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# Long-term changes in cerebellar activation during functional recovery from transient peripheral motor paralysis

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ABSTRACT

Localized altered cerebellar cortical activity can be associated with short-term changes in motor learning that take place in the course of hours, but it is unknown whether it can be correlated to long-term recovery from transient peripheral motor diseases, and if so, whether it occurs concomitantly in related brain regions. Here we show in a longitudinal fMRI study of patients with unilateral Bell's palsy that increases in ipsilateral cerebellar activity follow the recovery course of facial motor functions over at least one and a half years. These findings hold true for changes in brain activity related to both oral and peri-orbital activation, even though these processes are differentially mediated by unilateral and bilateral brain connectivities, respectively. Activation of non-facial musculature, which was studied for control, does not show any change in cerebellar activity over time. The localized changes in cerebellar activities following activation of facial functions occur concomitantly with increases in activity of the facial region in the contralateral primary motor cortex suggesting that the cerebellum acts together with the cerebral cortex in long-term adaptation to transient pathological sensorimotor processing.



## Introduction

Plasticity mechanisms underlying compensation to neuropathology form an intense topic of modern neuroscience research. One of the main unresolved questions is to what extent these mechanisms mimic those that underlie regular forms of plasticity such as the processes that are involved in learning and memory formation (Konrad et al., 2006; Cheng et al., 2008). In general, the forms of plasticity that are supposed to underlie learning and memory include the modification of the strength of particular synapses in the relevant circuitry (De Zeeuw and Yeo, 2005). Therefore one might expect that plastic changes associated with a particular learning paradigm are stably localized within a particular brain region (Cheng et al., 2008). Yet, during compensations in most neuropathological disorders changes are often not precisely fixed to one brain region, because often CNS disorders include *permanent* damage to one or more, central or peripheral area(s) causing a rerouting of the neuro-anatomical pathways involved (Konrad et al., 2006; Miall and King, 2008). Here, we investigated in a longitudinal study changes in activation in the cerebellum and motor cortex of Bell's palsy patients with a *transient* unilateral peripheral motor disease. Patients with Bell's palsy suffer from an idiopathic peripheral facial paralysis, and about 70% of them recover completely within 6 months without medication (Engstrom et al., 2008). Interestingly, the facial nucleus contains two different types of motor neurons. One type, which includes the motor neurons that innervate the oral muscles, receives a purely contralateral input from the cerebral cortex, and another type, which includes the motor neurons that innervate the peri-orbital muscles, receives a bilateral input from the cerebral cortex as illustrated in Fig. 1 (Morecraft et al., 2001). Thus, this unique division of innervations combined with a transient pathological process allows us to evaluate the question to what extent a non-permanent paralysis can lead to permanently altered activation in the cerebellum, and if so, whether we can correlate functional changes in the cerebellum to those in the cerebral cortex in the same subjects. We therefore measured changes in brain activation in Bell's palsy patients at four successive periods in one and a half years using functional magnetic resonance imaging (fMRI) while they were subjected to facial motor tasks of lip pursing and eyeblinking.

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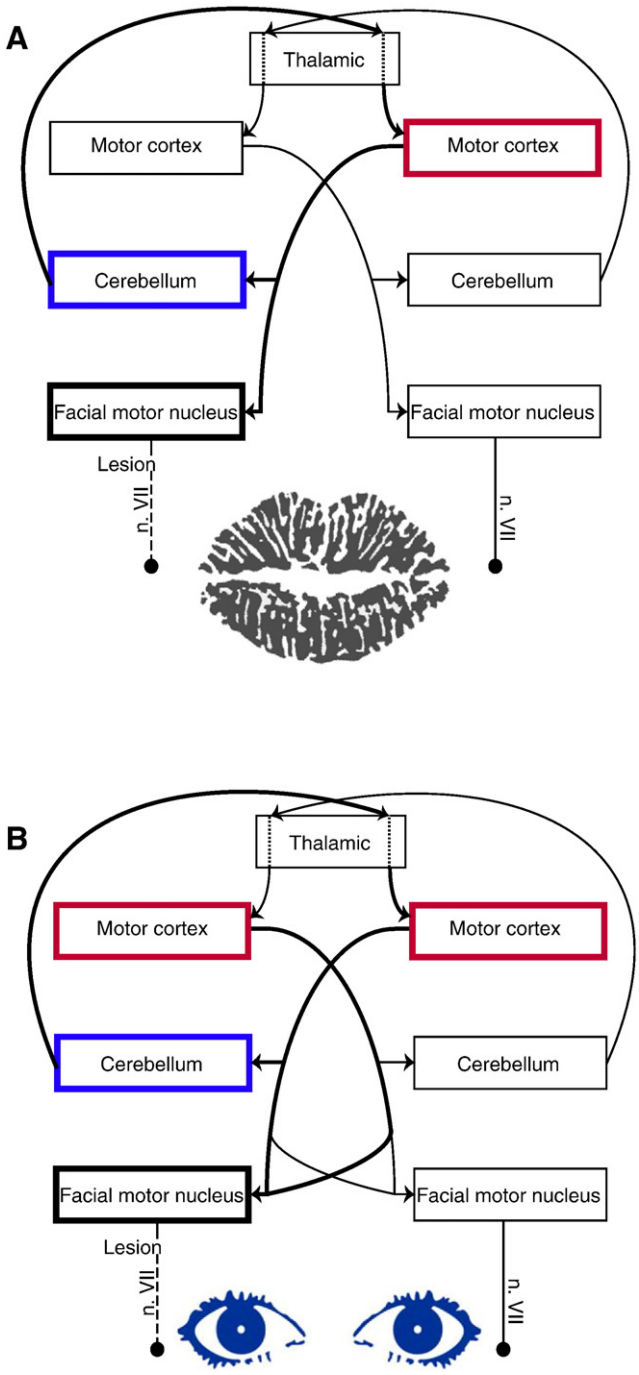


