P24 amplitudes was observed for patients between the asymptomatic side and the symptomatic side (Figs 1 and 2).

To build the dipolar models, we employed grand-average traces and used a sequential strategy, as described in detail elsewhere (Valeriani et al., 1997b, 1998). We divided the analysis time (from the subcortical P14 to the N30 response) into two intervals, choosing the peak of the N20 response as the division point. In the earlier interval, which was analysed first, one subcortical and two cortical dipolar sources were
Table 3 Dipolar coordinates

<table>
<thead>
<tr>
<th>Dipole 1</th>
<th>Dipole 2</th>
<th>Dipole 3</th>
<th>Dipole 4</th>
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</thead>
<tbody>
<tr>
<td>x y z θ φ</td>
<td>x y z θ φ</td>
<td>x y z θ φ</td>
<td>x y z θ φ</td>
</tr>
</tbody>
</table>

**Normal subjects**

- **Right median nerve SEPs**
  - Individual models (mean)
    - $-1.52$ $-22.9$ $-18.49$ $-64$ $-16.6$
    - $-43.11$ $-5.44$ $49.7$ $-82.56$ $66.22$
    - $-45.89$ $2.17$ $38.66$ $-13.8$ $-13.29$
    - $-17$ $-31$ $36.33$ $16.31$ $-0.16$
  - Individual models (SD)
    - $6.26$ $10.26$ $7.54$ $36.27$ $81.18$
    - $2.67$ $4.33$ $2$ $72.43$ $8.09$
    - $4.13$ $3.39$ $5.29$ $49.73$ $73.97$
    - $0$ $0$ $7.07$ $70.84$ $49.71$

- **Left median nerve SEPs**
  - Individual models (mean)
    - $0.18$ $-20.7$ $-19.92$ $-20.8$ $-32.53$
    - $-41$ $-6.32$ $51.01$ $-106$ $57.79$
    - $-41.89$ $3.21$ $38.77$ $-16.8$ $-21.39$
    - $-17.22$ $-32.44$ $36.08$ $48.5$ $-13.21$
  - Individual models (SD)
    - $8.84$ $12.71$ $8.36$ $49.27$ $69.13$
    - $5.43$ $5.25$ $3.99$ $13.78$ $7.58$
    - $6.79$ $4.95$ $5.98$ $64.57$ $70.8$
    - $0.67$ $4.33$ $8.47$ $59.63$ $56.61$

**Patients**

- **Symptomatic side median nerve SEPs**
  - Individual models (mean)
    - $2.75$ $-9.64$ $-17.96$ $-49.8$ $-54.92$
    - $-48.2$ $-4.22$ $46.36$ $-93.6$ $60.18$
    - $-44.4$ $-0.71$ $40.28$ $-34.8$ $8.18$
    - $-31.2$ $-14.2$ $48.24$ $-23.28$ $7.52$
  - Individual models (SD)
    - $7.38$ $40.71$ $13.5$ $16.9$ $34.6$
    - $5.4$ $4.58$ $8.18$ $32.2$ $18.23$
    - $8.62$ $10.77$ $7.41$ $103.7$ $41.3$
    - $10.85$ $6.18$ $8.74$ $34.78$ $39.11$

- **Asymptomatic side median nerve SEPs**
  - Individual models (mean)
    - $1.28$ $-29.74$ $-33.65$ $-50$ $-59$
    - $-47.6$ $-4.18$ $43.88$ $-104.4$ $68.6$
    - $-49.2$ $6.09$ $37.66$ $-52.4$ $-36.3$
    - $-25.2$ $-22$ $44.84$ $5.62$ $20.7$
  - Individual models (SD)
    - $9.9$ $22.41$ $24.83$ $13.62$ $24.32$
    - $3.58$ $2.86$ $2.79$ $10.78$ $12.2$
    - $9.26$ $5.41$ $2.13$ $15.67$ $29.47$
    - $9.2$ $7.7$ $11.54$ $57.6$ $71.03$
activated. In particular, two cortical sources were believed necessary on the basis of previous results showing the contributions of two different cortical generators to the SEP topography in the 20 ms latency range (Valeriani et al., 1997a). When we added the later interval to the analysis, another dipole was needed to explain the scalp SEP topography. This four-dipole model correlated well with the SEP distribution in the grand-average traces obtained from stimulation of the right median nerve in normal subjects (RV 4.2%; individual RV values ranged from 1.13 to 9.4%). In order to apply the same model to left median nerve traces, they were inverted off-line; in other words, traces from the left scalp were considered as recorded at the corresponding sites of the right scalp and vice versa, leaving traces from Fpz, Fz, Cz and Pz unaffected. When we applied the four dipole model to SEPs from left stimulation in normal subjects, we obtained RV values similar to those obtained from right median nerve traces (RV 4.98%; individual RV values ranged from 2.71 to 10.3%).

