Reorganization of Motor Execution Rather Than Preparation in Poststroke Hemiparesis

Holger Wiese, PhD; Philipp Stude; Robert Sarge; Katharina Nebel, MSc; Hans-Christoph Diener, MD; Matthias Keidel, MD

Background and Purpose—The aim of the present study was to examine movement-related potentials (MRPs) in patients in the “chronic” stage after cortical stroke with recovered hemiparesis compared with healthy control subjects.

Methods—Right index finger MRPs were derived from 12 patients 1 year after infarction in the territory of the left middle cerebral artery as well as from 12 control subjects. MRP components were compared between groups.

Results—In the patient group, the component directly preceding movement onset (negative slope [NS]) was significantly reduced over the lesioned hemisphere contralateral to the movement. Furthermore, increased motor potentials (MPs) were observed over the contralesional hemisphere during movement execution. No changes in the early MRP (Bereitschaftspotential) reflecting movement preparation were found.

Conclusions—Because the NS is supposed to be generated by the primary motor cortex, the decreased component over the lesioned hemisphere is interpreted to represent impaired contralateral M1 functioning in stroke patients. Contralesional activity has been reported as a probable sign of brain plasticity by functional imaging studies. Our results broaden these findings, giving new insights into the temporal course of movement-related brain activity in recovered cortical stroke patients. The data point to a functional reorganization of motor execution rather than preparation in poststroke hemiparesis. (Stroke. 2005;36:1474-1479.)

Key Words: electroencephalography ■ evoked potentials ■ paresis ■ recovery of function ■ stroke
temporal resolution of the method and of the possibility to 
examine self-initiated movements. To observe alterations of 
the temporal or spatial distribution of the MRP and differen-
tial effects on the MRP subcomponents after lesions of the 
cortical motor areas, we examined recovered patients with 
cortical lesions after infarction in the territory of the left 
middle cerebral artery, leaving the basal ganglia and thalamus 
intact.

Methods

Stroke patients were recruited from the neurological department 
of the University Clinic of Essen, Germany, and gave their informed 
consent to the examination. The study was approved by the local 
ethics committee.

The patient group consisted of 12 men with a mean age of 61.8 
(±5.5 SD) years after their first infarct of the left middle cerebral 
artery (Figure 1; Table 1).

The examination took place ≥1 year (mean 28.2±13.1 SD 
months) after stroke. The patients' lesions were mostly restricted to 
neocortical areas, leaving subcortical structures, such as the basal 
ganglia, intact. Strength of the paretic limb was measured according 
to the Medical Research Council (MRC) Motor Strength Scale. 
Moreover, Barthel indices were derived.

All patients experienced paresis in the initial phase after the insult. 
The mean initial MRC Motor Strength Scale score for finger 
abductions (m. interossii) was 3.0 (±0.9 SD) at the time of 
admission to the stroke unit. At the time of EEG examinations, MRC 
Motor Strength Scale scores had improved significantly (mean 
outcome MRC Motor Strength Scale score 4.3±0.7 SD; Wilcoxon Z 
−2.7; P=0.007).

To achieve a homogenous, defined population, all patients with 
previous brain disorders or psychiatric disorders were excluded. 
None of the patients were medicated with central acting analgesics, 
anticonvulsants, neuroleptics, or antidepressants at the time of 
examination.

Twelve age-matched healthy volunteers were examined as a 
control group (mean age 55.9±5.7 SD years). Exclusion criteria 
were neurological diseases or psychiatric disorders and intake of 
central-acting drugs. All subjects were right-handed according to the 
Edinburgh Handedness Inventory.15

Subjects were instructed to execute self-initiated brisk abductions 
of their right index finger about every 15 seconds. To control for the 
ocurrence of mirror movements, subjects were monitored during 
task performance.

