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Utility of EEG measures of brain function in patients with acute stroke

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Abstract

EEG has been used to study acute stroke for decades; however, because of several limitations EEG-based measures rarely inform clinical decision-making in this setting. Recent advances in EEG hardware, recording electrodes, and EEG software could overcome these limitations. The present study examined how well dense-array (256 electrodes) EEG, acquired with a saline-lead net and analyzed with whole brain partial least squares (PLS) modeling, captured extent of acute stroke behavioral deficits and varied in relation to acute brain injury. In 24 patients admitted for acute ischemic stroke, 3 min of resting-state EEG was acquired at bedside, including in the ER and ICU. Traditional quantitative EEG measures (power in a specific lead, in any frequency band) showed a modest association with behavioral deficits [NIH Stroke Scale (NIHSS) score] in bivariate models. However, PLS models of delta or beta power across whole brain correlated strongly with NIHSS score (R^2 = 0.85–0.90) and remained robust when further analyzed with cross-validation models (R^2 = 0.72–0.73). Larger infarct volume was associated with higher delta power, bilaterally; the contralesional findings were not attributable to mass effect, indicating that EEG captures significant information about acute stroke effects not available from MRI. We conclude that *1*) dense-array EEG data are feasible as a bedside measure of brain function in patients with acute stroke; *2*) high-dimension EEG data are strongly correlated with acute stroke behavioral deficits and are superior to traditional single-lead metrics in this regard; and *3*) EEG captures significant information about acute stroke injury not available from structural brain imaging.

Keywords: dense-array EEG, acute stroke, brain function, brain injury

ALTHOUGH MODERN MEDICINE has produced several excellent methods for measuring brain injury, current techniques for measuring brain function in complex medical settings are very limited. However, a technique that could provide a measure of neural function in such a setting accurately and rapidly could have high impact on clinical decision-making. This is likely to be particularly true in the setting of stroke, where both neural injury and neural function have been shown to contribute to impairment (Burke Quinlan et al. 2015; Finnigan and van Putten 2013; Kerr et al. 2011; Stinear et al. 2007). While valid methods for characterizing neural injury after stroke are well established and in routine clinical use, ideal methods for characterizing functional effects of stroke on the brain are still a research topic, particularly in the setting of acute stroke.

Traditional measures of neural function including functional MRI (Marshall et al. 2009; Saur et al. 2010), PET (Di Piero et al. 1992), and transcranial magnetic stimulation (Liepert et al. 2000) can provide useful insights into the physiological effects of a stroke. However, implementation of these techniques in the acute stroke setting remains challenging, underscoring the need for additional approaches for measuring brain function early after stroke and motivating the present study to examine the precision with which EEG captures effects of acute stroke on brain function.

EEG is useful for studying brain function safely and rapidly in complex medical settings and has been known for decades to provide insights into acute stroke effects (Astrup et al. 1977; De Weerd et al. 1988; Foreman and Claassen 2012; Macdonell et al. 1988; Marquardsen and Harvald 1964; Nunez and Srinivasan 2006). EEG metrics in this context, such as increased slow rhythms and decreased fast rhythms, are directly linked with neuronal metabolism and so rapidly reflect ischemic injury (Astrup et al. 1977; Foreman and Claassen 2012). Broad adoption of EEG into acute stroke clinical practice remains limited because of a number of factors such as long times needed to mount traditional AgCl EEG electrodes (Finnigan et al. 2007) and uncertainty regarding choice of EEG metric (Finnigan et al. 2007; Sheorajpanday et al. 2009; Xin et al. 2012).

Advances in EEG hardware, recording electrodes, and software analysis methods may be able to overcome these barriers (Tucker 1993). Dense-array systems with up to 256 electrodes show improved spatial resolution (Luu et al. 2001; Petrov et al. 2014), saline-based leads can be rapidly applied, and newer computational methods provide improved resolution of task-related brain function (Giacino et al. 2014); for example, recent studies using partial least squares (PLS) regression outperformed traditional EEG methods in terms of capturing behavioral variation in stroke and nonstroke populations (Wu et al. 2014, 2015).

The present study of patients admitted for acute stroke builds on these findings. The primary aim of the present study was to determine how well EEG captures behavioral effects of acute stroke. Specific study hypotheses were that *1*) dense-array EEG acquired acutely (hours to days) after stroke onset with a saline lead cap and analyzed with PLS models of whole brain function is feasible and is significantly related to impairment level [NIH Stroke Scale (NIHSS) score] and *2*) these PLS models capture impairment better than traditional quantitative EEG metrics (such as spectral power within a specific lead). Two secondary hypotheses examined were that these EEG-behavior relationships vary according to extent of injury (i.e., infarct volume) and that a model combining a measure of neural function (dense-array EEG) and a measure of neural injury [acute computerized tomography (CT) or MRI] is more closely related to impairment level than either measure alone, in line with prior studies (Burke Quinlan et al. 2015; Finnigan and van Putten 2013; Kerr et al. 2011; Stinear et al. 2007).