The first dipole (dipole 1), whose peaking activity had the same latency as the P14, was placed at the base of the skull; the other three dipoles had perirolandic locations. Dipole 2 was oriented tangentially and was activated at the latencies of both the N20/P20 and, with inverted polarity, P24/N24 potentials. Dipole 3 showed an early peak of activity slightly preceding the first peak of dipole 2; later, it was activated with opposite polarity at the same latency as the P22 response. Dipole 4 reached a radial orientation and a medial location and showed a late peak of activity at the latency of the frontocentral N30.

This model was applied to the grand-average traces obtained from all five patients, and was further applied to SEPs recorded in each patient. The four-dipole model correlated well with the SEP distribution in grand averages (RV 2.78 and 2.77% for grand-average traces from the asymptomatic and symptomatic sides, respectively) as well as in individual traces (RV 2.24–10.8%).

Statistical analysis of the individual BESA parameters in controls did not show any significant side difference (Table 3 and Fig. 3). In contrast, the individual BESA models obtained from patients (Figs 4, 5 and 6) showed that the strength of the second peak of dipole 2 was significantly weaker after stimulation of the symptomatic side than of the asymptomatic side (paired t-test, P < 0.01). No significant side differences were found for the other dipole parameters (location and orientation).

Inter-side asymmetry values of the dipole strengths obtained in patients did not show any significant correlation with the motor impairment expressed as total deficit score; in particular, no significant correlation was found between the inter-side asymmetry of the second peak of dipole 2 and the total deficit score (Spearman test, r = 0.205, P = 0.74).

**Discussion**

The main finding of the present study is that, after stimulation of the symptomatic side, patients with unilateral cerebellar damage demonstrate definite SEP abnormalities primarily in the positive parietal response P24 and the negative frontal response N24. These abnormalities may be related to the reduced activity of a dipolar source in the primary somatosensory cortex (SI).

Side differences after unilateral cerebellar damage were clearly shown by dipolar modelling. The strength of the second peak of activation of dipole 2, which was likely to generate both N24 and P24 waves (Valeriani et al., 1998), was significantly weaker after stimulation of the symptomatic side than of the asymptomatic side. Possible influences of physiological side differences were ruled out, because no significant side differences in SEPs were observed in control subjects. Subclinical involvement of somatosensory tracts at subcortical levels were discarded because both the P14 wave, which is thought to reflect the ascending volley in the medial lemniscus (Yamada et al., 1986), and the N20 response, which is generally agreed to represent the arrival of the somatosensory volley to the cortex (Desmedt et al., 1987; Allison et al., 1991a, b), were normal in all patients. We can also easily discard the hypothesis that SEP modifications might be related to the motor impairment, because patients presented very low motor impairment (Table 1) and no significant correlation was found between motor deficit scores and the reduction in dipole activity.