A 30-channel EEG as well as vertical electro-oculogram (EOG) 
and surface electromyogram (EMG) of the right index finger (m. 
interosseus I) were recorded using a SynAmps amplifier (Neuro-
Scan). For EEG recording, Ag/AgCl electrodes were placed accord-
ing to the extended international 10-20 system and were referenced 
to linked earlobe electrodes (A1/A2). A bandpass filter was set from 
DC to 100 Hz for EEG data and from 5 to 250 Hz for the EMG. Data 
were sampled with a frequency of 500 Hz. Impedance was kept <5 
kΩ. All data were digitized, displayed, and stored by a PC system. At 
least 50 artifact-free trials per subject were collected.
All data processing was performed using BrainVision Analyzer software (Brainproducts). EMG onset for each artifact-free movement was identified by visual analysis and marked. EMG was rectified and averaged. The difference between EMG maximum amplitude and EMG onset amplitude, divided by the time of maximum EMG relative to onset, was determined (EMG slope). EMG measures were compared between the groups using 2-sample t tests.

EEG data were segmented from $-2.5$ to $+1.5$ s relative to EMG onset, high-pass filtered at 0.01 Hz (12 decibel/octave), low-pass filtered at 50 Hz (12 db/oct), and baseline-corrected using the first 200 ms as baseline. Trials confounded with blink artifacts were removed after visual inspection. No additional algorithms for blink artifact correction were used. The different subcomponents of the MRP were identified visually in the grand averages. Area measures of individual subjects were calculated for the time intervals derived from the grand averages (Figure 2).

For statistical analysis, 15 electrodes of interest were determined, namely 10-20 system positions Fz, FCz, Cz, CPz, Pz, F3, F4, FC3, FC4, C3, C4, CP3, CP4, P3, and P4.

Repeated-measures ANOVAs with the within-subjects factors “anterior/posterior position” (frontal, frontocentral, central, centrotemporal, and parietal electrodes) and “left/right position” (left, middle, and right electrodes), as well as the between-subjects factor “group” (patients versus control group) were calculated for the 3 MRP subcomponents. All F-ratios associated with the repeated-measures factors were assessed using degrees of freedom corrected with the Greenhouse–Geisser procedure for controlling type I error. In case of significant interactions, reduced models were set up for further analysis. All statistics were performed with the Statistical Package for Social Sciences (SPSS 11).

### Results
No mirror movements were detected during the experiment. In the control group, a mean EMG slope of 0.72 μV/ms (±0.57 SD) was observed. In the patient group, the average EMG slope was 0.27 μV/ms (±0.24 SD). A 2-sample t test revealed significantly decreased slopes in the patient group ($T_{22}=2.5; P=0.025$).

In control subjects, the averaged EEG waveform departed from baseline $-2050$ ms relative to movement onset at electrode Cz. From approximately $-300$ ms on, a steeper increase in negativity appeared (NS), which reached its maximum at $-50$ ms. From that time on, a further steep increase in negativity was observed (MP), peaking $150$ ms after EMG onset at Cz (Figure 3).

In the patient group, BP onset was observed $-2040$ ms before movement onset. A reduced NS, demonstrating only a small increase in slope, was observed $-300$ ms before EMG onset. The MP component appeared shortly before EMG onset in the patient group (Figure 3). Maximum negativity was observed at electrode Cz $210$ ms after EMG onset.

The repeated-measures ANOVA calculated for the BP component did not reveal a significant main effect or interaction for the between-groups factor.

In the repeated-measures ANOVA calculated for the NS component, a significant interaction “left/right position×group” was found. A repeated-measures ANOVA with the factors “anterior/posterior positions” and “group” calculated for electrodes F3, FC3, C3, CP3, and P3 revealed a significant main effect for the factor “group.”

In the repeated-measures ANOVA calculated for the MP component, a significant main effect for the factor “group,” as well as a significant interaction “left/right position×group” was detected. A repeated-measures ANOVA with the factors “anterior/posterior positions” and “group” calculated for electrodes...
F4, FC4, C4, CP4, and P4 revealed a significant main effect for the factor “group.”

