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EEG correlates of P300-based brain–computer interface (BCI) performance in people with amyotrophic lateral sclerosis

Joseph N Mak[1,6], Dennis J McFarland[2], Theresa M Vaughan[2], Lynn M McCane[2], Phillippa Z Tsui[3,6], Debra J Zeitlin[4], Eric W Sellers[5] and Jonathan R Wolpaw[2]

[1] NeuroSky (Hong Kong) Co. Ltd, Hong Kong, People's Republic of China
[2] Laboratory of Neural Injury and Repair, Wadsworth Center, New York State Department of Health, Albany, NY, USA
[3] Yan Chai Hospital, Hospital Authority, Hong Kong, People's Republic of China
[4] Center for Rehabilitation Technology, Helen Hayes Hospital, West Haverstraw, NY, USA
[5] Brain–Computer Interface Laboratory, East Tennessee State University, Johnson City, TN, USA

E-mail: josephnfmak@gmail.com

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Abstract
The purpose of this study was to identify electroencephalography (EEG) features that correlate with P300-based brain–computer interface (P300 BCI) performance in people with amyotrophic lateral sclerosis (ALS). Twenty people with ALS used a P300 BCI spelling application in copy-spelling mode. Three types of EEG features were found to be good predictors of P300 BCI performance: (1) the root-mean-square amplitude and (2) the negative peak amplitude of the event-related potential to target stimuli (target ERP) at Fz, Cz, P3, Pz, and P4; and (3) EEG theta frequency (4.5–8 Hz) power at Fz, Cz, P3, Pz, P4, PO7, PO8 and Oz. A statistical prediction model that used a subset of these features accounted for >60% of the variance in copy-spelling performance ($p < 0.001$, mean $R^2 = 0.6175$). The correlations reflected between-subject, rather than within-subject, effects. The results enhance understanding of performance differences among P300 BCI users. The predictors found in this study might help in: (1) identifying suitable candidates for long-term P300 BCI operation; (2) assessing performance online. Further work on within-subject effects needs to be done to establish whether P300 BCI user performance could be improved by optimizing one or more of these EEG features.

(Some figures may appear in colour only in the online journal)

Introduction

A brain–computer interface (BCI) allows users to communicate with or control the external world by thought alone. It provides a new output pathway for the brain that is different from the conventional neuromuscular pathways of peripheral nerves and muscles (Mak and Wolpaw 2009, Wolpaw *et al* 2002). Brain signals reflecting the intent of the user are detected, and then analyzed and translated into device commands that indicate the desire of the user. BCI technology holds promise to restore the communication and control ability of people who are suffering from the most severe motor disabilities (Daly and Wolpaw 2008, Mak and Wolpaw 2009). Potential users include people with amyotrophic lateral

[6] Formerly of Wadsworth Center.

sclerosis (ALS), spinal-cord injury, stroke, and other serious neuromuscular diseases or injuries. These people may be locked into their bodies, i.e. cognitively intact but with minimal or no useful muscle function.

Restoration of communication has been a main focus of BCI research to date (Birbaumer *et al* 1999, Krusienski and Wolpaw 2009, Kubler and Neumann 2005, Mak and Wolpaw 2009, Ramoser *et al* 1997). Several specific electroencephalography (EEG) features have been proposed as control signals for such BCI communication systems. The BCI user may learn to modulate EEG features in the time domain (Birbaumer *et al* 1999, 2000), or in the frequency domain (McFarland *et al* 2008, Wolpaw and McFarland 2004) to represent his or her intent. Alternately, the BCI system may use event-related potentials (ERPs) elicited by external stimuli to determine the user's intent (Donchin *et al* 2000, Gao *et al* 2003, Krusienski *et al* 2008, Wang *et al* 2006). See Mak and Wolpaw (2009) for a more detailed review of BCIs.

The P300-based BCI (P300 BCI) system detects the P300 ERP to infrequent target stimuli, and thereby allows users to select items from a matrix consisting of letters, numbers, and function calls (Donchin *et al* 2000, Farwell and Donchin 1988). Previous studies have attempted to improve P300 BCI system performance in terms of speed and accuracy by optimizing the visual presentation paradigm (Salvaris and Sepulveda 2009, Sellers *et al* 2006, Townsend *et al* 2010), the feature extraction method (Rivet *et al* 2009, Serby *et al* 2005, Xu *et al* 2004), and/or the classification algorithm (Krusienski *et al* 2006, Lenhardt *et al* 2008, Rakotomamonjy and Guigue 2008).