**Fig. 1.** Main neuro-anatomical connections between thalamus, cerebral motor cortex, cerebellum and peripheral facial targets. A. Oral facial circuitry; oral motor neurons receive purely ipsilateral and contralateral input from the cerebellum and motor cortex, respectively; B. Orbital facial circuitry; orbital motor neurons receive ipsilateral and bilateral input from the cerebellum and motor cortex, respectively. Note that the oral facial and orbital representations are both ipsilaterally located in the cerebellum.

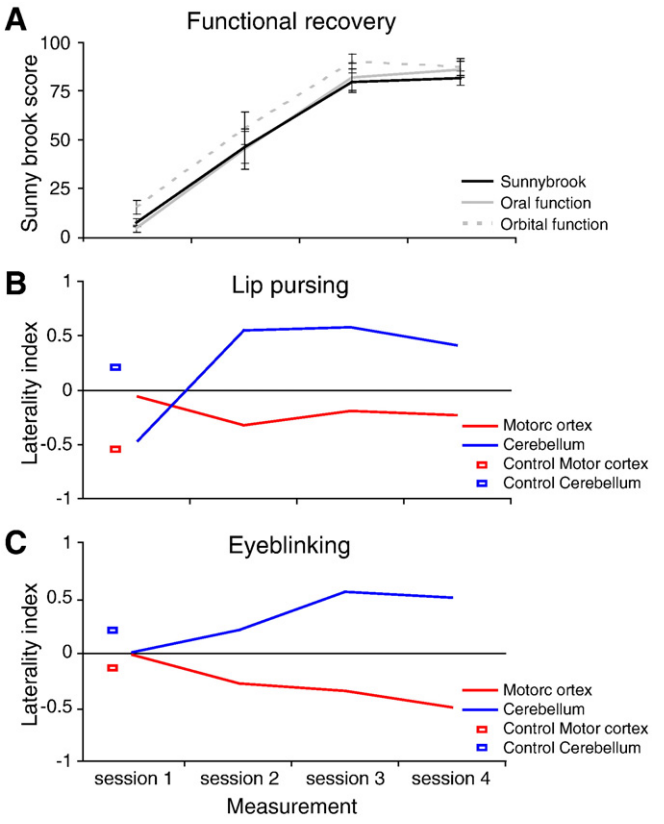


**Fig. 2.** Behavioral recovery of facial function. A. Recovery of 9 Bell's palsy patients as determined by the Sunnybrook Grading System. The scores of their facial muscle function were scaled from 0 (no function) to 100 (perfect functioning). At the onset and end of affliction, the mean scores for oral functions (solid gray line) were 3 (range 0–10) and 76 (range 38–100), while the orbital functions (dashed gray line) were rated at 16 (range 0–20) and 86 (range 46–100), respectively. Solid black line indicates overall Sunnybrook score. B. Changes in laterality index (LI) of fMRI activities in the motor cortex and cerebellum during lip pursing (statistical threshold was set at $p<0.001$). Bell's palsy patients were measured at four different sessions over a period of 1.5 years after onset of Bell's palsy, whereas controls were only measured once. The LI was computed according to the formula $(k_{left}-k_{right})/(k_{left}+k_{rightt})$, where k represents the number of voxels within the region of interest above threshold in the left and right hemisphere. Positive and negative LI's correspond to more or less ipsilateral activation, respectively. C. Changes in LI of fMRI activities in the motor cortex and cerebellum during eyeblinking (statistical threshold was set at $p<0.01$).

## Methods

### *Subjects*

Nine Bell's palsy patients (four men and five women, average age at onset of the paralysis; $41.7\pm12.3$ years, range; 20–59 years) participated in this study. Bell's palsy patients were recruited from the Department of Otolaryngology of the Erasmus MC, University of Rotterdam. Inclusion criteria were: Acute idiopathic unilateral facial nerve paralysis (onset and deterioration within 48 h), no medical treatment, and complete facial nerve denervation as defined by House Brackmann grade V–VI (Kanerva et al., 2006). Patients who presented with viral Herpes simplex I, Varicella zoster or a history of neurological, psychiatric, otological disorders or cerebral vascular accident were excluded. Additional exclusion criteria were pregnancy, substance abuse and claustrophobia. As a control group fourteen healthy subjects (nine men and five women; average age $39.6\pm15.0$ years; range 25–64 years) were studied. All participants signed an informed consent form prior to the study that was approved by the Medical Ethics Committee. The Subjects' consent was obtained according to the Declaration of Helsinki (BMJ 1991; 302:1194).

