A Pilot Study of Event-Related Functional Magnetic Resonance Imaging of Monitored Wrist Movements in Patients With Partial Recovery

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Background and Purpose—Previous functional imaging studies of motor recovery after stroke have investigated cerebral activation during periods of repetitive, often complex, movement. This article reports the use of an event-related approach to study activation associated with isolated simple movements (wrist extension). This allows investigation of the pattern of the motor response and corresponding brain activation on a trial-by-trial basis. Patients with partial recovery can be assessed, and allowance can be made for abnormalities in the shape of hemodynamic responses.

Methods—Functional MRI at 3 T was performed during a series of isolated, near-isometric wrist extension movements. A visual tracking procedure was used to elicit forces of 10% and 20% of maximum voluntary contraction. Force output from both wrists was monitored continuously. A voxel-wise procedure was used to fit the optimum hemodynamic response functions in each case.

Results—Three chronic stage patients with partial recovery were successfully scanned and compared with 8 healthy controls. The patients showed well-lateralized motor responses but inaccurate control of force. During movement of the paretic wrist, we observed excessive activation of the ipsilateral primary motor cortex and increased relative activation of the supplementary motor area compared with movement of the nonparetic side. In the primary motor area, hemodynamic responses peaked more quickly on the ipsilateral side in 2 patients for movements of the paretic hand, whereas controls showed the opposite trend.

Conclusions—An event-related approach can be used to study the relationship between motor responses and cerebral activation in patients with partial recovery. These preliminary findings suggest that excessive activation in ipsilateral motor cortex and secondary motor areas remains evident under these tightly controlled conditions and cannot be ascribed to mirror movements or abnormalities in the timing of the blood oxygen level–dependent (BOLD) response. However, close monitoring of motor responses also makes evident continuing impairment in motor skill, which makes comparison with activation in normal controls difficult. (Stroke. 2002;33:2881-2887.)

Key Words: magnetic resonance imaging ■ motor activity ■ stroke outcome

The mechanisms responsible for long-term motor recovery after stroke are still unclear. Functional imaging has been an important development for investigation of these mechanisms. Patients with recovery of hand function have been studied with positron emission tomography and, more recently, with functional MRI (fMRI). These studies have indicated that recovery after damage to the primary motor cortex and its descending fibers is associated with activation of alternative cortical motor areas such as increased primary sensorimotor activation in the intact hemisphere or increased activation in secondary motor areas.

One limitation of these studies is that comparable task performance during testing of each hand is only possible in patients with good hand recovery because the majority of tasks involved prolonged periods of relatively complex motor activity. Patients often had to have recovered well enough to make fine-finger movements, such as rapid sequential finger-thumb opposition, to match performance between hands. This is not typical of long-term recovery; the majority of those with significant subacute motor impairment still have limited range or rate of finger movement at 1 year. Recent progress in fMRI, combined with the development of high-field scanners, has seen a shift from the “blocking” of activity, which is essential in positron emission tomography and popular in fMRI studies, toward “event-related” paradigms. In studies of motor function, an event-related approach...
involves interleaving single movements with long rest periods instead of contrasting long epochs of repetitive activity with rest epochs. Averaging over trials provides a reliable measure of the hemodynamic response associated with such isolated movements. With the use of simple, single-joint movements in an event-related design, it should be possible to study patients with moderate recovery without fatigue or depreciation of movement quality. In addition, trials in which the correct movement is not made can be excluded from further analysis.

The purpose of this pilot study was to investigate the feasibility of using event-related fMRI at 3T in patients with partial recovery of upper-limb motor function. By studying activation during closely monitored simple movements (wrist extension), we sought to determine abnormalities in the pattern and timing of cerebral activation that were independent of any abnormality in motor performance or the blood oxygen level–dependent (BOLD) response.

**Subjects and Methods**

The study was approved by the local ethical committee, and informed written consent was obtained from all subjects.

