Correlation of Quantitative EEG in Acute Ischemic Stroke With 30-Day NIHSS Score
Comparison With Diffusion and Perfusion MRI

Simon P. Finnigan, PhD; Stephen E. Rose, PhD; Michael Walsh, FRACP; Mark Griffin, PhD; Andrew L. Janke, PhD; Katie L. McMahon, PhD; Rowan Gillies, RN; Mark W. Strudwick, PhD; Catharine M. Pettigrew, BSpPath; James Semple, PhD; John Brown, MA, MD, FRCP, FMedSci, FRES; Peter Brown, MD, FRCP; Jonathan B. Chalk, FRACP, PhD

Background and Purpose—Magnetic resonance imaging (MRI) methods such as diffusion- (DWI) and perfusion-weighted (PWI) imaging have been widely studied as surrogate markers to monitor stroke evolution and predict clinical outcome. The utility of quantitative electroencephalography (qEEG) as such a marker in acute stroke has not been intensively studied. The aim of the present study was to correlate ischemic cortical stroke patients’ clinical outcomes with acute qEEG, DWI, and PWI data.

Materials and Methods—DWI and PWI data were acquired from 11 patients within 7 and 16 hours after onset of symptoms. Sixty-four channel EEG data were obtained within 2 hours after the initial MRI scan and 1 hour before the second MRI scan. The acute delta change index (aDCI), a measure of the rate of change of average scalp delta power, was compared with the National Institutes of Health Stroke Scale scores (NIHSSS) at 30 days, as were MRI lesion volumes.

Results—The aDCI was significantly correlated with the 30-day NIHSSS, as was the initial mean transit time (MTT) abnormality volume ($\rho=0.80, P<0.01$ and $\rho=0.79, P<0.01$, respectively). Modest correlations were obtained between the 15-hour DWI lesion volume and both the aDCI and 30-day NIHSSS ($\rho=0.62, P<0.05$ and $\rho=0.73, P<0.05$, respectively).

Conclusions—In this small sample the significant correlation between 30-day NIHSSS and acute qEEG data (aDCI) was equivalent to that between the former and MTT abnormality volume. Both were greater than the modest correlation between acute DWI lesion volume and 30-day NIHSSS. These preliminary results indicate that acute qEEG data might be used to monitor and predict stroke evolution. (Stroke. 2004;35:899-903.)

Key Words: magnetic resonance imaging, perfusion-weighted electroencephalography stroke assessment magnetic resonance imaging, diffusion-weighted

A key aim for acute stroke therapy and research is the accurate identification and prediction of cerebral infarct evolution and clinical outcome. Using diffusion- (DWI) and perfusion- (PWI) weighted magnetic resonance images (MRI) acquired in patients with acute stroke, the volume of the DWI lesion or of the ischemic territory delineated on PWI mean transit time (MTT) maps has been shown to be correlated with National Institutes of Health Stroke Scale (NIHSS) or Canadian Neurological Scale (CaNS) scores. However, MRI is not practical for continuous investigations of the progression of brain pathophysiology in the crucial acute poststroke period. Electroencephalogram data can be serially acquired from patients in their hospital beds during this period. In stroke patients there is a substantial increase in the power of delta (1- to 4-Hz) rhythms. Quantitative electroencephalography (qEEG) techniques, such as topographic power maps, when compared with conventional EEG methods have demonstrated improved detection and localization of ischemic brain pathophysiology. In addition, qEEG data acquired within 72 hours after stroke possessed a higher prognostic value than did the CaNS. However, unlike MRI, qEEG data have not been acquired within several hours of

Received July 2, 2003; final revision received November 19, 2003; accepted December 23, 2003.

From the Centre for Magnetic Resonance (S.F., S.E.R., M.W., M.G., A.L.I., K.I.M., R.G., M.W.S., J.B.C.), the Department of Speech Pathology and Audiology (C.M.P.), and the Department of Medicine (J.B.C.), University of Queensland, Brisbane, Australia; the Translational Medicine and Technology Group (J.S., J.B.), GlaxoSmithKline, Cambridge, United Kingdom; the Academic Department of Psychiatry (J.S.), University of Cambridge, Cambridge, United Kingdom; and the Sobell Department of Motor Neuroscience and Motor Disorders (P.B.), Institute of Neurology, London, United Kingdom. Correspondence to Dr Simon P. Finnigan, PhD, Centre for Magnetic Resonance, Gehrmann Building, Research Road, University of Queensland, Brisbane, Queensland 4072, Australia. E-mail finnigan@cmr.uq.edu.au.