Functional recovery in patients was assessed with the Sunnybrook grading system (Kanerva et al., 2006), while simultaneous eyelid kinematics and OO-muscle activity recordings were performed with the search coil technique and OO-EMG (VanderWerf et al., 2007). The patients were subjected to four fMRI scans throughout their recovery to monitor changes in activation in the motor cortex and cerebellum. Functional MRI experiments were performed after about 15 days ($\pm12$), 4 months, 1 year and 1.5 years with respect to the onset of affliction. The timing of the scans should reflect the four phases that can be distinguished during blink recovery (VanderWerf et al., 2007): phase one is the period of the first few weeks during which

deterioration of the facial nerve is prominent; the second phase, i.e. month two to four, is the period during which the peripheral nerve sprouts towards its target; phase three starts in the fifth month and represents the period in which new nerve–muscle contacts are created as can be deduced from OO-EMG overshoots; and finally in phase four fine-tuning of the newly formed motor units occurs, which can be followed by subtle increases in the peak amplitude and velocity of blinks. The control group was subjected to the same functional imaging experiments using the same tasks, but only once. Patients and control subjects were permanently observed during the scan in order to ensure proper task performance.

### *Sunnybrook scale*

The Sunnybrook facial grading system was used to document clinically significant changes in facial function in Bell's palsy patients (Kanerva et al., 2006). The Sunnybrook facial grading system is a standard protocol of facial expressions to determine the grade of affliction. The protocol includes observation of the face at rest, followed by observation of five facial expressions; lifting the eyebrows, closing eyes gently and then more powerfully, wrinkling the nose, smiling with an open mouth and puckering of the lips. These facial expressions were often accompanied by synkinesia. All elements were scored and the sum resulted in the grade of affliction.

### *Functional imaging experiments*

Imaging data was acquired on a 1.5T MR scanner (Sigma CV/I, General Electric, Milwaukee, USA) with a standard head coil. An anatomical reference image was obtained using a 3D FSPGR T1-weighted sequence with the following parameters: TR/TE/TI 9.8/1.9/400 ms, 224×320 matrix size, field of view 24 cm, 1.6 mm thick slices, no gap). For functional images a T2*-weighted gradient echo EPI sequence was used (TR/TE 3000/40 ms, field of view 26 cm, 96×96

**Table 1**
Localizations and changes of activated areas in the cerebellum and the motor cortex during functional recovery of Bell's palsy patients. The laterality index (LI) of lip pursing flipped in the first 4 months from the right to the left cerebellar hemisphere. The LI of blinking deviates from the fourth month on towards the left cerebellar hemisphere and towards the right hemisphere in the motor cortex. Note that the side of affliction is left. The LI indicates the number of above threshold voxels (k), and the weighted location in MNI coordinates (CoM XYZ), in the ipsilateral (left) and contralateral (right) hemisphere in the two regions of interest, the motor cortex and the cerebellum, for the lip pursing, blinking and finger tapping tasks. Each patient underwent four measurements during the study conform the standard protocol. The weighted location (CoM XYZ) was computed as the centre of mass activation within a hemispheric region, by weighing the coordinate of each voxel with its associated T-value. XYZ coordinates of the highest activation within a hemispheric region are expressed in millimetres.