Our current knowledge about the mechanisms underlying the generation of cortical SEPs allows us to speculate on which kind of cortical dysfunction is specifically reflected by the SEP abnormality observed after cerebellar damage. So far, only a few studies have addressed the physiological meaning of the N24 and P24 scalp responses. The activities of both potentials are usually embedded in larger, long-lasting potentials; for example, the frontal N24 is often described as a small notch on the rising slope of the later N30 frontocentral wave (Rossini et al., 1987; Garcia Larrea et al., 1992) or is merely identified with this latter wave (Tsuji and Murai, 1986; Allison et al., 1991a, b). Regarding
Fig. 6 Four-dipole spatiotemporal solution for median nerve SEPs after stimulation of the symptomatic (A) and asymptomatic (B) side; Patient 2. SEPs obtained by left median nerve stimulation were inverted off-line for right upper limb SEPs before modelling. The residual variance is 7.2 in A and 6 in B. The source potentials of the dipoles are shown on the left. On the right, three views of the head illustrate the locations and orientations of the dipoles. The top row shows the source potential and location of the dipole at the base of the skull (dipole 1). The source potential and location of the tangential perirolandic dipole are shown in the second row. The third and fourth rows show source potentials and locations of the other two perirolandic dipoles. Note that the second peak of the tangential perirolandic dipole (dipole 2) is notably weaker after symptomatic than after asymptomatic side stimulation (arrows).
the late P25 response, corresponding to the parietal P24 in our traces, Rossini and colleagues suggested that ‘this peak might in part reflect the slow processes of electrotonic invasion of the apical dendrites due to current spread from the cell body with polarity inversion along the pyramidal cells of area 3b, which possibly generate a tangential dipole of opposite value compared to the one described for wave N20’ (Rossini et al., 1987). BESA confirmed that the frontal N24 and the parietal P24 are generated by the opposite poles of the same tangential dipolar source (Valeriani et al., 1998), demonstrating that the N24 and P24 responses represent the opposite ends of the same dipolar source generating the N20/P20 potentials (Valeriani et al., 1997b, 1998). Thus, N24/P24 are generated from the same cortical area that generates N20/P20 parietofrontal potentials, i.e. the 3b area (Arezzo et al., 1981; Desmedt et al., 1987; Allison et al., 1991a, b, Restuccia et al., 1999). Overall, these data indicate that cerebellar-induced SEP alterations can be localized within 3b processing.

As stated above, N24 and P24 waves are generated by the same source as the N20/P20 potentials, whose activity inverts its polarity. Reversal of the polarity of a dipolar activity has been explained as the transition of excitatory and inhibitory phases in different layers of the same cortical area (Creutzfeldt and Houchin, 1974). Confirmation of the inhibitory nature of the N24/P24 responses has derived from the dissociation between a normal N20/P20 and a reduced N24/P24 induced by stimulation at a high frequency (Valeriani et al., 1998) that selectively reduces inhibitory responses (Nacimiento et al., 1964). Therefore, our results strongly suggest that the cerebellum can influence the functional status of the primary somatosensory cortex, and, in particular, the function of the cortical circuitry that regulates the inhibitory phase that follows the primary depolarization of pyramidal cells.

If the cerebellum is involved in the early phases of somatosensory processing, it remains to be explained how the cerebellum exerts its influence on the somatosensory cortex. Two alternative hypotheses can be put forward. The first is that the impaired efficacy of somatosensory processing is a consequence of the lack of a general tonic influence of the cerebellum over the contralateral cerebral cortex. Different lines of evidence contradict this interpretation. The selectivity of the functional impairment limited to a specific SEP response, as well as the differences between the cerebellar-induced physiological modifications in M1, mainly affecting excitatory circuits (Di Lazzaro et al., 1995), versus SI, mainly affecting inhibitory phases, clearly argue in favour of the specificity of the cerebellar influence over cortical processing. The second hypothesis is that the reduction of SI inhibitory processing is specifically linked to the nature of the cerebellar input to this area. So far, no disynaptic cerebellar–SI projections have been reported through the cerebellar recipient thalamic relay nuclei. Nevertheless, cerebellar influences can reach SI through the intralaminar nuclei that are known to receive massive cerebellar input and to project to SI. It is worth noting that, although relay nuclei reach mainly the granular cortical layer, intralaminar cells project to the infragranular as well as to the superficial layers (Bentivoglio et al., 1988).

Thus, the characteristics of the cerebellar disynaptic input to area 3b are consistent with the above demonstrated influences on the later processing of the incoming volley. On the other hand, in the cortical area, where the cerebellar afferents mainly reach layer IV, as in MI, the effect of cerebellar damage is limited to the excitatory circuitry (Di Lazzaro et al., 1995).

Several SPECT (single-photon emission computed tomography) reports have pointed out that cerebellar lesions can cause the functional involvement of remote cortical cerebral areas. This remote involvement is commonly considered the reverse of the cerebrocerebellar diaschisis phenomenon described by Baron and colleagues (Baron et al., 1981); thus, it has been labelled as ‘crossed cerebrocerebellar diaschisis’. Several authors have described significant reduction of regional cerebral blood flow not only in frontal regions but also in postcentral regions contralateral to cerebellar damage (Sönmezoglu et al., 1993; Komaba et al., 2000). The present data provide clues for a better understanding of the mechanisms sustaining the diaschisis phenomenon.

References


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