© 2004 American Heart Association, Inc.

Stroke is available at http://www.strokeaha.org DOI: 10.1161/01.STR.0000122622.73916.d2
stroke onset and correlated with clinical outcome. This was the focus of the present study. Sixty-four-channel EEG data were collected from a cohort of stroke patients at times within 8 and 15 hours after stroke. Resultant qEEG measures were correlated with NIHSSS at 30 days after stroke. In addition, DWI and PWI data were acquired from these patients before and after these times, and these were correlated with 30-day NIHSSS and acute qEEG data. This comprehensive, multimodal approach allowed both the assessment of the capability of acute qEEG data to monitor infarct evolution and predict functional outcome and furthermore a comparison with the DWI and PWI examinations.

Materials and Methods

Patient Selection and Serial Imaging Protocol

Patients with acute focal motor neurologic symptoms together with symptoms such as speech impairment or inattention or impaired cognition consistent with ischemic cortical stroke were recruited. Approval to carry out the study was obtained from the local university and hospital Human Experimental Ethics committees. The patient or legally authorized person gave informed consent for the study. The “acute measurement time” was defined as the time elapsed between the last time the patient was known to be without neurologic deficit (accurate to within 1 hour) and the time of the initial MRI scans or initial EEG recordings. Patients were excluded if they presented with fever; seizures; a cerebral hemorrhage on computed tomography scan; a preexisting neurologic condition that would confound clinical or MR assessment, such as radiologic evidence of a previous stroke; EEG abnormalities consistent with encephalitis; or use of medications that could confound EEG assessment, such as benzodiazepines, tricyclic antidepressants, or neuroleptic medications. Patients underwent DWI and PWI scans within 6 hours, 15±3 hours, and 30 days after stroke onset. Sedation was not permitted for MRI scanning. The NIHSS was administered on admission and at 30±2 days after stroke.

Control Participants

EEG was acquired from 6 control participants, each of whom was matched with 1 patient in terms of age, sex, and the times of recording. These participants were previously found to be healthy on neuropsychological and MRI screening.

MRI Data Acquisition and Analyses

All patients received serial diffusion tensor imaging sequence. Imaging parameters were 21 angiography examinations with a 1.5-T Siemens Sonata MRI scan. All patients received serial diffusion, perfusion, T2, and MR screening. EEG was acquired from 6 control participants, each of whom was enrolled in the present study. The patient or legally authorized person gave informed consent for the study. The “acute measurement time” was defined as the time elapsed between the last time the patient was known to be without neurologic deficit (accurate to within 1 hour) and the time of the initial MRI scans or initial EEG recordings. Patients were excluded if they presented with fever; seizures; a cerebral hemorrhage on computed tomography scan; a preexisting neurologic condition that would confound clinical or MR assessment, such as radiologic evidence of a previous stroke; EEG abnormalities consistent with encephalitis; or use of medications that could confound EEG assessment, such as benzodiazepines, tricyclic antidepressants, or neuroleptic medications. Patients underwent DWI and PWI scans within 6 hours, 15±3 hours, and 30 days after stroke onset. Sedation was not permitted for MRI scanning. The NIHSS was administered on admission and at 30±2 days after stroke.

EEG Data Acquisition and Analyses

An elastic cap (Quik-Cap, Neuromedical Supplies) in which were embedded 62 sintered Ag/AgCl scalp electrodes was fitted to the patient’s head. Electrode locations corresponded to the 64-channel montage of the international 10-20 system. Note that we do not assume that use of electrode caps, nor of such a high-density montage, is essential in this context. Eye movements and blinks were monitored with appropriately placed bipolar vertical and horizontal electro-oculogram electrodes. At acquisition, all electrode signals were referenced to a linked pair of electrodes, 1 positioned on each mastoid process. Electrode impedances were predominantly 10 to 20 kΩ or less. Recordings were made with a Neuroscan SynAmps 64-channel EEG system. EEG data were digitized at a rate of 500 Hz and filtered online (bandpass, 0.01 to 100 Hz). EEG data were acquired both at the earliest practical time after the initial MRI scan and before the second MRI scan. In general, the patients were awake during these times but resting quietly and lying still in their beds with their eyes closed.