To examine a possible effect of the delayed MP peak in the patient group, an additional analysis on peak latency was carried out. A 3-way repeated-measures ANOVA revealed no significant between-groups effects. Indices of all statistical tests are given in Table 2.

**Discussion**

The present study examined recovered hemiparetic patients’ MRPs after cortical infarction of the territory of the left middle cerebral artery compared with healthy control subjects. Two main results can be summarized. (1) The NS, directly preceding movement onset, was reduced in the patient group over the lesioned hemisphere contralateral to the movement. (2) The MP, defined as the area under the curve between movement onset and peak negativity, was significantly increased in the patient group, especially over the contralesional hemisphere.

In a recent review, Toma and Hallett concluded that the NS component is generated by the anterior bank of the central sulcus, corresponding to the primary motor cortex (M1). This structure is damaged in most of our patients. Accordingly, the decreased NS component over the lesioned hemisphere is interpreted to represent impaired M1 functioning in cortical stroke patients.

This finding is in line with Kitamura et al., who examined 2 patients with vascular lesions of the internal capsule and the basal ganglia. They found bilaterally distributed NS components preceding movements of the recovered paretic arm. Because the NS is lateralized toward the hemisphere contralateral to upper extremity movements in healthy control subjects, this finding is in line with the reduced NS components in our patients. NS components that were shifted toward the ipsilateral hemisphere have also been reported by Honda et al.

In our patients, enhanced MP areas over the contralesional hemisphere ipsilateral to the movement were observed. The MP has been suggested to be generated by postcentral area 3 by dipole modeling studies. On the other hand, intracranial recordings demonstrated activity of contralateral M1 during the MP phase. In light of functional brain imaging studies, which demonstrated enhanced activity of the ipsilateral premotor and sensorimotor areas in stroke patients, our finding of enhanced MP areas might reflect increased and prolonged activity in the contralesional hemisphere during movement execution.

The role of contralesional motor areas in recovery from hemiparesis has been investigated extensively in former studies. Green et al. observed activity of contralesional generators in the majority of their patients during the MP phase in an EEG dipole study. Chollet et al. found bilateral activations in the sensorimotor cortices after striatocapsular infarct, concluding that the lateralized motor system controlling movements of the healthy side also participated in motor execution of the recovered fingers. Weiller et al. principally replicated these findings. However, movements of the unaffected hand, so-called mirror movements, were observed to be associated with ipsilateral sensorimotor cortex activity. Although we did not observe any overt mirror movements in
our patients, we cannot exclude the possibility that covert muscle activity in the contralesional hand might explain the enhanced neuronal activations in the healthy hemisphere. In a functional MRI study that controlled for movements of the unaffected hand, Cao et al.\(^20\) came to the conclusion that synkinesia alone cannot explain ipsilateral M1 activations. In a functional MRI study on cortical stroke patients, Cramer et al.\(^3\) found ipsilesional premotor cortex activation. Feydy et al.\(^21\) described different patterns of reorganization over time, with an initial or progressive focalization of ipsilesial SM1 activity mainly seen in subcortical stroke and a persisting recruitment of areas outside the ipsilesional SM1, including the contralesional motor cortex, mainly observed in cortical stroke. Finally, Luft et al.\(^22\) found alternative networks involving the ipsilateral postcentral as well as mesial hemisphere regions and areas at the rim of the stroke cavity recruited to a higher extent after cortical stroke.

Our finding of enhanced MP areas in cortical stroke patients is in good agreement with the above-cited literature. These studies demonstrate the lesion-dependent limitation of functional reorganization in the physiological contralateral motor network after cortical stroke compared with subcortical stroke patients.