**Patients**

Five patients with partial motor recovery after a first ischemic stroke were scanned; all had an initial severe impairment/complete loss of arm function (Rivermead Arm Assessment score <15). At the time of the fMRI scans (>6 months after stroke) some function had returned, at least to the extent of controlled wrist extension. Of the 5 patients scanned, 2 were omitted from the analysis: one because of excessive head motion and the other because of poor task compliance. Details of the remaining patients are shown in Table 1. Differences in wrist extension strength are shown in terms of left maximum voluntary contraction (MVC) as a percentage of right MVC. Figure 1 shows the site of stroke damage in each patient.

**Control Subjects**

The control group included 5 young adults (mean age, 25.4 years) recruited from the university community and 3 older adults (mean age, 59.7 years) recruited by advertisement in the local community. All control subjects were healthy and had no history of neurological disease.

**Image Acquisition**

Gradient echo-planar imaging was performed at 3.0 T with the use of a linear head coil. T2*-weighted coronal images with 128×64 matrix size, 3-mm in-plane resolution, and 9-mm slice thickness were acquired with echo time of 30 ms. Ten contiguous slices were acquired every 1.87 seconds. Anatomic localization was achieved with the use of multislice inversion recovery echo-planar data sets of the whole brain with gray matter nulled (3-mm isotropic voxels), as well as T2-weighted images.

**Motor Activation Task**

Subjects lay with their arms extended and forearms strapped firmly in foam rubber cradles so that the hands were mid-supinated (little finger downward).

**TABLE 1. Patient Details**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53</td>
<td>60</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>Infarct location</td>
<td>Right internal capsule</td>
<td>Right M1 and white matter</td>
</tr>
<tr>
<td>Carotid Doppler</td>
<td>No Doppler examination</td>
<td>Completely occluded right internal carotid artery</td>
</tr>
<tr>
<td>Days since stroke and Rivermead Arm Assessment Score (max=15)</td>
<td>12/4</td>
<td>1/0</td>
</tr>
<tr>
<td>Day</td>
<td>Score</td>
<td>Day</td>
</tr>
<tr>
<td>101</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>196</td>
<td>13</td>
<td>280</td>
</tr>
<tr>
<td>276</td>
<td>13</td>
<td>276</td>
</tr>
<tr>
<td>Days since stroke at time of scan</td>
<td>276</td>
<td></td>
</tr>
<tr>
<td>Wrist extension force at time of scan (% of nonparetic wrist)</td>
<td>105</td>
<td>42</td>
</tr>
</tbody>
</table>

**Figure 1.** Lesion maps for the 3 patients (Pat.), shown on a standard Talairach brain. Labels in millimeters indicate distance of transaxial slice above the anterior commissure–posterior commissure line. Neurological convention: right=right.
A pressure bulb was positioned in light contact with the back of each hand to allow compression by near-isometric wrist extension. The area of the hand contacting the pressure bulb was limited by a rigid plastic disk so that the force generated was proportional to the pressure exerted. The pressure produced an electric signal that was sampled every 187 ms and recorded on a computer. Wrist extension strength was measured before scanning. Subjects were asked to extend each wrist to the maximum limit 3 times; the MVC for each wrist was defined by the median amplitude. During scanning, feedback of the force amplitude to the subject was via a thermometer-type display viewed through prismatic glasses and was updated with each sampling of the electric signal. The experiment was conducted in 2 blocks, 1 for movements of each hand. Each trial began with the appearance of 2 arrows on the display that cued the movement and the required force. Subjects extended their wrists until the pressure level matched the target arrows and then relaxed, allowing the pressure level to return to baseline. The arrows disappeared either when the target force had been met or exceeded or 6 seconds into the trial if no motor response occurred. There were 28 trials per block, each lasting 18.7 seconds. Two target force levels were alternated within each block: 10% and 20% of the measured MVC. The nonparetic hand of the stroke patient was always tested first.

**Image Analysis**

All analysis was on an individual case basis, thus avoiding the need for transformation of images to a standard brain space. All images were corrected for motion with the use of a 3-dimensional registration algorithm (AIR; MEDx, Sensor Systems Inc) and globally normalized. The images were spatially smoothed with a gaussian distribution of 6 mm full-width-at-half-maximum. The fMRI time series was convolved with a Gaussian distribution of 3 seconds full-width-at-half-maximum and was high pass filtered to exclude frequencies lower than twice the trial presentation rate.