There was a peak in the delta band at or incorporating 1.5 Hz in the resulting spectra for all patients from the initial and, for most patients, the second time point. To compute an acute delta change index (aDCI) reflecting the relative direction and rate of change of average scalp delta power across the acute poststroke period, the power value associated with this frequency from the initial time point (D1) was subtracted from that at the final time point (D2). This difference was then divided by D1 and by the time (in hours) that had elapsed between these 2 time points.

Statistical Analyses

Because the data were not normally distributed, Spearman’s correlation coefficient was computed between the aDCI, MRI volumes, and outcome NIHSSS. The Bonferroni correction for multiple comparisons was applied to maintain the total type I error rate at a sufficiently low level. In this case, 5 comparisons were performed; thus, only outcomes of P<0.01 were considered statistically significant.

Results

Patient demographics and times of initial MRI scanning and EEG recording are given in Table 1. Eleven patients (5 men; mean age, 74.5; range, 55 to 87 years) were recruited. The mean initial time to MRI was 5.0 (range, 3 to 7) hours and for EEG, 6.6 (range, 5 to 8) hours. The mean time between the initial and second EEG data time points was 7.7 (range, 6 to 11) hours. Ten patients had acute DWI lesions encompassing both gray and white matter, whereas 1 patient (No. 6) had a deep white-matter DWI lesion. All patients possessed an MTT abnormality extending to the cortical surface. Two patients died within 12 days. One patient was treated with intravenous recombinant tissue-type plasminogen activator (r-tPA) at 5 hours. All patients demonstrated DWI abnormalities consistent with findings of the initial clinical presentation. All patients scored 0 (alert) or 1 (not alert but arousable by minimal stimulation) on NIHSSS item 1a during the initial and second EEG time points, and no patient’s score changed between these times, except for patient 9, who scored 2 (not alert) at the second time point. Eight patients had a reduced NIHSSS at 30 days, whereas 3 patients’ scores subsequently
increased. Two of these latter patients were deceased by 30 days after stroke, and the maximum NIHSSS of 42 was used. The correlations were computed on ranked data (see next section), and therefore, the ranks of these deceased patients’ 30-day NIHSSS would have been the highest of all patients in the study, regardless of the exact 30-day score used.

MRI and aDCI measures are given in Table 2. Delta power decreased over time (negative aDCI) in patients who subsequently recovered but increased (positive aDCI) in patients who subsequently died. There was a significant positive correlation between the aDCI and 30-day NIHSSS ($r=0.80$, $P<0.01$) (Figure 1A). A modest correlation was obtained between the aDCI and 15-hour DWI lesion volume ($r=0.62$, $P<0.05$; Figure 1B). Modest correlations were obtained between the 30-day NIHSSS and both the initial and 15-hour DWI lesion volumes ($r=0.61$, $P<0.05$ and $r=0.73$, $P<0.05$), respectively; Figure 1C). A significant correlation was obtained between 30-day NIHSSS and the initial MTT volume ($r=0.79$, $P<0.01$).

Figure 2 shows topographic delta power maps and MRI data from the patient (No. 2) with the most negative aDCI. It shows only marginal expansion of the diffusion lesion (C and G), with the 30-day T2-weighted scan revealing only a small infarct (H). The negative aDCI is illustrated in the delta maps (compare A and B with E and F). That is, the number of electrodes exhibiting abnormally high delta power (indicated by the red background) and as a corollary, average scalp delta power, decreased between the 2 acute time points.

In contrast, MRI data from patient 3, who died at 12 days, revealed very large DWI and PWI abnormalities (see Figure 3). A substantial expansion in DWI lesion volume over time