| Task | Cerebellum | Parameter | Patient | | | | Control |
|---|---|---|---|---|---|---|---|
| | Hemisphere | | Measurement 1 | Measurement 2 | Measurement 3 | Measurement 4 | Measurement |
| Lip pursing | | LI | −0.46 | 0.55 | 0.58 | 0.41 | 0.20 |
| | Left (ipsilateral) | K | 11 | 48 | 56 | 77 | 271 |
| | | CoM X Y Z (mm) | −20 −63 −25 | −21 −63 −23 | −20 −61 −27 | −22 −62 −31 | −19 −66 −27 |
| | | X Y Z (mm) | −3 −81 −24 | −24 63 −27 | −27 −63 −33 | −30 −66 −24 | −21 −63 −27 |
| | Right (contralateral) | K | 30 | 14 | 15 | 32 | 179 |
| | | CoM X Y Z (mm) | 22 −64 −26 | 22 −60 −23 | 29 −29 −15 | 23 −63 −32 | 20 −63 −24 |
| | | X Y Z (mm) | 30 −63 −27 | 24 −63 −27 | 27 −57 −30 | 18 −63 −24 | 24 −63 −30 |
| Blinking | | LI | 0.01 | 0.21 | 0.56 | 0.50 | 0.20 |
| | Left (ipsilateral) | K | 517 | 162 | 246 | 490 | 772 |
| | | CoM X Y Z (mm) | −20 −64 −24 | −16 −60 −22 | −18 −61 −28 | −19 −61 −32 | −19 −65 −25 |
| | | X Y Z (mm) | −6 −72 −24 | −15 −69 −21 | −36 −57 −36 | −15 −48 −45 | −21 −60 −30 |
| | Right (contralateral) | K | 510 | 106 | 70 | 162 | 513 |
| | | CoM X Y Z (mm) | 23 −64 −25 | 18 −62 −23 | 18 −63 −26 | 19 −62 −31 | 21 −65 −26 |
| | | X Y Z (mm) | 9 −75 −30 | 9 −75 −24 | 27 −60 −30 | 12 −66 −27 | 24 −63 −27 |
| Finger Tapping | | LI | −0.45 | −0.47 | −0.45 | −0.91 | −0.50 |
| | Left (ipsilateral) | K | 87 | 104 | 61 | 11 | 98 |
| | | CoM X Y Z (mm) | −21 −62 −26 | −21 −61 −23 | −19 −60 −26 | −22 −60 −27 | −19 −63 −24 |
| | | X Y Z (mm) | −3 −57 −18 | −9 −33 −15 | −24 −60 −27 | −24 −45 −24 | −24 −57 −33 |
| | Right (contralateral | K | 231 | 290 | 160 | 242 | 292 |
| | | CoM X Y Z (mm) | 22 −60 −26 | 21 −59 −22 | 22 −58 −28 | 21 −59 −27 | 20 −62 −25 |
| | | X Y Z (mm) | 15 −57 −24 | 21 −54 −27 | 15 −57 −21 | 12 −66 −21 | 9 −60 −21 |
| | Motor cortex | | | | | | |
| Lip Pursing | | LI | −0.06 | −0.32 | −0.19 | −0.23 | −0.55 |
| | Left (ipsilateral) | K | 24 | 39 | 89 | 81 | 95 |
| | | CoM X Y Z (mm) | −41 −7 48 | −41 −8 46 | −44 −4 41 | −42 −6 45 | −41 −9 49 |
| | | X Y Z (mm) | −48 −6 54 | −54 −9 33 | −54 −3 42 | −54 −9 33 | −45 −9 57 |
| | Right (contralateral) | K | 27 | 76 | 131 | 130 | 323 |
| | | CoM X Y Z (mm) | 44 −8 46 | 43 −9 46 | 50 −1 38 | 44 −8 46 | 45 −8 46 |
| | | X Y Z (mm) | 51 −9 39 | 60 0 27 | 57 3 36 | 54 −9 42 | 57 −12 42 |
| Blinking | | LI | −0.02 | −0.28 | −0.35 | −0.50 | −0.14 |
| | Left (ipsilateral) | K | 294 | 66 | 82 | 72 | 201 |
| | | CoM X Y Z (mm) | −40 −6 47 | −42 −6 45 | −41 −6 46 | −42 −6 46 | −42 −6 45 |
| | | X Y Z (mm) | −45 −6 60 | −45 −6 45 | −48 −6 51 | −48 −3 51 | −39 −6 51 |
| | Right (contralateral) | K | 305 | 118 | 171 | 216 | 268 |
| | | CoM X Y Z (mm) | 42 −6 45 | 45 −2 40 | 46 −3 40 | 45 −12 42 | 45 −5 43 |
| | | X Y Z (mm) | 39 −9 48 | 60 3 33 | 45 −6 48 | 45 −12 42 | 54 −12 39 |
| Finger Tapping | | LI | 0.52 | 0.75 | 0.56 | 0.43 | 0.42 |
| | Left (ipsilateral) | K | 266 | 181 | 368 | 273 | 445 |
| | | CoM X Y Z (mm) | −37 −12 53 | −36 −13 53 | −37 −12 52 | −36 −14 55 | −38 −12 52 |
| | | X Y Z (mm) | −48 −6 54 | −36 −18 63 | −36 −15 51 | −36 −24 57 | −30 −21 60 |
| | Right (contralateral) | K | 84 | 26 | 103 | 109 | 181 |
| | | CoM X Y Z (mm) | 41 −9 51 | 44 −7 46 | 45 −6 46 | 45 −5 47 | 44 −7 48 |
| | | X Y Z (mm) | 51 0 42 | 42 0 45 | 60 6 30 | 57 9 33 | 30 −9 54 |

matrix size, 5 mm thick slices, 1 mm interslice gap). All scans were oriented in the axial plane and covered the whole brain.

*fMRI paradigms*

All tasks were designed according to a block design with two conditions (active and rest). Each condition was alternated for 5 periods of 30 s during which 10 volumes were acquired. The total scan time per experiment was five minutes. The onsets of the rest and active conditions were indicated verbally using simple words (start, rest) generated by a computer program (Matlab 7.1; Mathworks, Sherborn, Mass). Auditory stimuli were presented to the patients through a MRI compatible headphone. The lip pursing task was a self-paced repetitive kiss-like movement with the lips; subjects were instructed not to use other facial muscles. The eyeblinking task consisted of fast, gentle, self-paced bilateral closure of the eyelids. Here too, the subjects were instructed not to use other facial muscles in the movement. A finger-tapping task, which was studied for control, consisted of a self-paced serial movement with the digits of the right hand. A series was a movement of index finger to thumb, middle finger to thumb, ring finger to thumb, little finger to thumb, ring finger to thumb and middle finger to thumb. During the experiments the subjects were asked to keep their eyes closed, except during the blinking task, and relax. Prior to the fMRI experiments subjects received exact instructions and practiced the tasks to ensure correct task execution.