METHODS

Study design. Inpatients with radiologically confirmed acute ischemic stroke were recruited from UC Irvine Medical Center. Subjects provided written informed consent to protocols approved by the Institutional Review Board and then underwent EEG assessment. Inclusion criteria included acute ischemic stroke, age >18 yr, and English speaking. Exclusion criteria included significant problems with attention, alertness, or cognitive function and inability to communicate. As standard stroke center procedure, all subjects had the NIHSS scored on admission by personnel certified in this assessment.

EEG acquisition and analysis. A dense-array surface EEG (256 electrodes, EGI) was used to acquire 3 min of eyes-open, resting-state brain activity. A HydroCel net applied all 256 electrodes onto the scalp at the same time. As a result, start-to-finish time for EEG preparation (including head measurement, net preparation in the saline conducting solution, net placement, and net adjustments), 3 min of EEG recording, EEG removal, and cleanup was typically 20 min. Data were collected with a high-input impedance amplifier at 1,000 Hz sampling rate, without digital filters.

EEG preprocessing.

EEG data were exported to MATLAB 7.8.0 (MathWorks, Natick, MA) for preprocessing and analyses. In line with previously described methods (Wu et al. 2014, 2015), preprocessing steps included applying a second-order 50-Hz low-pass Butterworth filter, mean detrending, and rereferencing to the average signal across all channels. Continuous EEG data were then binned into 180 sequential, nonoverlapping, 1-s epochs. After a visual inspection to remove trials contaminated by overt movement and speaking, the time series was subjected to an Infomax independent component analysis [EEGLAB (Delorme and Makeig 2004)], from which components containing characteristic extrabrain artifacts (including eyeblinks, eye movements, and cardiac rhythms) were identified and removed (Delorme et al. 2007). The remaining components were then transformed back to channel space before undergoing a subsequent visual inspection to ensure absence of all extrabrain artifacts in the remaining data. Across the 24 EEG recordings, 167.9 ± 20.4 (mean ± SD) of the 180 epochs per EEG exam (88.2%) were retained for subsequent analysis.

Traditional quantitative EEG metrics. Two traditional quantitative EEG metrics were examined, spectral power and coherence in individual leads. Spectral power measures were extracted by submitting the time series in each channel to a discrete fast Fourier transform and then normalizing by epoch length. Average absolute power at each electrode was calculated for a 1–30 Hz frequency band in 1-Hz bins, then expressed as relative power, i.e., divided by total power across 1–30 Hz at each electrode. Based on prior studies of EEG in acute brain injury, relative delta (1–3 Hz) power was selected as the primary measure of spectral power; relative power in theta (4–6 Hz), alpha (7–12 Hz), beta (13–19 Hz), and high beta (20–30 Hz) bands was also examined.

Recent findings suggest that connectivity measures better represent complexity in human cortical processing and thus may demonstrate a stronger association with behavior (Bullmore and Sporns 2012). In the present study, functional connectivity between brain regions was estimated with EEG coherence between electrodes overlying corresponding brain regions (Nunez and Srinivasan 2006). Coherence is a dimensionless metric that ranges from 0 to 1 and describes the degree of correspondence between signals in phase and amplitude at one frequency. Specifically, a coherence value near 0 for a given pair of electrodes indicates a random difference in phase and amplitude, while a coherence value equal to 1 indicates no difference in phase and amplitude across all time points. Similar to spectral power, coherence is a frequency-specific measure, and so mean coherence was calculated for each of the five frequency bands of interest. For individuals with infarcts in the right hemisphere, power arrays and coherence matrices were flipped across the midline for subsequent analyses. Since the NIHSS scale is weighted toward motor impairments (Lyden et al. 2004), the present study focused on mean coherence with a seed cluster of seven electrodes overlying ipsilesional sensorimotor cortex (SMC); the SMC seed was defined as the C3 lead, which largely reflects activity from precentral gyrus (Homan et al. 1987), and its six immediately surrounding electrodes.

PLS modeling. PLS analyses have advantages for analyzing large data sets such as neuroimaging data, in which multicollinearity across a large number of predictors can reduce statistical power (Krishnan et al. 2011). The present study used a previously described implementation of the N-way toolbox for MATLAB (Andersson and Bro 2000) to examine the correlation between behavioral measures and whole brain EEG measures (Wu et al. 2014, 2015) with PLS regression analysis. EEG measures examined consisted of the same five power and five coherence measures examined in the traditional quantitative EEG analyses above.