### Table 1. Patient Demographics, Vascular Territories, Times of MRI and EEG Acquisition, and NIHSSS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y/Sex</th>
<th>Vascular Territory</th>
<th>Acute Measurement Time, h</th>
<th>MRI, EEG Initial</th>
<th>NIHSSS 30 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>83/F</td>
<td>RPCA</td>
<td>3.5</td>
<td>5.5</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>57/F</td>
<td>LMCA</td>
<td>5.0</td>
<td>6.5</td>
<td>7</td>
</tr>
<tr>
<td>3*</td>
<td>83/F</td>
<td>RMCA</td>
<td>7.0</td>
<td>8.0</td>
<td>22</td>
</tr>
<tr>
<td>4</td>
<td>55/M</td>
<td>RICA</td>
<td>3.0</td>
<td>5.0</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>87/F</td>
<td>RMCA</td>
<td>5.5</td>
<td>7.5</td>
<td>19</td>
</tr>
<tr>
<td>6</td>
<td>64/M</td>
<td>LMCA</td>
<td>4.5</td>
<td>6.0</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>85/M</td>
<td>LMCA</td>
<td>5.5</td>
<td>7.5</td>
<td>25</td>
</tr>
<tr>
<td>8†</td>
<td>67/M</td>
<td>LMCA</td>
<td>4.5</td>
<td>6.0</td>
<td>21</td>
</tr>
<tr>
<td>9*</td>
<td>86/F</td>
<td>LMCA</td>
<td>4.5</td>
<td>6.3</td>
<td>33</td>
</tr>
<tr>
<td>10</td>
<td>86/F</td>
<td>LPCA</td>
<td>5.0</td>
<td>6.5</td>
<td>18</td>
</tr>
<tr>
<td>11</td>
<td>66/M</td>
<td>LMCA</td>
<td>7.0</td>
<td>8.0</td>
<td>11</td>
</tr>
</tbody>
</table>

L indicates left; R, right; MCA, middle cerebral artery; PCA, posterior cerebral artery; and ICA, internal carotid artery.

*Patient died before 30-day follow up scan.
†Patient received r-PA after initial MRI scan.

### Table 2. MRI and EEG Indices

<table>
<thead>
<tr>
<th>Patient</th>
<th>Lesion Volumes, mL</th>
<th>DWI, 5 Hours</th>
<th>MTT, 5 Hours</th>
<th>DWI, 15 Hours</th>
<th>T2, 30 Days</th>
<th>QEEG aDCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.6</td>
<td>14.8</td>
<td>7.7</td>
<td>6.0</td>
<td>−0.10</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>25.3</td>
<td>188.3</td>
<td>29.8</td>
<td>9.0</td>
<td>−0.17</td>
<td></td>
</tr>
<tr>
<td>3*</td>
<td>205.7</td>
<td>424.8</td>
<td>263.9</td>
<td>NA</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>26.6</td>
<td>50.4</td>
<td>29.5</td>
<td>22.9</td>
<td>−0.10</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>32.8</td>
<td>108.2</td>
<td>46.9</td>
<td>46.3</td>
<td>−0.04</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>11.1</td>
<td>98.1</td>
<td>12.4</td>
<td>7.4</td>
<td>−0.06</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>35.7</td>
<td>228.5</td>
<td>46.4</td>
<td>37.0</td>
<td>−0.08</td>
<td></td>
</tr>
<tr>
<td>8†</td>
<td>134.5</td>
<td>199.8</td>
<td>143.0</td>
<td>167.3</td>
<td>−0.05</td>
<td></td>
</tr>
<tr>
<td>9*</td>
<td>224.3</td>
<td>483.1</td>
<td>298.5</td>
<td>NA</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>5.1</td>
<td>14.6</td>
<td>9.1</td>
<td>0.9</td>
<td>−0.09</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>5.1</td>
<td>NA</td>
<td>14.0</td>
<td>144.7</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

aDCI indicates acute delta change index.

*Patient died before 30-day follow-up scan.
†Patient received tissue r-PA after initial MRI scan and EEG recording.
is evident. The delta maps (compare A and B with E and F) illustrate a positive aDCI.

Figure 4 shows data for the patient given r-tPA. The 15-hour MR angiographic examination revealed recanalization of the middle cerebral artery. Initial MRI scans revealed a large DWI lesion with a large territory of hypoperfused brain tissue. The follow-up DWI scan revealed only marginal expansion of the lesion; the NIHSSS improved significantly from the initial to the final score. The posttreatment delta maps illustrate a negative aDCI.

Age-, sex-, and time-matched control EEG data (2 men and 4 women; age range, 58 to 82 years) revealed the mean average scalp delta power to be 2.77 μV², whereas in patients this was value was 33.95 μV² at 7 hours (t = 4.68, P < 0.001). In addition, each control participant’s aDCI (range, −0.002 to +0.008) was at least 1 order of magnitude lower than the lowest patient aDCI (range, −0.17 to +0.15).

Discussion

A number of novel findings have emerged from this study. First, we have demonstrated that an acute qEEG metric, the aDCI, is strongly correlated with patients’ 30-day NIHSSS (Figure 1A). This correlation was equivalent to that between acute MTT abnormality volume and 30-day NIHSSS, and both aforementioned correlations were greater than those obtained between the latter clinical outcome score and acute DWI lesion volumes (Figure 1C).