Despite recent progress in optimizing P300 BCI system performance, studies in both healthy (Guger *et al* 2009) and severely disabled subjects (Nijboer *et al* 2008, Sellers and Donchin 2006) report highly variable online performance across users. Indeed, some people, including those in target populations (Vaughan *et al* 2006), have been unable to use a P300 BCI due to low online classification accuracies (McCane *et al* 2009). Similar phenomenon has also been observed and reported in motor-imagery-based BCIs (Vidaurre and Blankertz 2010). Often, the reasons for poor BCI performance are not clear. Specifically, there is limited knowledge about which EEG features determine, or reflect, successful use of an EEG-based P300 BCI. Because successful BCI operation depends on the interaction between the user and the BCI system (Wolpaw *et al* 2002), specific features of the EEG are likely to correlate with performance. The purpose of this study was to identify the EEG features that best correlate with P300 BCI performance.

Methods

Subjects

Twenty subjects (16 men, 4 women; mean age 56.9 ± 8.6 years) with advanced ALS were included in this study. Most were extremely disabled (mean ALSFRS scores: 6.89 ± 6.89 (Brooks *et al* 1996)). Fourteen out of 20 subjects used mechanical ventilation and retained little or no voluntary muscle control (i.e. no more than eye movement or movement of a single digit). At the time of the study, 10 subjects communicated using high-technology assistive devices operated via small body movements (e.g. eye, neck or head). The remaining 10 communicated using low-technology, e.g., visual letter boards. A detailed inclusion criterion for initial user of our BCI system can be found in Vaughan *et al* (2006). The study was reviewed and approved by the Helen Hayes Hospital Institutional Review Board, and all subjects provided informed consent.

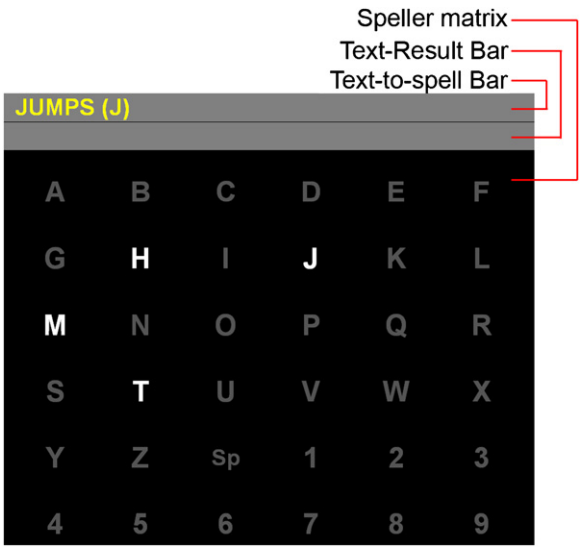

Figure 1. The 6 × 6 P300 BCI matrix used in this study. Groups of items in the speller matrix flashed successively in a random manner beginning 0.5 s after the presentation of the target selection listed in parentheses at the end of the character string (i.e. '*J*' in this case). In online testing runs, the classification results were displayed immediately in the text-result bar.

Data acquisition

EEG was recorded using a cap (Electro-Cap International, Inc.) embedded with 16 electrodes (F3, Fz, F4, T7, C3, Cz, C4, T8, CP3, CP4, P3, Pz, P4, PO7, Oz, PO8) based on the modified international 10-20 system (Sharbrough *et al* 1991). The recordings were referenced to the right mastoid and grounded to the left mastoid. The EEG was bandpass filtered at 0.5–30 Hz, amplified with a g.USBamp (Guger Technologies OEG, Graz, Austria), digitized at a rate of 256 Hz, and stored. Electrode impedances were kept below 10 kΩ. BCI operation and data collection were controlled by BCI2000, a general-purpose BCI software platform (Schalk *et al* 2004).

Experimental protocol

Subjects were seated in their home environment facing a computer screen. As showed in figure 1, the visual presentation was divided into three parts: (1) the Text-to-Spell Bar, (2) the Text-Result Bar, and (3) the 6 × 6 Speller matrix containing 36 items (letters and numbers). All data were collected in copy-spelling mode (Krusienski *et al* 2008, Sellers *et al* 2006). The word(s) the user was asked to copy-spell were displayed in the Text-to-Spell bar, with the current target letter shown

Table 1. EEG features extracted from each EEG channel used for online classification.