A voxel-wise fitting procedure was used to locate significant activations and assess variations in the hemodynamic response. The optimum hemodynamic response function for each voxel was determined by convolving a delta function representing the motor event with a gamma-variate function. The gamma-variate function is described by the equation \( S(t) = (t/\tau_p)^{\alpha} \times \exp[-\alpha(t/\tau_p)] \), where \( t \) is the time since the visual cue (ie, \( t = 0 \) when the visual cue appears), \( \tau_p \) is the time point where the signal \( S \) attains maximal intensity, and \( \alpha \) is a factor that determines the slope of the curve. A least-squares minimization routine was used to find the optimum values of \( \tau_p \) and \( \alpha \) to describe the trial-averaged time course of each voxel. The optimized parameters for each voxel were then used to create the fitted time course for all trials by convolving a series of delta functions corresponding to each movement. Statistical maps were created with the use of the correlation coefficient between the MR signal time course for the whole experiment and the fitted time course. Significantly correlated voxels were identified by thresholding the statistical maps at \( P < 0.001 \) uncorrected. The statistical maps were not corrected for multiple comparisons because only activated voxels within the confines of the predefined cortical motor system were reported.

The inversion recovery images for each subject were used to define anatomic regions of interest (ROIs) for the primary motor area (M1) and lateral premotor areas in each hemisphere as well as for the supplementary motor area (SMA). The images were viewed in the 3 cardinal planes with the use of Analyze AVW. M1 was defined as the precentral gyrus, and the premotor area was delineated as the area between the precentral sulcus and the next sulcus. Both the M1 and premotor areas extended from the brain vertex to the Sylvian fissure. SMA was defined as the medial cortex lying above the cingulate sulcus and caudal to the line drawn through the anterior commissure perpendicular to the anterior commissure–posterior commissure line. The ROIs masks were then coregistered with the functional data sets of each subject.

To compare activity in contralateral versus ipsilateral M1, a laterality index (LI)† was calculated for movements of each hand for each subject. The LI was defined as \((C − I)/(C + I), \) where \( C \) and \( I \) represent the number of suprathreshold voxels in M1 contralateral or ipsilateral to the hand movement, respectively. Hence, the value of LI could range from 1.0 (all M1 activity was contralateral) to −1.0 (all M1 activity was ipsilateral). A similar measure was used to compare activity in a particular cortical area for movements of each hand and hence can be termed a task laterality index (TLI). The TLI was defined as \((L − R)/(L + R), \) where \( L \) and \( R \) represent the number of suprathreshold voxels in the ROI activated by movements of the left and right wrist, respectively. The value of TLI could range from 1.0 (all activity related to movement of the left wrist) to −1.0 (all activity related to movement of the right wrist).

**Results**

**Task Performance**

For controls, strength of wrist extension assessed before scanning was on average weaker on the nondominant left than on the right wrist (median, 87.5% MVC; range, 69% to 124%). Table 1 shows overlap of the range of relative wrist strengths of the patients with the range observed in the control subjects, although the relative strength for patient 2 was below the control range.

The characteristics of the motor responses are summarized in Table 2 and illustrated for patient 2 in Figure 2A and 2C. The 3 patients were able to comply with the task; they produced brief force pulses, of duration similar to those of the controls, with either wrist in response to the visual cue. Any force responses of the “resting” hand >1% of MVC were noted. Such events occurred only rarely for patients (3% of trials). None of these events occurred during force generation with the tested hand; all occurred later than 5.6 seconds after

<table>
<thead>
<tr>
<th>Wrist moved</th>
<th>Mean Duration, s</th>
<th>Mean Overshoot, % MVC</th>
<th>SD of Overshoot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>0.7</td>
<td>23</td>
<td>12</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1.0</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Patient 3</td>
<td>0.8</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>Controls</td>
<td>0.8</td>
<td>5†</td>
<td>3†</td>
</tr>
</tbody>
</table>