On the basis of MRI data from patient 2 (Figure 2), considerable expansion of the DWI lesion into the surrounding penumbral territory could be expected, together with a decline in functional outcome. However, the aDCI was negative and correctly predicted an improved functional outcome. In patient 3, who died, the DWI lesion expanded significantly (Figure 3) and the aDCI was positive, correctly predicting a worsening outcome. The aDCI also allowed assessment of the effects of r-tPA treatment. In patient 8, who received r-tPA, the aDCI was negative (Figure 4), and this result was correlated with an improved 30-day NIHSSS; this clinical outcome appeared unlikely based on acute MRI measures.

This is the first reported demonstration that there is a correlation between an acute qEEG measure and 30-day NIHSSS. Other qEEG variables derived from data acquired within 72 hours of stroke were correlated with 3-month CaNS. However, in contrast to the aDCI, the calculation of those qEEG variables requires the use of a population EEG database. We have further demonstrated a modest correlation between aDCI and 15-hour DWI lesion volume (Figure 1B). This is the first reported correlation between any qEEG and MRI data in the acute poststroke period.

Significant correlations between MRI measures and clinical scores have been reported previously. Using a stringent, nonparametric statistical approach, we have demonstrated a modest correlation between the 30-day NIHSSS and acute DWI lesion volumes and a significant correlation between the former and the MTT abnormality volume. Baird et al. used the same approach but obtained a nonsignificant correlation between MTT volume and follow-up NIHSSS. This discrepancy might be due to the greater mean acute scanning and follow-up times (and greater ranges thereof) in the latter study.

Figures 2, 3, and 4 illustrate the correspondences between the locations of electrodes exhibiting greatest delta power and the stroke-affected brain regions, as has been demonstrated previously. However, the aDCI per se is not a localization metric but a measure of change in average scalp delta power; hence, its correlation with 30-day NIHSSS should generally hold, regardless of cortical stroke location. Indeed, it is noteworthy that the current small sample comprises a range of DWI/PWI abnormality volumes and locations. It might be that average scalp delta power indexes the volume of brain tissue exhibiting delta pathophysiology, but this remains unresolved.

A potential confounding factor in the present study is the impact of drowsiness or sleep on the aDCI, because delta rhythms are present during deep, non–rapid eye movement sleep. Three patients were awake at the first time point but asleep at the second time point, yet all 3 exhibited a negative aDCI, which is in the opposite direction to that expected if sleep were confounding the aDCI. Patient 9 scored 2 on NIHSS item 1a, indicating drowsiness was present at the second time point. However, removal of this patient’s data from analysis did not diminish the significance of the correlation between the aDCI and 30-day NIHSSS. Yokoyama et al. reported that delta power during sleep was correlated with that obtained during wakefulness after hemispheric
stroke. Hence, it appears that any possible confounding effect of drowsiness- and/or sleep-related delta activity on the aDCI, if it were to exist, would not be of sufficient magnitude to significantly diminish the utility of this metric in the prognosis of functional outcome after stroke.

Further evidence that the observed delta power changes were not simply due to changes in alertness or indeed eye movements is provided by the specific delta topographies, which consistently colocalized with MRI lesions at both EEG time points. Similarly, these delta topographies extend quite posteriorly and laterally; this would argue against an index of eye movement artifacts, which were in any case removed or attenuated via an appropriate algorithm.

This novel study on a small patient sample has found that EEG, a relatively resource-efficient methodology, permits the bedside monitoring of acute stroke patients and thus might improve our understanding of the evolution of poststroke brain pathophysiology. However, we do not propose that EEG replace MRI in this context. MRI permits better detection and definition of penumbral tissue for example. The present study has focused on a delta power metric. Further analyses of EEG data, eg, coherence, source calculations, and registration of EEG source and MRI data sets, might permit new insights into stroke evolution. Specifically, the latter approach has the potential to determine whether delta oscillations are generated by brain regions exhibiting diffusion and/or perfusion abnormalities and whether or not there is a relation between scalp delta power and the volume of brain tissue defined as abnormal.

Acknowledgments
We acknowledge the support of Dr Stephen Read and the Stroke Units of the Royal Brisbane and Wesley Hospitals, Australia. We also acknowledge funding from GlaxoSmithKline Pharmaceuticals. GlaxoSmithKline employees were involved in the conceptual design of the study as well as interpretation of the data.

References