*fMRI data analysis*

Analysis of fMRI data was performed with the statistical parametric mapping (SPM5, Welcome department of Cognitive Neurology, London, UK) software implemented in Matlab (Math Works Inc., Natick, MA). For individual analysis, all T2*-weighted functional images were realigned to correct for the participant's motion during data acquisition and were co-registered with the high-resolution T1-weighted anatomical image (Friston et al., 1996). The functional and anatomical images were normalized to the standard brain space defined by the Montreal Neurological Institute (MNI) as provided within SPM5, using affine and nonlinear registration (Ashburner and Friston, 1999) and resulting in resampled voxel sizes of $3\times3\times3$ mm$^3$ for the functional and $1\times1\times1$ mm$^3$ for the anatomical images. The normalized functional images were smoothed with 3D Gaussian filter of $8\times8\times8$ mm$^3$ Full Width Half Maximum (FWHM) to increase the signal-to-noise ratio, correct for interindividual anatomical variation and to normalize the data. For each task and each acquisition, individual statistical parametric maps were calculated using the general linear model by modeling the conditions as a box car function convolved with the hemodynamic response function, corrected for temporal autocorrelation and filtered with a high-pass filter of 128 s cut-off. Motion parameters were included in the model as regressors of no interest to reduce potential confounding effects due to motion. For each subject t-contrast maps were calculated between the active and rest condition. These individual t-contrast images were then used for second-level random effects group analyses. For interpretation of the data contrast maps of the lip pursing and eyeblinking experiments data sets were mirrored when patients were paralyzed on the right side ($n=3$). We used 1-sample t-tests for each of the experiments, uncorrected. All tests were thresholded at $p<0.001$ except for the eyeblinking where a threshold of $p<0.01$ was used. We focused on two regions of interest (ROIs); the primary cerebral motor area and the cerebellum as defined by the automated anatomical labeling (AAL) program (Tzurio-Mazoyer et al., 2002). For both regions we calculated the laterality index (LI), which expresses the relative activity in one hemisphere compared to the other, with the formula: $(k_{left}-k_{right}/k_{left}+k_{right})$. The values of $k_{left}$ and $k_{right}$ are the number of voxels above the threshold in the left and right hemisphere, respectively. In patients, an increase in LI therefore corresponds to a relative increase in activation in the hemisphere ipsilateral to the side of affliction.

## Results

We investigated functional recovery and associated brain activation in 9 Bell's palsy patients with a transient motor disturbance of one of their facial nerves. The facial functional recovery in these patients, which was quantified at 4 defined periods with the use of the Sunnybrook scale, was, as shown in Fig. 2A, in agreement with previous observations (VanderWerf et al., 2007). In the first 4 weeks recovery of facial nerve function was virtually absent, while measurements in the subsequent periods at 4 months, 1 year and 1.5 years showed an improvement of the Sunnybrook scale up to a