For each PLS model, the objective is to maximize representation of the variance in the dependent measure in as few components of the independent measure as possible. This is accomplished by optimizing a least-squares fit of a partial correlation matrix between the independent and dependent measures. In the present study, the independent variables were the EEG measures of brain function and the dependent variable was NIHSS score. As a preprocessing step, data were mean centered and then submitted to a direct orthogonal signal correction (Westerhuis et al. 2011). As with previous studies that use PLS (Esteban-Diez et al. 2004; Krishnan et al. 2013), this step allows for more efficient PLS models that are built with fewer components by removing the single largest component of the independent measure that is most orthogonal to the behavioral data. In the PLS regression, a series of models with successively more components were generated that

maximally accounted for variance in NIHSS score. In PLS analysis, similar to other component-based statistical methods, a nonlinear increase in percentage of total variance explained is accounted for with each additional component. The resultant models each represent a complex linear regression where each electrode is associated with a correlation coefficient. The magnitude (absolute value) and direction (negative or positive) of the correlation coefficient represent the degree and direction of correlation between variance in the EEG measure and variance in the dependent measure (NIHSS score). As previously (Wu et al. 2014, 2015), the fitted PLS model included as many components as were required to explain 80% of the variance in the dependent variable. This 80% cutoff was chosen on the basis of previous experience in our group demonstrating that there is a significant decrease in added variance accounted for in PLS models that include greater than two components. Furthermore, it has been our experience that PLS models that include additional components beyond the 80% cutoff never survive leave-one-out and predict cross-validation.

To identify specific clusters of leads where variance in the EEG measure of interest was most strongly correlated with variance in the dependent measure, a threshold was predefined and applied to the correlation coefficients in each PLS model. With a previously detailed approach (Menzies et al. 2007), regression coefficients were thresholded at $|r_i| > 0.75 \times r_{max}$, where r_i is the correlation coefficient at the ith electrode and r_{max} is the largest $|r_i|$ value across all electrodes. Clusters were required to have a minimum of two contiguous electrodes exceeding the threshold. EEG measures were then averaged across clusters of leads and regressed against the dependent measure, using bivariate correlations.

Magnetic resonance imaging. As part of the acute stroke imaging protocol at the UC Irvine Medical Center Stroke Center, all subjects had diffusion-weighted imaging performed, from which infarct volume was calculated with previously described methods (Burke Quinlan et al. 2015).

Statistical analyses. Parametric methods were used, as measures were normally distributed or could be transformed to a normal distribution. Significance was two-tailed, set at $P < 0.05$, and tested via MATLAB 7.8.0. At each electrode, traditional quantitative EEG metrics were evaluated by using linear regression to compare 10 measures (power and coherence with ipsilesional SMC in each of 5 frequency bands), with the dependent measure being NIHSS score, with Bonferroni correction for multiple comparisons. Strength of these quantitative EEG results was compared to strength of PLS models by comparing the R^2 values.

To test the ability of a given model to extrapolate to a test case, a leave-one-out and predict cross-validation was performed for each linear regression model and for each fitted PLS model. In this validation method, data from a single subject are iteratively removed from the model set. Then, the behavioral data from the removed subject (test case) are predicted from his/her EEG data with either the linear regression model or the PLS model generated from the remaining $n - 1$ subjects. The reported validated R^2 was calculated from the sum of errors across all n iterations of the leave-one-out and predict sequence. This method has established utility for accurately assessing a model's potential to generalize to an independent data set (Huang et al. 2011).

RESULTS

Subjects. Twenty-five stroke patients were recruited and signed informed consent. EEG recordings were acquired in diverse settings that included ER, ICU, and stroke ward. One patient was excluded because of hardware malfunction during data acquisition. The remaining 24 patients were age 60.9 ± 13.1 yr (mean ± SD, range 35–88 yr), 16 men/8 women, 20 right-handed/4 ambidextrous and were studied 3.4 ± 3.0 days (range 3 h–12 days) after stroke. Infarcts were heterogeneous: 22.6 ± 43.6 cc (range 0.14–166.1 cc), with 15 in left and 9 in right hemisphere, and with admission NIHSS scores ranging from 1 to 19 (median [IQR] = 5.5 [3–7]).

PLS models are more closely related to acute stroke impairment than traditional quantitative EEG metrics.

When NIHSS score was compared with each of the 10 EEG measures (power in 5 frequency bands and coherence with ipsilesional SMC in 5 frequency bands) by bivariate linear regression, one was significant: power in the high beta band, within an electrode cluster overlying a contralesional frontoparietal region (Table 1); however, this did not survive cross-validation.