*Paretic side for patients.
†Mann-Whitney U exact probability test for controls vs patients, \( P < 0.05 \). All others not significant.
the start of the trial, and 80% of these events occurred during testing of the nonparetic hand, which was always tested first. Failures to respond to the visual cue or production of double responses occurred only rarely for patients (3% of trials) and controls (2% of trials). These noncompliant trials were omitted from the activation analysis. In contrast to their good control of side and timing of responses, the patients’ control of force output was poor on both the paretic and nonparetic sides. Table 2 shows that they tended to overshoot the target force more than controls and showed greater variability in amount of overshoot ($P < 0.05$, Mann-Whitney $U$ test, exact probability). Because 10% and 20% trials could not be clearly segregated, separate analysis of the 2 force levels was not possible, and these 2 trial types were combined for the image analysis stages.

**Activation Patterns of Control Subjects**

As expected, the motor task resulted in robust asymmetrical activation of the primary motor area (Table 3), and the degree of activation in contralateral M1 exceeded that in the ipsilateral M1 for movements of either wrist in all subjects, as demonstrated by the positive LIs. All control subjects showed activation of the SMA for both tasks (Table 4), and 7 of the 8 control subjects also showed some bilateral activation of the lateral premotor areas. TLIs, calculated for each of the secondary motor areas for each subject, revealed large variation in extent of lateral premotor activation (right premotor area: median, −0.01; range, −0.71 to 0.86; left premotor area: median, −0.09; range, −0.71 to 0.86) (Figure 3). However, in the SMA, spatial extent of activation was similar for both hands (median, −0.12; range, −0.48 to 0.19).

**Activation Patterns of Patients**

For movements of the nonparetic wrist, primary motor area activation was similar to that of controls, with contralateral M1 consistently more activated than its ipsilateral counterpart (Table 3). For movement of the paretic wrist, there was some activation in contralateral M1 in all cases, but the relative activation compared with the ipsilateral side was different from controls. For patients 1 and 2, contralateral activation was less than on the ipsilateral side. Patient 3 had identical laterality ratios for movements of either hand, although the absolute level of activation was greater in both primary motor areas during movement on the paretic side. As a group, the patients showed greater ipsilateral M1 activation during movement of the paretic wrist than controls ($P < 0.05$, Mann-Whitney $U$ test, exact probability). Figures 2B and 2D illustrate the measured and fitted time courses of activated pixels in contralesional M1 of patient 2 for movements of the nonparetic and paretic hands, respectively.

**TABLE 3. Number of Significantly ($P < 0.001$) Activated Voxels in M1**

<table>
<thead>
<tr>
<th>Wrist moved</th>
<th>Left M1</th>
<th>Right M1</th>
<th>Laterality Index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left*</td>
<td>Right</td>
<td>Left*</td>
</tr>
<tr>
<td>Patient 1</td>
<td>8</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>Patient 2</td>
<td>28</td>
<td>39</td>
<td>3</td>
</tr>
<tr>
<td>Patient 3</td>
<td>19</td>
<td>10</td>
<td>48</td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>5†</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>Young, range</td>
<td>5–9</td>
<td>26–71</td>
</tr>
<tr>
<td></td>
<td>Older, range</td>
<td>2–11</td>
<td>20–35</td>
</tr>
</tbody>
</table>

*Paretic side in patients.
†Mann-Whitney $U$ exact probability test for controls vs patients, $P < .05$. All others not significant.
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Table 4. Number of Significantly (P<0.001) Activated Voxels in Secondary Motor Areas

<table>
<thead>
<tr>
<th>Wrist moved</th>
<th>Supplementary Motor Area</th>
<th>Left Premotor Area</th>
<th>Right Premotor Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left*</td>
<td>Right</td>
<td>Left*</td>
</tr>
<tr>
<td>Patient 1</td>
<td>6</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Patient 2</td>
<td>39</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>Patient 3</td>
<td>8</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Controls</td>
<td>Median</td>
<td>30</td>
<td>33†</td>
</tr>
<tr>
<td>Young, range</td>
<td>20–102</td>
<td>22–83</td>
<td>3–24</td>
</tr>
</tbody>
</table>

*Paretic side for patients.
†Mann-Whitney U exact probability test for controls vs patients, P<.05. All others not significant.