The present study revealed decreased NS but reorganized MP components in recovered stroke patients. These components have been suggested to reflect different processes. NS is supposed to represent the programming of specific movement characteristics (eg, the required force).\(^23\) Because contralateral M1 is assumed to be a generator of the NS, functional recovery of these processes may not be possible. This deficit might be partially compensated by enhanced activity during movement execution. The MP has been suggested to reflect afferent sensoric input from the periphery\(^16,23\) but also activity of the pyramidal neurons, which generate the final motor output to the spinal cord.\(^17\) These processes might be conducted by unaffected structures, especially in the contralateral hemisphere. Furthermore, varying effects on NS and MP on the lesioned side might be explained by vulnerability effects, depending on the functional properties of M1 neurons. However, because the present study represents a cross-sectional examination, such effects in the lesion area, which are supposed to occur in the acute stage, cannot be distinguished from processes of reorganization in the temporal course after stroke.

As described above, a large number of studies exist that investigated stroke patients with functional imaging techniques, allowing more precise localizations of activated brain areas. However, these techniques only provide limited temporal information. Block designs, and to a lesser extent, event-related functional MRI studies, are not able to differentiate between the diverse processes during movement preparation and execution. This may be important because in our study, early preparatory activity during the BP phase appears to be intact, which might be explained by intact supplementary motor areas in patients with infarctions of the MCA, but the subsequent processes (NS and MP) altered differentially in recovered cortical stroke patients.

In conclusion, by taking advantage of the superior temporal resolution of the MRP, we demonstrated reduced ipsilesional activity directly preceding movement onset and enhanced contralesional activity during movement execution in post-recovery cortical stroke patients, whereas the early component of the MRP (BP) reflecting motor preparation remained unchanged. These results are in line with the idea of prefrontally mediated early preparatory processes,\(^16,24,25\) presumably affected by medial structures,\(^26\) and a dominant role of the primary motor cortex for movement execution.

We suggest that plastic changes resulting in a partial compensation of impaired motor functions underlie the observed alterations of MRPs in cortical stroke patients. Our findings complement functional imaging studies and provide

### TABLE 2.

<table>
<thead>
<tr>
<th>Effect</th>
<th>df</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>0.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × group</td>
<td>2, 43.9</td>
<td>1.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.5, 32.6</td>
<td>3.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × anterior/posterior × group</td>
<td>3.9, 86.5</td>
<td>1.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>NS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>1.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × group</td>
<td>1.8, 38.5</td>
<td>7.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.4, 31.3</td>
<td>0.04</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × anterior/posterior × group</td>
<td>3.6, 78.8</td>
<td>1.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>MP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>4.4</td>
<td>0.047</td>
</tr>
<tr>
<td>Interaction left/right × group</td>
<td>1.8, 40.1</td>
<td>4.0</td>
<td>0.029</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.3, 28.8</td>
<td>3.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × anterior/posterior × group</td>
<td>3.6, 79.2</td>
<td>1.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>NS (left electrodes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>5.2</td>
<td>0.032</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.5, 32.1</td>
<td>0.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>NS (middle electrodes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>1.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.8, 38.6</td>
<td>0.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>NS (right electrodes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>0.03</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.6, 35.4</td>
<td>0.09</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>MP (left electrodes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>1.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.6, 34.7</td>
<td>1.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>MP (middle electrodes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>2.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.4, 30.0</td>
<td>2.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>MP (right electrodes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>12.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.3, 29.6</td>
<td>1.7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>MP Peak Latency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main effect group</td>
<td>1, 22</td>
<td>0.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × group</td>
<td>1.3, 30.4</td>
<td>0.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction anterior/posterior × group</td>
<td>1.9, 42.9</td>
<td>0.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Interaction left/right × anterior/posterior × group</td>
<td>3.7, 85.6</td>
<td>2.5</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>
a further example of the successful application of the MRP to the study of vascular brain lesions. Future studies are hopefully encouraged to examine the probable relationship of the different MRP components with the recovery of motor function in stroke patients.

References


Reorganization of Motor Execution Rather Than Preparation in Poststroke Hemiparesis
Holger Wiese, Philipp Stude, Robert Sarge, Katharina Nebel, Hans-Christoph Diener and Matthias Keidel

Stroke. 2005;36:1474-1479; originally published online June 9, 2005;
doi: 10.1161/01.STR.0000170639.26891.30
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/36/7/1474

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/