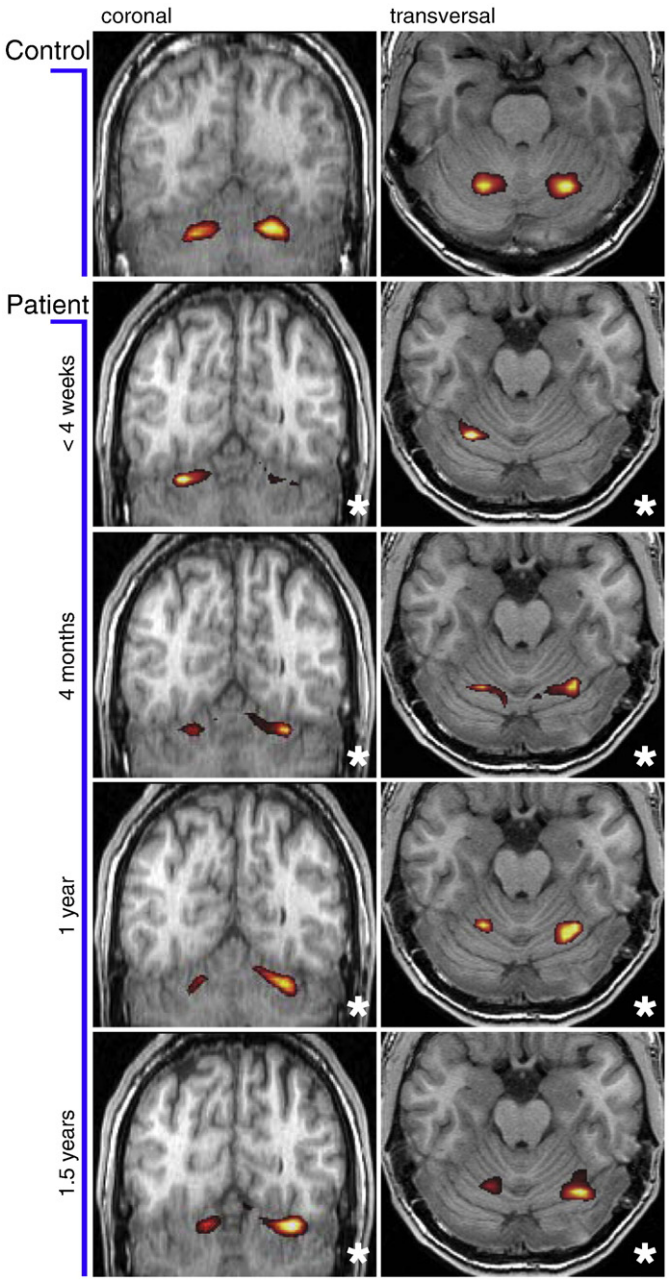


**Fig. 3.** Group analyses of brain activity induced by lip pursing illustrating activation in the cerebellum in a successive 1.5-year period. The asterisks indicate the side of affliction of the Bell's palsy patients. Note that at 4 months, the peak of the activation in lobule HVI of the cerebellum switches from the contralateral to the ipsilateral side.

stable level of approximately 75 % ($p<0.02$, $p<0.01$, $p<0.002$, respectively; t-test). Interestingly, within the first few weeks after onset of Bell's palsy the LI of cerebellar activities in the patients decreased compared to that of control subjects indicating that they moved towards the side of the brain that is contralateral to the affliction. Subsequently, over the next one and a half year their LI values returned, as shown in Figs. 2B and C, gradually towards their original dominance, i.e. towards the ipsilateral side with respect to the paralysis. In the cerebral motor cortex we observed the same changes except that the sides towards which the activities were shifted were opposite, which is in line with their crossed connections within the central nervous system. These relative shifts for cerebellar and cerebral activities held true both for the lip pursing and eyeblink tests (thresholded at $p<0.001$ and $p<0.01$, respectively). None of these changes was observed after the finger tapping task that was studied for control.

*Localization during lip pursing*

During lip pursing the control group showed clusters of activated voxels in circumscribed areas of the cerebellum (Table 1). Fig. 3 shows that the areas that were most prominently activated included lobule HVI in the hemisphere and lobule VII in the vermis with preponderance on the side that was ipsilateral to the side at which the task was performed. Small bilateral clusters of activation were also found in the lobules HIV and HV as well as the vermis lobules IV, V and VI that were adjacent to those in lobules HVI and VII. As indicated in Fig. 2B and Table 1 the changes in LI in the patients indicate that their ipsilateral activities were during the first few weeks shifted to the other side and that they returned over the subsequent period of one and a half years gradually back to the original side with a slight overshoot. The most prominent effects in this respect were observed in lobule HVI. Importantly, while the changes in the intensity and side of the activities in HVI were very prominent, the exact localization of its position within the cerebellar hemispheres remained as shown in Fig. 3, stable. Likewise the changes in activities that were observed in both the primary motor cortex and premotor areas around the central gyrus were also relatively stable, shown in Fig. 4 and Table 1. These exact sides matched well with those of the controls and with those that have been described previously (Hesselmann et al., 2004).

*Localization during eyeblinking*

During eyeblinking the control group also showed clusters of activated voxels in circumscribed areas of the cerebellum (Table 1). The areas in the cerebellar cortex that were most prominently activated during the eyeblinking tasks in the control group included lobules HVI and Crus 2 on both sides, which is shown in Fig. 4. Areas that were activated far less included Crus 1, lobules HIV and HV as well as vermis lobules IV, V and VI. In the patient group clusters of activated voxels were also found in the cerebellar lobules HVI on both sides, but as can be observed in Fig. 2C during lip pursing the intensity of the activities changed over time in that the LI increased over the course of the one and a half year of recovery. The only difference was that the initial shift in activities shortly after the onset of the disease was less prominent during eyeblinking than during lip pursing; this difference can be seen at the first session presented in Figs. 2B and C. Thus, the measurements at one year as well as at one and a half year yielded the largest cluster of activated voxels in lobule HVI, ipsilateral to the side of affliction. The lateralization of the activation in the cerebral cortex of the Bell's palsy patients followed the same pattern as that observed in the cerebellum, except that in accordance with the crossed nature of its connectivity, relative increases during the recovery period occurred again predominantly in the precentral gyrus region contralateral to the side of affliction (shown in Figs. 2C and 4). In the control group of healthy subjects we observed most clusters of activated voxels bilaterally in the primary motor cortex and premotor areas, in particular in the middle precentral gyrus area, which is compatible with previous studies (Kato and Miyauchi, 2003). We therefore concluded that the intensity and side of activation varies over time during recovery of Bell's palsy, but that the localization of these changes in both the cerebellar and cerebral cortex are relatively stable.