Figure 3 shows the TLIs for each of the secondary motor areas. Variation in the extent of premotor area activation among patients was within the range defined in control subjects. However, the TLI calculated for the SMA in patients 2 and 3 exceeds the range defined in control subjects (patient 2: TLI=0.7; patient 3: TLI=0.78) because of SMA activation of greater spatial extent for movement of the paretic hand relative to that observed for movements of the nonparetic hand, which was lower than for controls (Table 4).

Hemodynamic Parameters

When values for the significantly activated voxels in the motor system were averaged, the optimized hemodynamic parameters in patients were comparable to those seen in controls. The average times to response peak were 7.6 seconds for patient 1, 6.9 seconds for patient 2, and 7.4 seconds for patient 3 compared with a median for controls of 6.9 seconds (range, 4.8 to 9.1 seconds). The averages for breadth of response (α) were 5.7, 4.7, and 5.4, respectively, compared with a median for controls of 5.5 (range, 3.0 to 12.6).

Comparison of the hemodynamic parameters of suprathreshold voxels in the primary motor areas showed that the contralateral M1 response tended to peak faster than the ipsilateral M1 response in control subjects (median, 5.1 versus 6.4 seconds; P=0.05, Wilcoxon paired rank test). Figure 4 shows that this was also true for the nonparetic (right) wrist of all 3 patients, but the pattern was reversed for patients 1 and 2 on the paretic side. For all 3 patients moving the paretic wrist, the contralateral response was slower than seen for any control subject, whereas the ipsilateral response was within the control range.

There was no significant difference in the width of the hemodynamic response, α, between contralateral and ipsilateral M1 (median, 4.15 versus 4.85 seconds).

Discussion

We have shown that it is possible to use an event-related approach with selected patients with partial recovery. We observed extensive ipsilateral M1 activation in some patients, a finding consistent with previous studies using repetitive movement in patients with excellent recovery. In addition, we detected relative timing differences between areas of activation in M1 of each hemisphere, which were reversed in the patients showing increased involvement of ipsilateral M1.

Use of an event-related experimental design enabled categorization of individual trials according to performance, allowing elimination of noncompliant trials from the final

Figure 3. Scatterplot of TLIs for the secondary motor areas. Small open circles indicate young controls; filled circles, older controls. A positive TLI indicates that the majority of activation in the ROI is related to movements of the paretic/left hand. Diamonds indicate patient 1; squares, patient 2; and triangles, patient 3.

Figure 4. Time to peak for the hemodynamic response in M1. Solid line and error bars show the medians and ranges, respectively, for controls. Diamonds indicate patient 1; squares, patient 2; and triangles, patient 3.
analysis and better matching of patient and control task performance. The confounding effects of temporal differences in hemodynamic function between our subjects were limited by a flexible analysis method. The temporal characteristics of the BOLD response have been shown to vary between brain regions and between stroke patients and controls. Reference functions, such as the gamma-variate function in our analysis, are commonly used to model the delay between the neuronal activity and the fMRI signal change, as well as the smoothness of this change. Voxal-wise solutions that allow the temporal characteristics of the reference function to vary across subjects and regions, as used in this study, limit underestimation of fMRI-measured activation due to poor modeling of responses with preset, fixed functions. However, even with the experimental design and analysis used in this study, the interpretation of functional imaging data remains difficult; some of the key issues for theories of recovery are discussed below.

Increased activation of the ipsilateral M1 during movements of the paretic hand has been a common finding in neuroimaging studies. This pattern of activation has been reported for some patients in positron emission tomography studies and for a majority of patients in fMRI studies. An initial concern was that this increased ipsilateral activity might simply reflect inadvertent movements on the nonparetic side, although later studies reported that ipsilateral activation occurred in the absence of any obvious mirror movements. Similarly, continual monitoring of force output of both hands in the present study did not reveal the occurrence of mirror movements in our patients, despite the observation of extensive ipsilateral M1 activation.