The strength of the association between EEG data and admission NIHSS score was significantly improved with PLS regression. Table 2 presents results for each of the 10 EEG measures, with the fitted model R^2 representing the best fit correlation between all EEG electrodes and NIHSS score and with the validated model R^2 representing the strength of each PLS model obtained with leave-one-out and predict cross-validation. As expected, the R^2 values were consistently higher for models that are a simple fit compared with models that require validation. In addition, power outperformed coherence. Delta power was strongly related to admission NIHSS score (Fig. 1*A*; fitted $R^2 = 0.85$, validated $R^2 = 0.72$). In this PLS model, electrodes having the strongest correlation with NIHSS score were in two clusters, one overlying ipsilesional SMC, where higher delta power correlated with greater impairment (Fig. 1*B*; $R^2 = 0.35$, $P = 0.002$ in this cluster of leads), and the other overlying contralesional frontoparietal areas, where higher delta power again correlated with greater impairment (Fig. 1*C*; $R^2 = 0.28$, $P = 0.008$ in this cluster of leads). Beta power was also robustly related to admission NIHSS score (Fig. 1*D*; fitted $R^2 = 0.90$, validated $R^2 = 0.73$). In this PLS model, electrodes having the strongest correlation with NIHSS score were in a single cluster, in a region overlying ipsilesional SMC, where lower beta power correlated with greater impairment (Fig. 1*E*; $R^2 = 0.45$, $P = 0.0004$ when analysis is restricted to only this cluster of leads). Similar results were found for beta power for electrodes overlying a contralesional parietal area (Fig. 1*F*; $R^2 = 0.41$, $P = 0.0008$).

MRI assessment of neural injury and acute stroke impairment. Injury measures outperformed clinical variables as correlates of impairment in simple linear regression analyses. Thus time from stroke onset to EEG acquisition ($P > 0.7$) and age ($P > 0.4$) did not correlate significantly with NIHSS score, while an injury measure did (infarct volume, $r = 0.41$, $P = 0.046$) although infarct volume did not survive cross-validation.

Combining measures of neural injury and neural function improves strength of their association with acute stroke impairment.

A model combining an MRI-based measure of neural injury with an EEG-based measure of neural function explained acute impairment better than either measure alone. Structural and functional measures were combined by two methods.

First, adding an MRI-based measure of neural injury to EEG measures of neural function in PLS models significantly improved the strength of the association with acute impairment (i.e., with admission NIHSS score). Infarct volume correlated significantly with NIHSS score ($R^2 = 0.17$, $P = 0.046$). When infarct volume was added as a predictor to the PLS model of delta power, validated prediction improved (from $R^2 = 0.72$ to $R^2 = 0.77$) to an extent that was statistically significant ($F_{0.05,1,22} = 4.35$, $P < 0.05$). Similarly, when infarct volume was added as a predictor in the PLS model of beta power, validated prediction improved (from $R^2 = 0.73$ to $R^2 = 0.81$), a boost in R^2 that was also significant ($F_{0.05,1,22} = 10.7$, $P = 0.004$).

Second, adding EEG measures of neural function to an MRI-based measure of neural injury also improved the linear model. Injury- and region-specific functional measures were combined with a forward stepwise multivariate linear regression approach (0.1 to enter, 0.15 to leave the model). The EEG measures examined in the forward stepwise model were delta power within the key ipsilesional and contralesional regions defined in the above PLS model and beta power within the key ipsilesional region defined in the above PLS model (see Fig. 1 and Table 2); the MRI measure examined in the model was infarct volume. A measure of neural function (ipsilesional SMC beta power) and a measure of neural injury (infarct volume) survived the model (Table 3). The resultant model ($R^2 = 0.54$, $P = 0.0003$) was less robust than the PLS models,

emphasizing that the higher EEG dimensionality representation with PLS modeling provides improved brain-behavior relationships.

EEG markers of acute stroke impairment vary with extent of injury. An additional analysis examined whether EEG markers of impairment varied according to extent of injury. The EEG markers examined were delta power within key ipsilesional and contralesional regions and beta power within the key ipsilesional region, as defined in the above PLS models focused on admitting NIHSS score (Fig. 1 and Table 1). The injury measure examined was infarct volume. In the ipsilesional and contralesional regions of the delta power map that best explained NIHSS (Fig. 1, *A–C*), EEG markers varied directly with injury (Table 4). These findings indicate that, in the most behaviorally salient regions of the delta power EEG map on both sides of the brain, larger injury was associated with higher delta power. Results were overall similar for beta power in the ipsilesional hemisphere.

Additional brain imaging was reviewed to clarify whether higher contralesional delta power simply reflected mass effect from the stroke onto the contralesional hemisphere. All brain CT and MRI images obtained throughout the acute stroke admission were reviewed for the nine patients with medium (4–50 cc) and large (>50 cc) strokes, among whom EEG was acquired 2.3 ± 1.2 days after stroke onset and time between EEG and any brain imaging averaged 2.8 ± 4.7 days. No mass effect or edema was present in the contralesional hemisphere in eight of these subjects, while a single subject showed mild mass effect (Fig. 2).

