Differential Infraslow (<0.1 Hz) Cortical Activations in the Affected and Unaffected Hemispheres From Patients With Subacute Stroke Demonstrated by Noninvasive DC-Magnetoencephalography

Stefanie Leistner, MD; Tilmann Sander, PhD; Michaela Wachs, MD; Martin Burghoff, PhD; Gabriel Curio, MD; Lutz Trahms, PhD; Bruno-Marcel Mackert, MD

**Background and Purpose**—Sustained mass depolarization of neurons, termed cortical spreading depolarization, is one electrophysiological correlate of the ischemic injury of neurons. Cortical spreading depolarizations spread in the gray matter at a rate of approximately 3 mm/min and are associated with large infraslow extracellular potential changes (<0.05 Hz). Moreover, smaller infraslow potential changes accompany functional activation and might help to assess neuronal repair after stroke. The objective of the present pilot study was to investigate whether it is feasible to apply noninvasive near-DC-magnetoencephalography to detect and monitor infraslow field changes in patients with acute stroke.

**Methods**—A simple motor condition was used to induce physiological cortical infraslow field changes. Five patients in a subacute state after ischemic stroke performed self-paced simple finger movements (30-second periods of finger movements, always separated by 30-second periods of rest, for a total of 15 minutes). Near-DC-magnetoencephalography signals were recorded over the contralateral primary motor cortex for the affected and unaffected hemisphere, respectively.

**Results**—In all patients, the time courses of the contralateral cortical field amplitudes in the infraslow frequency range followed closely the motor task cycles revealing statistically significant differences between finger movement and rest periods. In 4 of 5 patients, infraslow field amplitudes were significantly stronger over the unaffected hemisphere compared with the affected hemisphere.

**Conclusions**—This study demonstrates that cortical infraslow activity can be recorded noninvasively in patients in the subacute state after ischemic stroke. It is suggested that near-DC-magnetoencephalography is a promising tool to also detect cortical spreading depolarization noninvasively. *(Stroke. 2009;40:1683-1686.)*

**Key Words:** infraslow (<0.1 Hz) potentials ■ MEG ■ stroke
after neuronal injury. Functional restitution after stroke is
governed by several factors such as lesion localization,
adaptive and compensatory processes, and local reorganiza-
tion. Little is known about if and how neurovascular mech-
amisms after stroke are modified. In particular, longitudinal
studies after stroke are missing. The longitudinal poststroke
assessment of infraslow neuronal changes using near-DC-
MEG could allow deriving possible prognostic factors.

The present feasibility study examined if near-DC-MEG
can be performed and cortical field changes in the infraslow
frequency range can be recorded also in patients with stroke.
The feasibility to qualitatively and quantitatively analyze
infraslow cortical signals in patients with stroke would open
up the avenue to further develop the technology for the
monitoring of CSDs in patients with stroke and to assess the
progress of repair in rehabilitation studies.

Materials and Methods

The study was approved by the local ethics committee and performed
in accordance with the recommendations of the Helsinki Declaration.
Baseline characteristics of the patients cohort are given in the Table.
The patients were mildly to moderately disabled (mean National
Institutes of Health Stroke Scale 3.2). Inclusion criteria were an (1) arm paresis due to (2) a subacute
infarct; AH, affected hemisphere; MCA, middle cerebral artery.

Table. Clinical and CT Morphological Baseline Characteristics and Strength of Motor-Related MEG Amplitudes (B/FT±SD) of the Patient Cohort

<table>
<thead>
<tr>
<th>S</th>
<th>Age, F/M</th>
<th>Infarct Territory</th>
<th>Infarct Size, mm</th>
<th>Infarct Sub-/Cortical Localization</th>
<th>Infarct Etiology</th>
<th>Stroke, Days</th>
<th>BMRC Arm</th>
<th>NIHSS</th>
<th>mRS</th>
<th>BI</th>
<th>UH FT±SD</th>
<th>AH FT±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60 M</td>
<td>Left MCA 10×20</td>
<td>Cortical</td>
<td>MCA territory</td>
<td>Large artery</td>
<td>11</td>
<td>4-</td>
<td>3</td>
<td>2</td>
<td>90</td>
<td>691±76</td>
<td>88±8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>61 M</td>
<td>Right MCA 20×20</td>
<td>Sub-/cortical</td>
<td>MCA territory</td>
<td>Large artery</td>
<td>6</td>
<td>3-</td>
<td>7</td>
<td>3</td>
<td>70</td>
<td>337±51</td>
<td>55±13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>55 M</td>
<td>Left MCA 25×20</td>
<td>Subcortical</td>
<td>Peri-insular</td>
<td>Large artery</td>
<td>14</td>
<td>2</td>
<td>10</td>
<td>4</td>
<td>60</td>
<td>305±65</td>
<td>168±47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>70 M</td>
<td>Right MCA 5×5</td>
<td>Subcortical</td>
<td>Internal capsule</td>
<td>Lacunar</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>95</td>
<td>707±105</td>
<td>584±119</td>
<td>0.03</td>
</tr>
<tr>
<td>5</td>
<td>69 M</td>
<td>Right MCA 8×5</td>
<td>Subcortical</td>
<td>Internal capsule</td>
<td>Lacunar</td>
<td>7</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>95</td>
<td>440±54</td>
<td>469±70</td>
<td>0.3</td>
</tr>
</tbody>
</table>

BMRC indicates British Medical Research Council; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; BI, Barthel Index; UH, unaffected hemisphere; AH, affected hemisphere; MCA, middle cerebral artery.