*Localization during finger tapping*

The outcome of the experiments described above suggests that changes in the activities of specific regions in the cerebellar cortex and cerebral cortex follow transient peripheral paralysis of the facial nerve. However, some of these changes might be aspecific and due to general activation or stress factors that might occur in these patients. We therefore subjected both the patient group and control group also to a test that does not depend on activation of the facial nerve, but

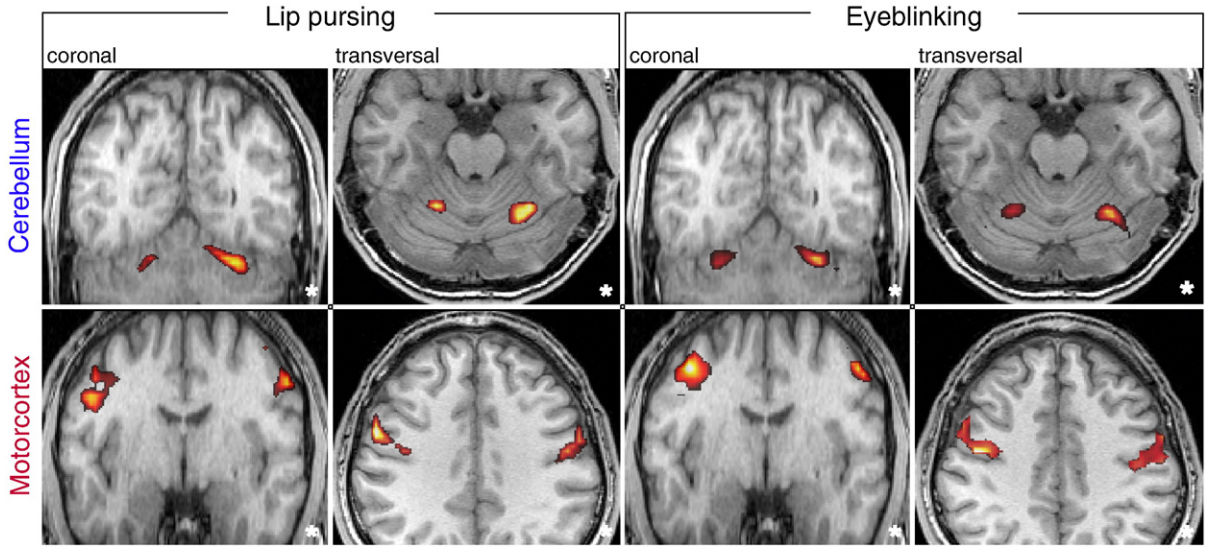


**Fig. 4.** Group analyses of brain activity induced by lip pursing and eyeblinking illustrating clusters of activated voxels in the cerebellum and motor cortex one year after onset of the affliction. Both during lip pursing and eyeblinking most activation is observed ipsilateral in lobule HVI of the cerebellum and contralateral in the motor cortex in the precentral gyrus. Asterisks indicate the side of affliction.

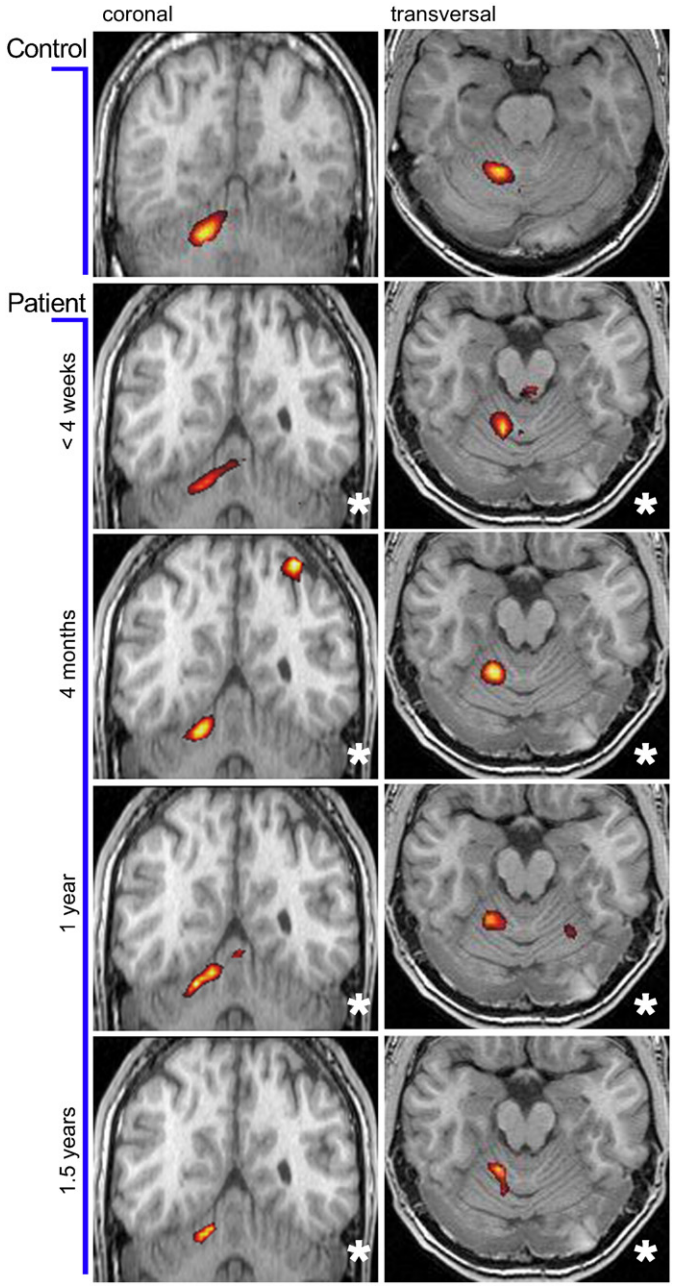


**Fig. 5.** Group analyses of brain activity induced by right hand finger tapping illustrating activation in the cerebellum in a successive 1.5 year period. Asterisks indicate the side of affliction. Note that the finger tapping cluster remained relatively stable throughout the study in lobules HIV and HV of the cerebellum.