DISCUSSION

Evidence suggests that a measure of brain function provides useful insights in the setting of stroke (Burke Quinlan et al. 2015; Di Piero et al. 1992; Kerr et al. 2011; Marshall et al. 2009; Saur et al. 2010); however, candidate techniques such as functional MRI and PET are challenging to implement in the acute care setting for reasons such as accessibility and cost. EEG has established value for measuring altered brain function in the acute stroke setting (Astrup et al. 1977; De Weerd et al. 1988; Foreman and Claassen 2012; Macdonell et al. 1988; Marquardsen and Harvald 1964; Nunez and Srinivasan 2006) and overcomes many of these challenges but has not been widely adopted. Building on advances in EEG hardware, recording electrodes, and software methods, the present study found that dense-array EEG analyzed with PLS modeling was a powerful correlate of behavioral status, performing better than traditional quantitative EEG metrics or measures of brain injury in the present cohort of 24 patients admitted for acute ischemic stroke. In addition, infarct volume was associated with differences in EEG findings, including the finding that larger infarct volume was associated with higher contralesional delta power, a result that indicates that EEG captures significant information regarding acute stroke effects not available from MRI. Acquisition of dense-array EEG in acutely ill patients was feasible in wide-ranging clinical settings including the ER and ICU. Together these findings suggest that dense-array EEG provides an accessible measure of brain function that is superior to traditional single-lead metrics, and is complementary to injury measures, for understanding behavioral effects of acute brain injury such as stroke.

Previous studies of patients with acute stroke have found that EEG changes correlate with behavioral status (Finnigan et al. 2007; Sheorajpanday et al. 2009) and, compared with neuroimaging alone, provide an improved understanding of clinical course (Finnigan and van Putten 2013). The present study builds upon these efforts, addressing issues that have limited broad adoption of EEG in the acute stroke setting. First, use of a single saline net, rather than the traditional application of 20 separate electrodes with paste, shortens the time to begin acquiring EEG signals (Tucker 1993). Second, use of dense-array (256 electrodes) EEG increases spatial resolution compared with 10-20 lead montages (Luu et al. 2001; Petrov et al. 2014). Third, use of PLS analyses maximizes statistical power by maintaining dimensionality and spatial resolution of the data (Wu et al. 2014, 2015). As such, several PLS models were very strongly related to acute behavioral deficits (Table 2); for example, the PLS model of delta power was robust ($R^2 = 0.72$ in the leave-one-out model validation). In contrast, across the 10 traditional quantitative EEG measures examined, none survived leave-one-out and predict model validation.

The ability of EEG to capture acute stroke impairment was significantly improved when a measure of neural injury was added to the EEG PLS model. This is consistent with prior studies that found that a multimodal approach incorporating both neural function and neural injury explained poststroke behavior better than either measure alone (Burke Quinlan et al. 2015; Kerr et al. 2011). Thus in the present study adding a measure of neural injury (infarct volume) to the PLS model of beta power significantly increased the strength of the leave-one-out and predict validation model, from $R^2 = 0.73$ to $R^2 = 0.81$. These results indicate that both neural function and neural injury are related to impairment early after stroke and confirm that an approach combining the two is significantly better than either measure alone for understanding behavior.

The present approach also provides neurobiological insights into the functional anatomy of acute stroke impairment. EEG markers of acute stroke impairment increased with larger infarct volume. For example, delta power within contralesional frontoparietal areas related to acute impairment (Fig. 1, *A* and *C*) was significantly higher with increasing infarct volume (Table 4). These differences in the weighting of EEG map topography could potentially identify therapeutic targets or serve as biomarkers in a pathophysiologically specific manner. Prior studies have reached mixed results regarding the presence and significance of contralesional changes in relation to behavioral state early after stroke (Assenza et al. 2013; Juhasz et al. 1997; Macdonell et al. 1988; Tecchio et al. 2007), and some have suggested that EEG measures of contralesional dysfunction in acute stroke strictly reflect mass effect (Macdonell et al. 1988; Newey et al. 2013). Present analyses suggest the need for an alternative interpretation, as contralesional frontoparietal delta power was not a consequence of mass effect from the stroke onto the contralesional hemisphere (Fig. 2). Such EEG changes in behaviorally relevant contralesional brain areas early after stroke may therefore be a marker of diaschisis (Juhasz et al. 1997), downstream effects of reduced intracortical inhibition within the ipsilesional hemisphere (Liepert et al. 2000), altered interhemispheric inhibition (Butefisch et al. 2008), or changes in cortical excitability within the contralesional hemisphere (Di Lazzaro et al. 2010 2015).