However, abnormal ipsilateral M1 activation in recovered stroke patients might reflect increased involvement of bilaterally represented proximal muscles. Part of the normal pattern of motor control is that generation of force at the hand is accompanied by automatic stabilization of the arm by recruitment of shoulder muscles. However, in the present study we studied very simple movement at a low proportion of MVC and with the arms held in a rigid cradle, which avoids the large increase in area of cortical activation with increasing force output that is seen during more complex, less controlled tasks and that may reflect shoulder muscle involvement.

Stabilization is not the only possible cause of ipsilateral activation. Turton and Lemon found that ipsilateral responses in healthy adults occurred preferentially in wrist extensors and elbow flexors but to a lesser extent in finger and wrist flexors. By using a less dexterous motor task than other neuroimaging studies, observation of extensive ipsilateral activations in M1 are more likely in patients in the present study because recruitment of bilaterally represented wrist extensors could mask loss of function in unilaterally represented distal muscles. The usefulness of ipsilateral pathways in recovery may be limited to control of proximal muscles because of their relatively stronger representation in ipsilateral M1. This suggestion is in agreement with evidence that extensive ipsilateral M1 responses are associated with poor recovery. Serial neuroimaging studies of recovering hemiparetic patients have found that recovery was associated with a shift toward more positive LIs for movements of the paretic hand. In addition, a longitudinal study of upper limb motor responses to transcranial magnetic stimulation showed that ipsilateral responses from the undamaged hemisphere were more common in poorly recovered patients. Similarly, patient 2 in our study, who experienced the poorest recovery and had widespread damage undercutting M1, showed the strongest ipsilateral bias in M1 activity.

Determination of the hemodynamic response characteristics of activated pixels adds a new dimension to the investigation of motor control. The time to peak of the BOLD signal was reduced in contralateral M1 compared with ipsilateral M1 in control subjects and in patients for movements of the nonparetic wrist. However, this hemodynamic pattern was reversed in the 2 patients who showed a shift in the LI for movements of the paretic hand. For these patients, the peak BOLD response in ipsilesional, right M1 was delayed, relative to responses in left M1, for movements of either wrist. In terms of absolute rather than relative timing, all 3 patients showed abnormally delayed M1 responses in the damaged hemisphere when moving the paretic wrist. One hypothesis would be that these abnormalities in relative and absolute timing reflect reorganization of the motor system; alternatively, they might be effects of impaired perfusion due to vascular disease. The limited information on the vascular status of the patients in this pilot study means that this issue cannot be settled here. However, a recent study has shown that impaired autoregulation resulting from carotid atherosclerotic disease may be responsible for the complete uncoupling of neuronal activity from the normal hemodynamic response in some cases. Future fMRI studies after stroke may therefore need to combine measures of regional perfusion (using Doppler or MRI) with other neuroimaging techniques, such as magnetencephalography or evoked potentials, that do not rely on hemodynamic markers of neuronal activity to assess neuronal processing within such areas.

The potential importance of secondary motor areas in recovery has been demonstrated in most previous neuroimaging studies. Two of the patients showed abnormally large relative increases in spatial extent of activation in the SMA when moving the paretic arm. The SMA contributes substantial numbers of fibers directly to the corticospinal tract, forming parallel descending pathways in the internal capsule at spatially distinct sites from fibers originating in M1. It has been suggested that these pathways may be sufficient for control of motor function after damage to M1 or its underlying white matter. However, in normal subjects SMA activity increases with the difficulty of the motor task and given that our patients found matching target forces to be difficult, the observed difference in activation may only indicate a normal adaptation to performing a difficult motor task. Although we were able to improve the match between task performance of patients and control subjects by excluding noncompliant trials, the difference in overall accuracy remained a problem, and our reported differences in SMA activity may reflect this issue.

In summary, we have shown that event-related fMRI can be used to study selected patients with partial motor recovery. This technique allowed us to limit the influence of differences
in both task performance and hemodynamic response characteristics among our patients and control subjects. The observed abnormalities in cerebral activation of individual patients found with this method were in agreement with previous studies using traditional blocked paradigms in patients with excellent recovery, and we have identified changes in the relative timing of activation within the motor system in partially recovered patients. However, there are continuing uncertainties arising from abnormalities in the details of motor performance during scanning and questions over the functional value of abnormal activation.

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References
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