instead on stimulation of peripheral nerves that are required for finger tapping. We choose this type of activation, because it is known to robustly activate areas of the cerebellum and cerebral cortex that are close to those that are activated by stimulation of the facial nerve (Gizewski et al., 2007). During finger tapping with the right hand, clusters of the most prominently activated voxels were found on the ipsilateral side in lobule HVI of the cerebellum and adjacent areas in both the patient group and control group (Table 1). In contrast to the lip pursing and eyeblink experiments, the lateralization of the activations following finger tapping of the patients was as shown in Fig. 5, stable throughout their recovery period. In the cerebral cortex most prominent activity occurred on the contralateral side in the precentral gyrus. Here too no vast changes in lateralization occurred during the recovery period. Thus, the LI's of the four different measurements in the cerebellar and cerebral cortices in the patients did not differ from those obtained in the control group indicating that the differences described above for the lip pursing and eyeblinking experiments are probably not reflecting an artefact.

## Discussion

The current study provides for the first time longitudinal data on central plastic processes during transient damage to the peripheral nervous system resulting in a relative increase in activation of the cerebellar cortex during recovery, while it does not lead to a spatial reorganization of its functional activation. Remarkably, the functional reorganization that is present even after one and a half years, as illustrated by the sustained changes in LI, is not even accompanied by a sizeable spatial reorganization in the cerebral motor cortex. Therefore the effects of transient peripheral damage of motor nerves stand in marked contrast to that of permanent damage as can be observed for example after amputation or irreversible degeneration of central motor neurons (Konrad et al., 2006; Miall and King, 2008; Mohammadi et al., 2009a,b). The changes in cerebellar activation of Bell's palsy patients mimic much more closely those that can be observed following cerebellar motor learning such as classical conditioning of eyeblink responses (Schreurs et al., 1997; Cheng et al., 2008). Interestingly, because eyeblink conditioning also employs the facial motor nerve (VII) we can make a direct comparison between fMRI activation induced by this form of short-term motor learning and by the functional recovery to transient peripheral damage to the facial nerve as investigated in the current study. In both cases the cerebellar regions with increased activation included lobule HVI and in both cases no functional reorganization occurred in that the locus of peak activation remained relatively fixed during the learning or recovery process, respectively. Moreover, once these processes were fully ongoing in both cases cerebellar activation remained at a high level (Cheng et al., 2008). Both the resemblance between the central impact of recovery to transient peripheral damage and that of short-term cerebellar motor learning and the prominent difference between the impact of transient damage and that of permanent damage are even more striking, if one realizes that it takes at least a few months after onset of affliction before the facial nerve in Bell's palsy patients re-innervates the muscle (VanderWerf et al., 2007). In addition, the functional recovery was never complete and frequently guided by facial weakness and synkinesia (Valls-Solé, 2007), which one could expect to promote some compensatory central reorganization. Possibly the intact facial motor neuron cell bodies and dendritic arbors in facial nerve palsy allow the central nervous system to compensate for the transient peripheral pathology solely by modifying the strengths of existing synapses in the cerebellar and cerebral pathways, similar to the mechanisms involved in short-term motor learning (De Zeeuw and Yeo, 2005). Such mechanisms presumably require the pathways within the brain to be intact, and they probably can even explain why spatial shifts in representations actually can occur both in the cerebellum and cerebral cortex when the primary lesions are in the central rather than the peripheral nervous system, and when they are permanently rather than transiently (Riecker et al., 2002; Ramnani, 2006; Jain et al., 2008).

Despite the consistent global shifts in fMRI activities described above, there were still some minor, yet interesting differences. Question remains for example why the initial shift in LI was more robust during lip pursing than during eyeblinking. Possibly, this difference reflects the difference in input from the cerebral motor cortex to the different motor domains within the facial nucleus (N VII). Since the input from the cerebral cortex to the orbital domain of the facial motor neurons is bilateral, whereas that to the oral domain is contralateral as illustrated in Fig. 1, it might be possible that the

bilateral nature of the input connections of the orbital motor neurons initially promotes equality in the changes in activity and thereby dampens changes in LI. In other words, even though the transient lesions were unilateral, the eyeblinking task was performed with both eyes, and thereby we probably induced, at least shortly after the affliction, a balance in the change of activities on the left and right side. Possibly, at later stages the balance was still lost due to the impact of other unilateral inputs such as those from the cerebellum.

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