There are a number of limitations with the present study. As with all scalp EEG studies, spatial localization is limited and provides an imperfect anatomical relationship between EEG electrodes and specific brain structures. However, this concern is mitigated in part by use of dense-array (256 electrodes) EEG (Luu et al. 2001; Petrov et al. 2014) and by the fact that for electrodes C3 and C4 a particularly strong association exists between underlying cortical brain function and the signals measured at the scalp (Homan et al. 1987). Over the 24 study enrollees, EEG studies were not performed at the identical time as behavioral assessments or brain imaging, because of practical limitations; longer time intervals could suggest an increased role for supervening factors. The specific hardware and software choices employed in the present study are not likely ideal solutions for widespread application of the present results, and so one potential future direction for additional studies is to capture the present results with methods that can be widely adopted.

Rapid, noninvasive methods for measuring brain function that are accessible across the various settings of acute stroke care could provide useful insights for understanding interpatient differences and thus for driving therapeutic decision-making. The present study presents a novel application of dense-array EEG combined with PLS analyses in an acute stroke population and was found to outperform traditional measures, such as infarct volume and quantitative EEG measures within specific leads, in terms of capturing behavioral deficits early after stroke. EEG findings related to impairment varied according to infarct volume. EEG captured significant information about acute stroke injury not available from structural brain imaging, the nature of which might be a candidate marker for stroke-induced transhemispheric diaschisis. EEG is safe and relatively inexpensive and can be performed rapidly in complex clinical settings. Dense-array EEG may have a role for measuring behaviorally relevant derangements in brain function early after stroke.

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DISCLOSURES

S. L. Small has performed editorial work for Elsevier Publishers. S. C. Cramer has served as a consultant for Dart Neuroscience, RAND Corporation, MicroTransponder, and Roche and is cofounder of personalRN.

AUTHOR CONTRIBUTIONS

J.W., E.B.Q., and S.C.C. performed experiments; J.W., R.S., E.B.Q., A.S., S.L.S., and S.C.C. analyzed data; J.W., R.S., E.B.Q., A.S., S.L.S., and S.C.C. interpreted results of experiments; J.W. and S.C.C. prepared figures; J.W., R.S., and S.C.C. drafted manuscript; J.W., R.S., E.B.Q., A.S., S.L.S., and S.C.C. edited and revised manuscript; J.W., R.S., E.B.Q., A.S., S.L.S., and S.C.C. approved final version of manuscript; R.S., E.B.Q., A.S., S.L.S., and S.C.C. conception and design of research.

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Figures and Tables

Table 1.

Correlation coefficients between traditional quantitative EEG measures and NIHSS score

Quantitative EEG Measure	Min R^2	Max R^2	No. of Significant Electrodes
Delta power	<0.0001	0.35	0
Delta coherence with ipsilesional SMC	<0.0001	0.37	0
Theta power	<0.0001	0.07	0
Theta coherence with ipsilesional SMC	<0.0001	0.41	0
Alpha power	<0.0001	0.17	0
Alpha coherence with ipsilesional SMC	<0.0001	0.38	0
Beta power	0.04	0.50	0
Beta coherence with ipsilesional SMC	<0.0001	0.32	0
High beta power	0.02	0.64	7*
High beta coherence with ipsilesional SMC	<0.0001	0.31	0

SMC, sensorimotor cortex. Significance was defined as $P < 0.05$ after correction for multiple comparisons. Results are provided for bivariate analyses. Note that no traditional quantitative EEG measure remained significant in the cross-validation model.

*For the 7 electrodes surviving Bonferroni correction, mean R^2 value was 0.61 and mean P value <0.0001; note that these electrodes did not survive in the cross-validation model.