Continuous EEG	RMS amplitude (RMS)	
	RMS amplitude at 60 Hz (RMS60)	
	Delta frequency band power (Delta)	
	Theta frequency band power (Theta)	
	Beta1 frequency band power (Beta1)	
	Beta2 frequency band power (Beta2)	
	Alpha1 frequency band power (Alpha1)	
	Alpha2 frequency band power (Alpha2)	
	Gamma frequency band power (Gamma)	
ERP	Target responses	Non-target responses
	Positive peak amplitude (TPeak)	Positive peak amplitude (NTPeak)
	Positive peak latency (TpLat)	Positive peak latency (NTpLat)
	Negative peak amplitude (TnPeak)	Negative peak amplitude (NTnPeak)
	Negative peak latency (TnLat)	Negative peak latency (NTnLat)
	Peak-to-peak amplitude (TPtP)	Peak-to-peak amplitude (NTPtP)
	RMS amplitude (TRMS)	RMS amplitude (NTRMS)

Features of continuous EEG:
RMS amplitude (μV), RMS amplitude at 60 Hz (μV), power at various frequency bands (dB)—Delta: 0.5–4 Hz; Theta: 4.5–8 Hz; Alpha1: 8.5–11 Hz; Alpha2: 11.5–14 Hz; Beta1: 14.5–25 Hz; Beta2: 25.5–35 Hz; Gamma: >35.5 Hz.
Features of ERP to target and non-target stimuli (analysis window: 800 ms post-stimulus):
positive peak amplitude (μV), positive peak latency (ms), negative peak amplitude (μV), negative peak latency (ms), peak-to-peak amplitude (μV), and RMS amplitude (μV).

in parentheses at the end of the character string. Beginning 0.5 s after the presentation of the target selection in parentheses, groups of items in the speller matrix flashed successively in a random order (Townsend *et al* 2010). The flash rate was 4 Hz (flash for 187.5 ms with 62.5 ms between flashes). Subjects were asked to attend to the target letter and to silently count the number of times it flashed. An average of 17.5 $\pm$ 4.89 flashes per selection were presented to subjects in this study.

Each subject performed one copy-spelling session comprised of nine 3–4 min runs. In each run, the user was asked to copyspell a word or a character set. The words and character sets were the same across subjects. The first five runs (21 characters in total) comprised a calibration phase in which no feedback was provided, and the next four runs (14 characters in total) comprised a testing phase in which feedback was provided (i.e. the letters spelled up to the current moment were displayed in the Text-Result Bar). It should be noted that, in cases where classification rate is low (<75%), feedback in testing phase was disabled to avoid frustration of subjects.

Online classification

A stepwise linear discriminant analysis (SWLDA) was applied to the data from the five calibration runs (i.e. training set; runs 1–5) to determine the classifier weights (i.e. classifier coefficients) (Donchin *et al* 2000, Farwell and Donchin 1988, Krusienski *et al* 2006). These weights were then applied during the subsequent four testing runs (i.e. testing set; runs 6–9). Individuals who achieved success (classification 75%) on run 6 (i.e. first testing run) were provided feedback for the remaining three runs. The time epoch used for analysis was 800 ms with a decimation frequency of 20 Hz (i.e. resulting in 16 samples in 800 ms). The SWLDA procedure derived classifier weights from a subset of eight channels (Fz, Cz, P3, Pz, P4, PO7, PO8, Oz). Previous exploratory work by Krusienski *et al* (2008) has shown reliable and satisfactory classification results with a P300 BCI using this eight-channel set. This electrode set requires less preparation time than the traditional 10–20 set while keeping classification optimal, and is therefore used as a standard for long-term home use of a P300-based BCI system (Sellers *et al* 2010, Vaughan *et al* 2006). However, it is possible that a different montage would be required for ALS patients in different stages of their disease. Therefore, an additional eight channels of EEG data was collected from each subject for further individualized offline analyses as it may require.

Data processing and analysis

In order to study the correlation between the subject's EEG activity and his/her P300 BCI performance, we analyzed EEG data collected from the four testing runs (runs 6–9) of each of the 20 subjects. EEG or ERP activity is characterized by frequency, amplitude, and the direction of major deflection, i.e. polarity (Tong and Thankor 2009). In this study, a total of 21 EEG features (table 1) were extracted from each of the eight EEG channels (Fz, Cz, P3, Pz, P4, PO7, PO8, Oz) used for online classification. These features formed a feature space of dimension 168 $\times$ 80 ((21 features $\times$ 8 channels) $\times$ (20 subjects $\times$ 4 runs)). The EEG features used, which include peak measurements, frequency band power, and average amplitude over time, are listed in table 1. They are classical, quantitative EEG/ERP measures that are commonly used in the field (Cacioppo *et al* 2007, Luck 2005, Tong and Thankor 2009, van Drongelen 2007).

EEG features in the feature space were divided into four groups, with a dimension of 168 $\times$ 20 each, corresponding to their run numbers (i.e. run 6, 7, 8, 9). