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Predicting functional outcomes after stroke: an observational study of acute single-channel EEG

Abstract

2019, 2019 Taylor & Francis Group, LLC. Background: Early and objective prediction of functional outcome after stroke is an important issue in rehabilitation. Electroencephalography (EEG) has long been utilized to describe and monitor brain function following neuro-trauma, and technological advances have improved usability in the acute setting. However, skepticism persists whether EEG can provide the same prognostic value as neurological examination. Objective: The current cohort study examined the relationship between acute single-channel EEG and functional outcomes after stroke. Methods: Resting-state EEG recorded at a single left pre-frontal EEG channel (FP1) was obtained from 16 adults within 72 h of first stroke. At 30 and 90 days, measures of disability (modified Rankin Scale; mRS) and involvement in daily activities (modified Barthel Index; mBI) were obtained. Acute EEG measures were correlated with functional outcomes and compared to an early neurological examination of stroke severity using the National Institute of Health Stroke Scale (NIHSS). Classification of good outcomes (mRS ≤ 1 or mBI ≥ 95) was also examined using Receiver Operator Curve analyses. Results: One-third to one-half of participants experienced incomplete post-stroke recovery, depending on the time point and measure. Functional outcomes correlated with acute theta values (r_s 0.45-0.60), with the strength of associations equivalent to previously reported values obtained from conventional multi-channel systems. Acute theta values ≥ 0.25 were associated with good outcomes, with positive (67-83%) and negative predictive values (70-90%) comparable to those obtained using the NIHSS. Conclusions: Acute, single-channel EEG can provide unique, non-overlapping clinical information, which may facilitate objective prediction of functional outcome after stroke.

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Predicting functional outcomes after stroke: An observational study of acute single-channel EEG

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ABSTRACT

Background: Early and objective prediction of functional outcome after stroke is an important issue in rehabilitation. Electroencephalography (EEG) has long been utilized to describe and monitor brain function following neuro-trauma, and technological advances have improved usability in the acute setting. However, skepticism persists whether EEG can provide the same prognostic value as neurological examination.

Objective: The current cohort study examined the relationship between acute single-channel EEG and functional outcomes after stroke.

Methods: Resting-state EEG recorded at a single left pre-frontal EEG channel (FP1) was obtained from 16 adults within 72 hours of first stroke. At 30- and 90-days, measures of disability (modified Rankin Scale; mRS) and involvement in daily activities (modified Barthel Index; mBI) were obtained. Acute EEG measures were correlated with functional outcomes and compared to an early neurological examination of stroke severity using the National Institute of Health Stroke Scale (NIHSS). Classification of *good* outcomes ($mRS \leq 1$ or $mBI \geq 95$) were also examined using Receiver Operator Curve analyses.

Results: One-third to one-half of participants experienced incomplete post-stroke recovery, depending on the time point and measure. Functional outcomes correlated with acute theta values (r_s 0.45-0.60), with the strength of associations equivalent to previously reported values obtained from conventional multi-channel systems. Acute theta values ≥ 0.25 were associated with *good* outcomes, with positive (67-83%) and negative predictive values (70-90%) comparable to those obtained using the NIHSS.

Conclusions: Acute, single-channel EEG can provide unique, non-overlapping clinical information, which may facilitate objective prediction of functional outcome after stroke.

Key words: activities of daily living; cerebrovascular disease; disability; outcomes; prognosis; stroke; quantitative electroencephalogram

1 INTRODUCTION

2 Stroke is associated with immediate brain changes resulting from the suppression of
3 oxygen and glucose supply, including a biochemical cascade that can lead to cell death and
4 cerebral infarction.¹⁻³ Electroencephalography (EEG) is sensitive to the effects of these acute
5 changes in cerebral blood flow^{4,5} and neural metabolism.^{6,7} Such changes can be identified
6 through the disruption or deterioration of normal electrical activity within the four classical
7 frequency bands: delta, theta, alpha, and beta. Delta and theta are primarily associated with a
8 low state of arousal, and a prominence of these slow frequency waves is reported in
9 individuals with neurological disease or injury.⁸ Faster frequency alpha waves are associated
10 with a state of relaxation and readiness, while beta waves mainly occur when an individual is
11 actively engaged in mental effort.⁸ In particular, EEG obtained in the acute stage after stroke
12 (i.e. <72 hours) is often associated with the rapid appearance of slow delta frequency waves
13 and attenuation of faster alpha frequency activity.⁹⁻¹³

14 Acute post-stroke EEG has demonstrated prognostic value, strongly correlating with
15 30-^{9,10} and 90-day¹²⁻¹⁶ mortality and morbidity. EEG measurements derived from frontal
16 electrodes may be particularly sensitive predictors of clinical outcome,¹⁴ suggesting an
17 alternative to conventional multi-electrode arrays, with lengthy set-up times that are not well
18 tolerated by acute neurological patients.^{17,18} Correspondingly, a single-channel, prefrontal
19 EEG system, offering rapid fitting and calibration procedures, is capable of detecting
20 associations between acute brain states and later cognitive performance,¹⁹ and in
21 discriminating various forms of ischemia.²⁰ However, the utility of single-channel EEG in
22 predicting post-stroke functional outcomes remains unclear.

23 Early and accurate prediction of functional outcomes is important to support patients
24 and their families, and guide rehabilitation planning.²¹ The aim of the current study was to
25 examine the prognostic value of acute, single-channel EEG with respect to 30- and 90-day

1 functional outcome. It was hypothesized that a single prefrontal channel of EEG data
2 collected within 72-hours of a first stroke would correlate with standardized scales of
3 disability (modified Rankin Scale; mRS) and daily living (modified Barthel Index; mBI),
4 commonly used to assess stroke outcomes.^{22,23} The predictive strength of acute EEG was
5 expected to be comparable to that of a gold-standard stroke severity prognosis tool, the
6 National Institute of Health Stroke Scale (NIHSS).²⁴

7

8 **MATERIALS & METHODS**

9 **Participants**

10 From July 2014 to December 2015, 16 consecutive patients admitted to the acute
11 stroke ward of a tertiary hospital in Sydney, Australia were recruited for participation.
12 Patients admitted within 72-hours of a first-ever stroke were eligible for participation. Time
13 of stroke onset was defined as the last time the participant was seen without stroke symptoms,
14 as indicated in the medical records. Exclusion criteria included a previous history of
15 neurological or psychiatric disorder, non-English speaking, or <18 years of age.

16

17 **Outcome measures**

18 Baseline stroke severity was quantified with the NIHSS,²⁴ an 11-item scale assessing
19 level of consciousness, visual, motor, sensory, and language function. Higher scores (max =
20 42) indicate more severe symptoms. The mRS and mBI were collected to monitor post-
21 stroke functional outcomes. The mRS²⁵ measures global disability on a scale of 0 (no
22 symptoms) to 6 (deceased), with higher scores reflecting poorer outcome. The mBI²⁶
23 assesses 10 domains of daily living (bowel control, bladder control, grooming, toilet use,
24 feeding, transfers, walking, dressing, climbing stairs, and bathing), with lower scores (range
25 0-100) indicative of greater dependence.

1 EEG data acquisition and analysis

2 Continuous EEG was obtained with the MindSet device (NeuroSky, San Jose,
3 California), a single-channel, wireless headset with demonstrated concurrent validity¹⁸ and
4 re-test reliability.²⁷ The MindSet device (Figure 1) consists of a ThinkGear microchip and
5 firmware, 10 mm dry stainless steel active electrode, and material reference and ground
6 electrodes contained within a set of headphones. The reference and ground electrodes are
7 housed within the left ear pad, while the EEG electrode is embedded in a flexible arm
8 extending from the left headband, positioned at the International 10–20 system site FP1.
9 Electrical potentials at the active and reference electrodes are subtracted through common
10 mode rejection to derive a single EEG channel signal which is amplified 8000 times.
11 Sampling and amplification of the raw 128 Hz data are carried out within the embedded
12 microchip and transmitted wirelessly by Bluetooth© to a computer for recording and
13 subsequent off-line quantitative analysis.

14 Using SCAN Edit version 3 software (Neuroscan™, USA), the raw EEG waveform
15 data was band-pass filtered (0.5-30 Hz), and manually inspected to identify any movement or
16 muscle artifact. Identified sections of artifact were excluded from further processing.
17 Remaining epochs containing amplitudes in excess of $\pm 100 \mu\text{V}$ were removed using an
18 artifact rejection filter included in the SCAN software. Artifact-free 4-sec EEG epochs (1/4
19 Hz resolution) were submitted to a Fast Fourier Transform with 10% Hamming window to
20 extract the absolute power in the delta (1.5–3.5 Hz), theta (3.5–7.5 Hz), alpha (7.5–12.5 Hz),
21 and beta (12.5–25 Hz) frequency bands. Relative power was calculated by summing absolute
22 power across the four bands to compute total power, and then dividing the absolute power for
23 each individual band by the total power, expressed as a percentage. EEG ratios previously
24 reported in the acute stroke literature, including delta/alpha ratio (DAR),¹³ delta/theta ratio

1 (DTR),¹⁹ and delta+theta/alpha+beta ratio (DTABR),²⁸ were also computed by summing and
2 dividing the relative power of the relevant frequency bands.

3

4 **Procedure**

5 The NIHSS and continuous EEG recordings were obtained at hospital bedside. After
6 minimizing signal impedance from the electrode, participants were asked to close their eyes
7 and relax for the 3-min EEG recording session. At 30- and 90-days post-ictus the mRS and
8 mBI were collected, with order counterbalanced. The research team were blind to acute EEG
9 results until analysis of the follow-up outcomes of all participants commenced. This research
10 was approved by University and Hospital Human Research Ethics Committees, and each
11 participant (or their carer/substitute decision maker) provided written informed consent. The
12 final manuscript was prepared in accordance with the 22-items of the Strengthening the
13 Reporting of Observational Studies in Epidemiology (STROBE) guidelines.²⁹

14

15 **Statistical analysis**

16 Spearman Rank Order Correlations (r_s) were calculated to test the relationship
17 between EEG measures and NIHSS data and the ordinal mRS, and mBI outcomes at 30- and
18 90-days. A bootstrapping method (sampled 1000 times) was used to estimate population
19 parameters and calculate 95% confidence intervals, bias corrected and accelerated (BCa).
20 One-tailed p values were selected to test directional *a priori* hypotheses. All analyses were
21 completed with IBM SPSS Statistics for Windows version 23 (IBM Corp., Armonk, N.Y).
22 Receiver Operator Curve (ROC) analyses were conducted using GraphPad Prism version 7
23 for Windows (GraphPad Software Inc, La Jolla, CA) to determine optimal EEG and NIHSS
24 criterion cut-offs for classifying post-stroke outcomes. *Good* outcomes were defined as an
25 mRS ≤ 1 or mBI ≥ 95 .^{22,23,30}

1 RESULTS

2 Demographic and descriptive information

3 Complete baseline and follow-up data was collected from 16 right-handed participants
4 (9 males and 7 females), with an average age of 66 ± 17 years (range 33-93 years). The
5 majority exhibited *minor to moderate* neurological impairment (81%), as classified by the
6 NIHSS on admission (range 0-10), and had sustained an ischemic stroke (75%). EEG was
7 obtained at bedside within the first 20-72 hours (mean 47 ± 21 hours). Participants were
8 subsequently followed up on average 37 ± 8 days and 96 ± 7 days post-ictus. See Table 1 for
9 additional demographic and baseline clinical characteristics.

10

11 Disability and functional outcomes

12 At 30-days, 44% of participants had a *poor* disability outcome (mRS >1) and 38%
13 had a *poor* daily functioning outcome (mBI <95). By 90-days post-stroke, the proportion
14 experiencing a *poor* disability outcome had increased to 50%. In contrast, the proportion
15 experiencing a *poor* daily functioning outcome had decreased to 31%. Baseline NIHSS
16 significantly correlated with the mRS and mBI at 30- and 90-days (Table 2), with lower
17 NIHSS scores (less neurological impairment) associated with less disability (lower mRS
18 scores) and superior daily functioning (higher mBI scores). Other demographic and clinical
19 characteristics (i.e. age, gender, years of education, stroke type, stroke hemisphere) were not
20 significantly associated ($p > 0.05$) with outcomes.

21

22 EEG prediction of functional outcomes

23 Relative power in the theta band significantly correlated with mRS and mBI outcomes
24 at 30- and 90-days (r_s range 0.45-0.60), with lower theta values associated with greater
25 disability (higher mRS scores) and dependence in daily activities (lower mBI scores).

1 Relative power in the delta, alpha, and beta bands, and the EEG ratios DAR, DTR, and
2 DTABR, were not correlated ($p > 0.05$) with either outcome measure at either time point
3 (Figure 2).

4 Baseline theta and NIHSS were not correlated [$r_s = -0.42$ (95% BCa CI -0.83 - 0.12),
5 $p = 0.11$]. For both the NIHSS and relative theta power, the strength of association with
6 outcomes diminished over the 30- to 90-day interval (Table 2). ROC analysis consistently
7 identified a theta band criterion cut-off of 0.25 as optimal for classifying post-stroke
8 outcomes (Table 3). Participants with theta values ≥ 0.25 were more likely to have an mRS
9 score ≤ 1 (*good* outcome) at 30-days ($p = 0.04$), and an mBI score ≥ 95 (*good* outcome) at 30-
10 ($p < 0.01$) and 90-days ($p = 0.05$). The cut-off failed to reach significance ($p = 0.09$) for 90-
11 day mRS scores. The sensitivity and specificity of the relative power theta criterion cut-off
12 was comparable to results obtained using an NIHSS cut-off score of ≤ 6 (Table 3).

13

14 **DISCUSSION**

15 EEG has long been available to monitor the effects of acute ischemic^{1,31} and
16 hemorrhagic^{32,33} stroke. However, broad adoption of EEG into acute stroke clinical care
17 remains limited,³⁴ and skepticism remains about whether EEG provides the same prognostic
18 value as neurological examination or imaging studies.^{7,35} Recent technological advances in
19 wireless EEG have improved usability and streamlined data analysis. The current study
20 therefore examined the capability of acute, single-channel EEG biomarkers to predict the
21 effects of stroke on sub-acute functioning, compared with conventional neurological
22 assessment using the NIHSS. Results showed that for a sample of patients suffering a first
23 stroke, acute EEG provided a unique predictor of outcomes, uncorrelated with the NIHSS.
24 Insights regarding the performance of the NIHSS and EEG as possible assessment tools for
25 predicting functional outcomes after stroke are discussed, in turn, below.

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Acute NIHSS Prognosis

In the current study, NIHSS scores ≤ 6 were associated with *good* mRS (≤ 1) and mBI (≥ 95) outcomes at follow-up (positive predictive power 67-100%; negative predictive power 80-90%). Higher NIHSS scores were associated with poorer functional outcomes. There is limited consensus regarding the optimal NIHSS cut-off: some reports suggest that scores up to 8-10 are associated with a more favorable outcome,³⁶⁻³⁸ while others support thresholds as low as 2-4 after stroke.³⁹⁻⁴¹ The current threshold fits within these upper and lower bounds..

Several weaknesses of the NIHSS are evident when examining its value as a prognostic measure. First, it is not always possible to reliably assess neurological status with a behavioral examination because specific deficits are not always noticeable upon observation,⁴² particularly in acute patients with minimal or fluctuating levels of consciousness. Second, as NIHSS scores are derived from behavioral observation, they are susceptible to examiner background, training, and experience.^{43,44} Third, the NIHSS has been criticized for its complexity,⁴⁵ with items of poor inter-rater reliability (ataxia)⁴³ or questionable face validity (dysarthria).⁴⁶ Fourth, baseline NIHSS assessment may not be the optimal time point for predicting functional outcomes,^{36,47,48} given variability in clinical observations over the first 24 hours after a stroke.^{49,50} These weaknesses may explain the alarmingly low NIHSS completion rates (12-28%) in acute stroke settings.^{51,52} Overall, the assessment validity and prognostic value of performing a neurological examination in isolation has been challenged by the view that other assessment methods and measures be included,⁵³ like concurrent physiological observations such as EEG.⁵⁴

Acute EEG Prognosis

1 Capitalizing on advances in EEG hardware and software, the current study
2 demonstrated that a single pre-frontal channel of EEG can yield metrics that predict
3 functional outcomes to a level comparable to that obtained using the NIHSS. Stroke
4 survivors exhibiting acute attenuation of relative theta power subsequently demonstrated
5 greater disability and dependence at 30- and 90-days. Frontally distributed theta typically
6 features prominently at rest in healthy individuals,^{27,55,56} with higher resting theta power
7 identified as a biomarker of healthy aging,⁵⁷ and greater likelihood of a benign course after
8 acute stroke.⁵⁸ In contrast, acute post-stroke reductions in theta are associated with
9 unfavorable stroke outcomes, and may reflect brain changes occurring as a result of
10 hypoperfusion below an ischemic threshold.²⁰

11 The corollary was that stroke survivors who exhibited acute relative theta values
12 ≥ 0.25 tended to experience *good* 30- and 90-day functional outcomes, as measured by an
13 mRS ≤ 1 or an mBI score ≥ 95 (positive predictive value 67-83%, negative predictive value
14 70-90%). For the other participants who fell below this threshold, post-stroke recovery was
15 incomplete, with long-term follow-up studies suggesting that the observed restrictions in self-
16 care and physical function were likely to be persistent, and accompanied by diminished
17 participation and lower health-related quality of life.^{59,60}

18 The mRS and mBI are the two most common instruments used in stroke outcome
19 studies,^{23,61,62} and the strength of these preliminary prognostic relationships to acute single-
20 channel EEG data is promising. Specifically, using commonly accepted cut-off values to
21 define *good* and *poor* outcomes,^{22,23,30} the predictive utility of acute theta values derived from
22 just a single pre-frontal EEG electrode were comparable to a gold standard prognostic tool.
23 Unlike the NIHSS, acquisition of EEG data is less likely to be susceptible to examiner bias
24 and experience.

1 Correlations between acute EEG data and sub-acute outcomes in the current study (r_s
2 0.45- 0.60) were also equivalent to those reported by recent studies^{14,15,19,28,63-65} using
3 conventional, multi-channel arrays (r_s 0.35-0.66; Table 4). It is unclear why earlier EEG
4 studies^{9,10,12} reported stronger associations with post-stroke functional outcomes (r_s 0.80-
5 0.91) than our study or contemporary multi-channel research. However, in an advancement
6 over both recent and older EEG research, the current study examined both disability and
7 participation outcomes. While measures of disability have traditionally been the primary
8 focus of practitioners, outcomes of participation in age-appropriate activities and valued roles
9 are typically of most importance to patients and their families,⁶⁶ and should also be
10 measured.^{67,68}

11 Whereas earlier EEG studies have typically reported significant correlations (r 0.33-
12 0.90) between early EEG and NIHSS values,^{10,28,34,64,69} our study found no relationship
13 between baseline NIHSS and relative theta power, suggesting EEG can provide non-
14 overlapping clinical information regarding brain function not captured by a neurological
15 exam.⁶³ The localized recording paradigm in the current study may have contributed to this
16 null finding, but this hypothesis requires deliberate testing.

17

18 **Limitations**

19 This study is based on a moderate sample of 16 participants. This sample size was
20 comparable with earlier studies in the area,^{9,10,14,15,19,63,70} and produced *medium to large*
21 correlations (r values ranging from 0.42-0.87),⁷¹ which suggests that our study was
22 adequately powered. However, replication in a larger sample is encouraged to allow an
23 analysis of potential moderators of *good* and *poor* functional outcomes (e.g. age, gender,
24 medical comorbidities, time to treatment, premorbid history),⁷² and to enhance the
25 generalizability of results. In particular, the current cohort was predominantly of *mild* to

1 *moderate* severity, due to ischemic stroke. While these characteristics are representative of
2 the natural incidence of stroke,^{73,74} it is uncertain how current findings apply to hemorrhagic
3 stroke and patients with severe neurological deficits at baseline. Notwithstanding this, even
4 individuals with “minor strokes” (e.g. NIHSS <5) experience significant problems that
5 impact their relationships with others, return to valued roles, and reintegration into
6 society,^{39,75} as such, it is important to identify tools sensitive to their outcomes as well. As
7 well, the merging of clinical and neurophysiological data with neuroimaging information may
8 enhance outcome prediction,⁷⁶ however this was not examined in the current study.

9 In regard to outcome measurement, the domain validity of both the mBI and mRS
10 have limitations. The mBI only examines functional independence in self-care.⁷⁷ Similarly,
11 while the mRS is one of the most widely used instruments in stroke research,⁶¹ outcomes
12 based on this instrument should be discussed in reference to physical disability and need for
13 physical assistance.⁷⁸ The current battery could be supplemented by other instruments to
14 provide a holistic examination of participation in instrumental activities of daily living and
15 quality of life.⁷⁹

16

17 **Conclusions**

18 Biomarkers of brain function that are derived from a single pre-frontal channel of
19 EEG data are associated with post-stroke functional recovery. Indeed, the explanatory power
20 of the EEG metric is largely independent to that provided by a neurological exam. This acute
21 EEG data compares well with prognosis based on initial stroke severity but has the advantage
22 of being unaffected by subjective interpretation of clinical observations using NIHSS ratings.
23 Due to the multifactorial nature of functional recovery, a single parameter is unlikely to be
24 sufficient to define and predict individual outcomes. Overall, these preliminary results re-
25 affirm EEG can uniquely inform understanding of the clinical course following stroke,⁸⁰ and

1 could be used in conjunction with a neurological exam. Larger scale studies are encouraged
2 to further examine the potential for single-channel EEG data to augment early prediction of
3 post-stroke outcomes, and to isolate moderators.

4

5

6

7 **Abbreviations:** BCa: bias corrected and accelerated; DAR: delta/alpha ratio; DTABR:

8 delta+theta/alpha+beta ratio DTR: delta/theta ratio; EEG: electroencephalography; mBI:

9 modified Barthel Index; mRS: modified Rankin Scale; NIHSS: National Institute of Health

10 Stroke Scale; ROC: Receiver Operator Curve

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5**Table 1.** Demographic and neurological characteristics of participants

Age ^a	65.75 (16.98), 33-93
Gender ^b	
Male	9 (56)
Female	7 (44)
Education Level ^b	
≤ 12 years	10 (62)
> 12 years	6 (38)
Baseline NIHSS score ^a	6.56 (6.45), 0-18
Minor (< 5) ^b	7 (44)
Moderate (5-15) ^b	6 (38)
Moderately severe (16-20) ^b	3 (18)
Ischemic Stroke ^b	12 (75)
Hemorrhagic Stroke ^b	4 (25)
Left-sided lesion ^b	7 (44)
Right-sided lesion ^b	9 (56)
Time to EEG recording (hours) ^a	46.63 (20.63), 20-72
30 day follow-up (days) ^a	37.06 (8.23), 28-45
90 day follow-up (days) ^a	95.56 (7.15), 88-111

^aMean (SD) range; ^bNo (%). Note: EEG: electroencephalography; NIHSS: National Institute of Health Stroke Scale.

Table 2. Spearman's *rho* correlations of prognostic EEG and functional outcome variables (mBI 0-100; mRS 0-6)

	NIHSS	RP Theta	30-day mRS	30-day mBI	90-day mRS	90-day mBI
NIHSS	1.00	-0.42 [-0.80, 0.07]	0.87** [0.73, 0.94]	-0.66** [-0.87, -0.32]	0.74** [0.39, 0.93]	-0.59** [-0.86, -0.06]
RP Theta		1.00	-0.54* [-0.88, -0.08]	0.60** [0.07, 0.86]	-0.53* [-0.86, 0.01]	0.45* [-0.03, 0.79]
30-day mRS			1.00	-0.78** [-0.93, -0.49]	0.86** [0.67, 0.96]	-0.79** [-0.95, -0.39]
30-day mBI				1.00	-0.69** [-0.92, -0.28]	0.82** [0.56, 1.00]
90-day mRS					1.00	-0.83** [-0.94, -0.45]
90-day mBI						1.00

Note: * $p < 0.05$ (one-tailed). ** $p < 0.01$ (one-tailed). Bootstrapped 95% confidence intervals reported in brackets. EEG: electroencephalography; mBI: modified Barthel Index; mRS: modified Rankin Scale; NIHSS: National Institute of Health Stroke Scale.

Table 3. Optimal Receiver Operator Curve criterion cut-offs for classifying good post-stroke functional outcomes (mRS ≤ 1 ; mBI ≥ 95)

Criterion and EEG Threshold		AUC	<i>p</i> value	Sensitivity	Specificity	PPV	NPV
30-day mRS	≥ 0.25	0.81	0.04	71.4%	88.9%	83.3%	80.0%
30-day mBI	≥ 0.25	0.90	<0.01	83.3%	90.0%	83.3%	90.0%
90-day mRS	≥ 0.25	0.75	0.09	62.5%	87.5%	83.3%	70.0%
90-day mBI	≥ 0.25	0.82	0.05	80.0%	81.8%	66.7%	90.0%
Criterion and NIHSS Threshold		AUC	<i>p</i> value	Sensitivity	Specificity	PPV	NPV
30-day mRS	≤ 6	0.98	<0.01	85.7%	100%	100%	90.0%
30-day mBI	≤ 6	0.90	<0.01	83.3%	90.0%	83.3%	90.0%
90-day mRS	≤ 6	0.84	0.02	71.4%	88.9%	83.3%	80.0%
90-day mBI	≤ 6	0.87	0.02	80.0%	81.8%	66.7%	90.0%

Note: AUC: area under curve; EEG: electroencephalography; mBI: modified Barthel Index; mRS: modified Rankin Scale; NIHSS: National Institute of Health Stroke Scale; NPV: negative predictive power; PPV: positive predictive power.