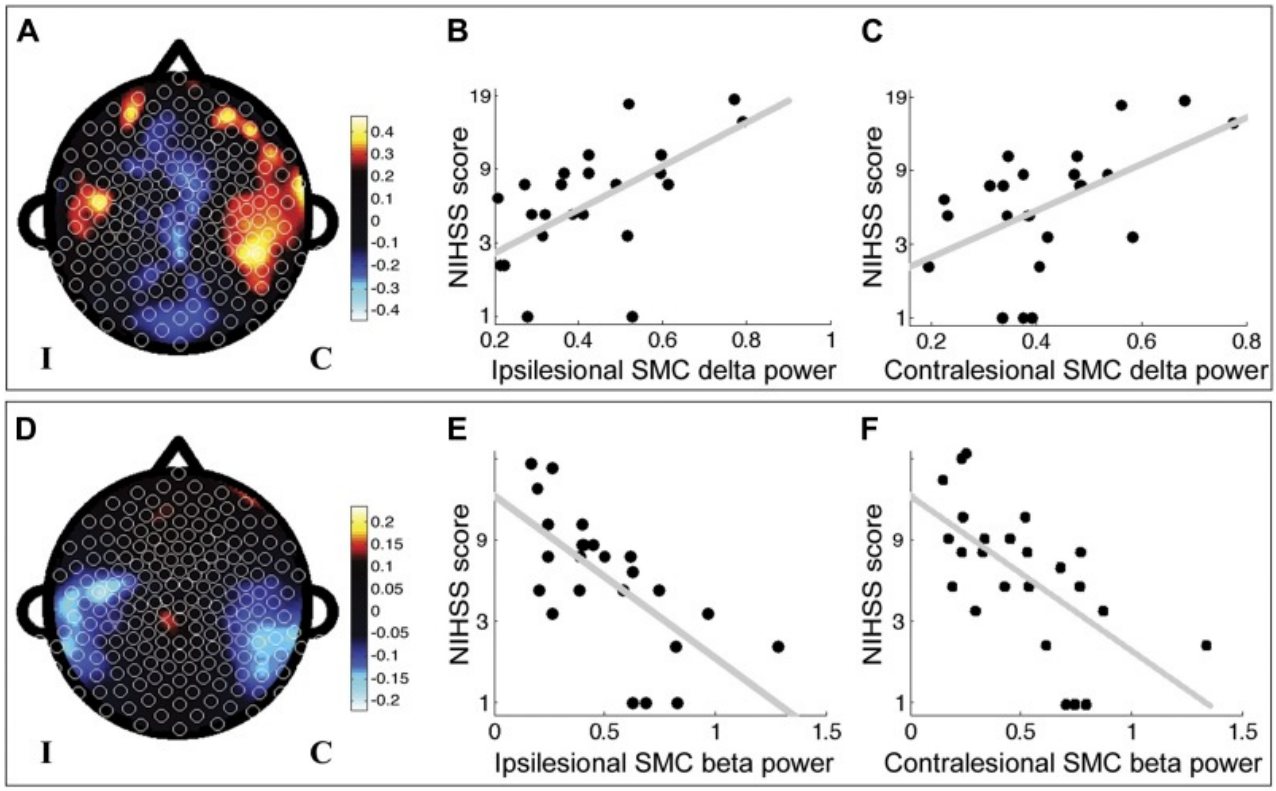
Table 2.

Fitted and validated R^2 for EEG whole brain PLS models correlating with acute NIHSS score

EEG Metric	Whole Brain Fitted Model R^2	Whole Brain Validated Model R^2
Delta power	0.85	0.72
Delta coherence with ipsilesional SMC	0.84	0.47
Theta power	0.88	0.36
Theta coherence with ipsilesional SMC	0.88	0.48
Alpha power	0.84	0.69
Alpha coherence with ipsilesional SMC	0.81	NS
Beta power	0.90	0.73
Beta coherence with ipsilesional SMC	0.87	NS
High beta power	0.81	0.70
High beta coherence with ipsilesional SMC	0.90	0.35

NS indicates a PLS model that did not survive in the cross-validation model.

Fig. 1.



EEG measurement of brain function in the delta frequency range was excellent at capturing admission NIHSS score. *A*: topographic map of correlation coefficients in the whole brain PLS model (fitted $R^2 = 0.85$, validated $R^2 = 0.72$), with higher delta (1–3 Hz) power correlating with higher admission NIHSS score (more severe behavioral deficits). *B*: the leads overlying ipsilesional SMC contributed to these whole brain findings, with higher delta power within these leads correlating with higher NIHSS score ($R^2 = 0.35$, $P = 0.002$ in this cluster of leads). *C*: the leads overlying a contralesional frontoparietal area also contributed to these whole brain findings, with higher delta power within these leads correlating with higher NIHSS score ($R^2 = 0.28$, $P = 0.008$ in this cluster of leads). *D*: topographic map of correlation coefficients in the whole

brain PLS model (fitted $R^2 = 0.90$, validated $R^2 = 0.73$), with lower beta (13–19 Hz) power correlating with higher admission NIHSS score (more severe behavioral deficits). *E*: the leads overlying ipsilesional SMC contributed to these whole brain findings, with lower beta power within these leads correlating with higher NIHSS score ($R^2 = 0.45$, $P = 0.0004$ in this cluster of leads). *F*: the leads overlying a contralesional parietal area also contributed to these whole brain findings, with lower beta power within these leads correlating with higher NIHSS score ($R^2 = 0.41$, $P = 0.0008$ in this cluster of leads). I, ipsilesional; C, contralesional; SMC, sensorimotor cortex.

Table 3.

Forward stepwise multivariate linear regression results

Variable	Estimate	Standard Error	*P*
Intercept	2.32	0.28	<0.0001
Infarct volume	0.12	0.06	0.06
Ipsilesional SMC beta power	−1.83	0.45	0.0005

Note that infarct volume and ipsilesional SMC beta power were not significantly correlated ($P > 0.4$).

Table 4.