Results

Five patients with clinically symptomatic subacute stroke
were investigated: Patient 1 with right sensorimotor hemipa-
resis, Patient 2 with left facial and sensorimotor hemiparesis,
Patient 3 with right facial and sensorimotor hemiparesis,
Patient 4 with left motor arm paresis, and Patient 5 with left
motor hand paresis (Table).

In all data sets, finger movements were accompanied by
motor-related infraslow magnetic field changes over the
contralateral motor cortex, which were clearly above noise
level. These infraslow field changes were characterized by a
fast increase of field strength at the beginning of activation,
sustained field amplitudes during the 30-second activation,
and a slower decrease after the end of the finger movement
(Figure 1).

In 2 patients (S1 and S2), motor output (using electromyo-
graphy) and heart rate were monitored. In patient S1, elec-
 tromyographic activity was approximately 60% stronger on
the healthy compared with the affected side, but muscle
action was clearly visible on both sides. Heart rate was
approximately 80 beats/min for both sides. In patient S2,
electromyographic strength was similar on the healthy and
affected sides with muscle action clearly visible. Heart rate was approximately 75 beats/min for both sides.

For the data analysis, averaged signals over 30 periods were used. (The recording technique allows also data analysis on a single trial basis.) The amplitudes of motor-related infraslow field changes were significantly stronger for the unaffected compared with the affected hemisphere in 4 of 5 patients (S1 to S4) and in one case approximately the same (S5; mean amplitude: 496.0 fT±70.0 versus 268.5 fT±51.3, paired t test; see Figure 1 and Table). Subjects with cortical infarcts (S1 and S2) showed the clearest difference in the motor-induced field changes.

In 3 patients, the spatial motor-related field patterns of the unaffected hemisphere had a predominantly dipolar structure compared with predominantly distorted patterns over the affected hemisphere (Figure 2). Thereby, the dipolar generator was individually located close to the N20 field pattern.

Discussion

The present study proved the feasibility and applicability of DC-MEG in patients with stroke. The application of DC-MEG to patients with stroke presents various difficulties. Patients with stroke cannot keep as still as healthy subjects. Especially, inadvertent head motions or eye movements can alter the MEG signal-to-noise ratio. As a consequence of these constraints, in the present first step, only patients with milder forms of stroke in a subacute stage were investigated.

By analyzing temporal dynamics, strength of amplitude, and field pattern, the physiological stimulus condition revealed stable and clearly separable activation-related infraslow field changes above noise level in all patients. The profiles of infraslow magnetic fields followed the motor activation closely during the 30-minute recording session as known from studies in healthy subjects.6,10,12,13 A fast increase of the amplitude was recorded at the beginning of
finger movements. Sustained elevated amplitudes were seen during the activation period over 30 seconds. A slower decrease characterized the period after the finger movements.

Beyond revealing stable signal changes, the noninvasive DC-MEG technique allowed to detect intraindividual differences. In 4 of 5 patients, the motor-related activation generated significantly stronger infraslow signals over the unaffected compared with the affected hemispheres. Thereby, the clearest difference was found for subjects with cortical lesions compared with subcortical lesions. Because cortical lesions affect a greater cerebral network, cortical lesions are expected to cause the greater reduction of activation-related amplitudes. However, because functional asymmetry, eg, caused by handedness or performance differences due to the degree of individual functional impairment, could also contribute to the differential results, follow-up studies have to further characterize these findings.

The reconstructed motor-related infraslow magnetic field pattern displayed a predominantly bipolar structure over the unaffected hemisphere, whereas the spatial pattern over the affected hemisphere was not bipolar or showed major distortions.

Summary

In this pilot study, a noninvasive modulation-based MEG measuring technique was able to monitor and to localize activation related infraslow activity in a patient sample with subacute ischemic stroke. In the next step, the noninvasive MEG method might allow to investigate also patients with stroke in the acute stage, eg, for monitoring of spontaneous pathological infraslow waves of cortical spreading depolarization occurring during ischemic stroke events. In addition, longitudinal DC-MEG studies of neuronal recovery after stroke could allow optimizing rehabilitation regimes.

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Disclosures

None.

References


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