Table 4. Summary of previous studies (in chronological order) examining the relationship between acute EEG data and post-stroke outcomes. Where available, the strength of outcome prediction using an alternate “gold standard” tool is provided, for comparison. All reported analyses were statistically significant ($p < 0.05$).

Author, Year (Location)	Study population, time to EEG	Primary EEG Metric	Primary Outcome Measure	Statistical Analysis	Comparator Analysis
Sainio ⁷⁰ 1983 (Finland)	15 ischemic stroke, within 48 hours	resting state global delta	30 month return to work	Fisher’s exact test $p < 0.01$	NR
Cillessen ⁸¹ 1994 (Netherlands)	55 ischemic stroke, within 1-10 days	resting state alpha asymmetry	12-month mRS	PPV 0.85-0.86	baseline mRS, PPV 0.52-1.00
Classen ¹¹ 2004 (USA)	34 hemorrhagic stroke, within 2-6 days	serial resting state global DAR	vasospasm and cerebral ischemia over first 2-weeks	PPV 0.60-0.67	NR
Finnigan ⁹ 2004 (Australia)	11 ischemic stroke, within 16 hours	resting state global delta	30-day NIHSS	$r_s = 0.80$	baseline MRI, $r_s =$ 0.79
Cuspineda ¹² 2007 (Cuba)	28 ischemic stroke, within 72 hours	resting state global delta	90-day mRS	$r = 0.89$	NR
Finnigan ¹⁰ 2007 (Australia)	13 ischemic stroke, within 48 hours	resting state global DAR	30-day NIHSS	$r_s = 0.91$	baseline NIHSS, $r_s =$ 0.92
Finnigan ⁸² 2008 (Australia)	2 ischemic stroke, within 4-8 hours	contralateral resting state global delta	rapid mortality	NR	NR
Sheorajpanday ²⁸ 2011 (Belgium)	110 ischemic stroke, within 1 week	resting state global DTABR	6-month mRS	$r_s = 0.47$	baseline NIHSS, $r_s =$ 0.59
Xin ⁶³ 2012 (China)	22 stroke, within 48 hours	resting state brain symmetry index	28-day mRS	$r = 0.44$	baseline NIHSS, $r =$ 0.74
Schleiger ¹⁴ 2014 (Australia)	20 ischemic stroke, within 4 days	resting state frontal DAR	90-day cognitive items from FIM/FAM	$r_s = - 0.66$	NR

Zappasodi ⁶⁴ 2014 (Italy)	36 ischemic stroke, within 4-10 days	resting state fractal dimension asymmetry	6-month NIHSS	$r = 0.35$	NR
Aminov ¹⁹ 2017 (Australia)	19 stroke, within 72 hours	resting state frontal DTR	90-day MoCA	$r = -0.57$	baseline NIHSS, r = -0.74
Schleiger ¹⁵ 2017 (Australia)	23 ischemic stroke, within 2-10 days	resting state posterior alpha	90-day MoCA	$r = 0.66$	NR
Bentes ⁶⁵ 2018 (Portugal)	150 ischemic stroke, within 72 hours	resting state global alpha	12-month mRS	$r = 0.54$	baseline NIHSS, r = 0.63

Note: DAR: delta/alpha ratio; DTABR: delta-theta/alpha-beta ratio; DTR: delta/theta ratio; EEG: electroencephalography; FIM/FAM: Functional Independence Measure/Functional Assessment Measure; NIHSS: National Institutes of Health Stroke Scale; NR: not reported; PPV: positive predictive value; MoCA: Montreal Cognitive Assessment; MRI: magnetic resonance imaging; mRS: modified Rankin Scale; TBI: traumatic brain injury.

Figure Legends

Figure 1. The NeuroSky MindSet consists of a single electrode embedded in a flexible arm extending from the left side of a pair of headphones (Image available via Creative Commons License BY-NC-SA 4.0).



Figure 2. Absolute values of the strength of association (Spearman’s *rho*) between EEG parameters and function outcome measures. *Only correlations with relative theta power were statistically significant ($p < 0.05$). Note: mBI: modified Barthel Index; mRS: modified Rankin Scale.