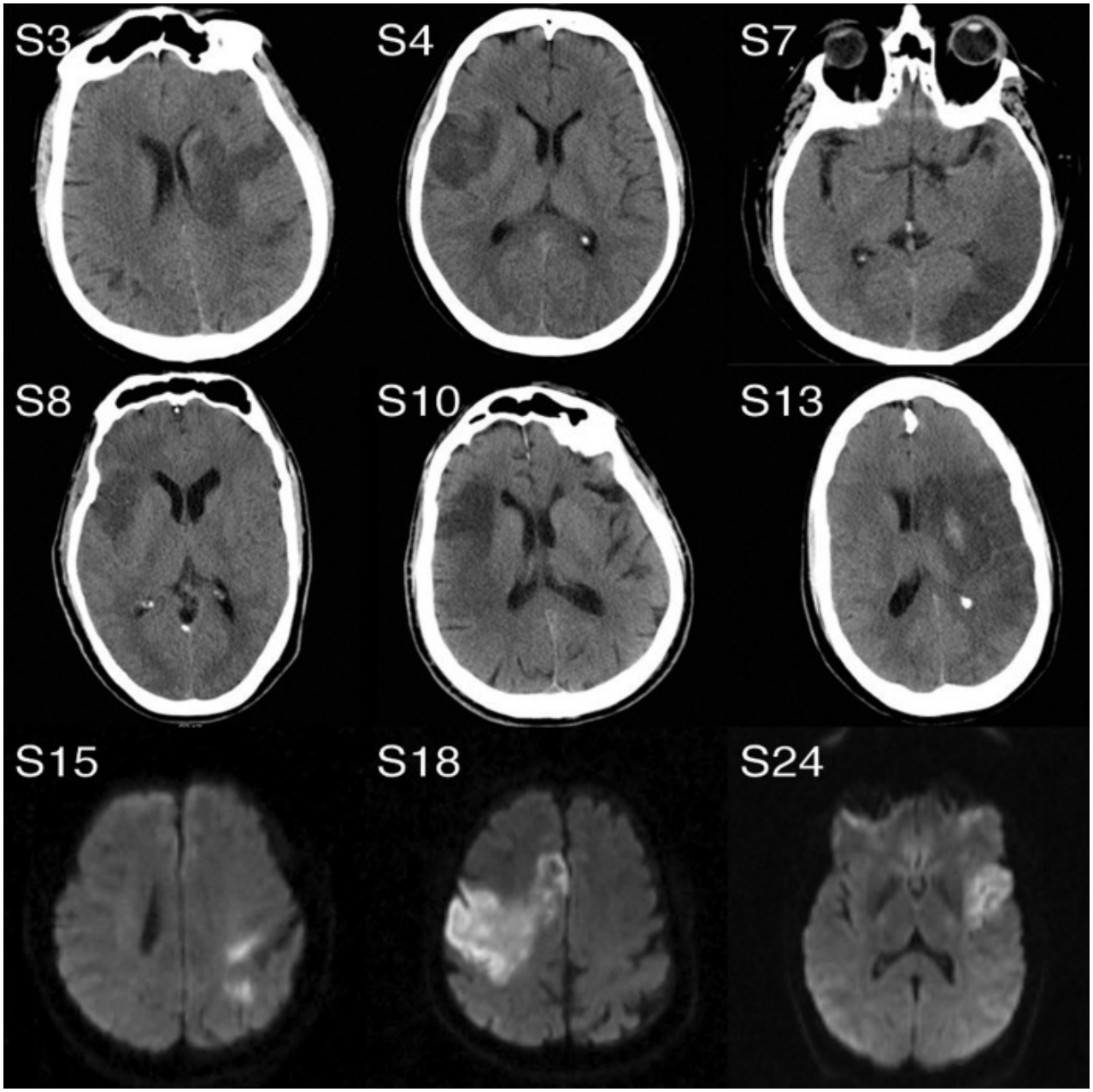
EEG markers of acute stroke impairment vary according to extent of neural injury

	Ipsilesional Delta Power (electrodes overlying SMC)	Contralesional Delta Power (electrodes overlying frontoparietal areas)	Ipsilesional Beta Power (electrodes overlying SMC)
Infarct volume	$R^2 = 0.51^{\dagger}$	$R^2 = 0.34^{*}$	$R^2 = 0.18$

Values indicate correlation between infarct volume and EEG measures in key regions.

$^{*}P < 0.05$,
$^{\dagger}P \leq 0.001$.

Fig. 2.



Representative images from the diffusion-weighted imaging MRI or CT taken at the closest time to EEG for the 9 subjects with medium or large infarcts. For the 9 subjects with infarct volume ≥ 4 cc, no important mass effect from the infarct onto the contralesional hemisphere is apparent, with the exception of *subject S13*.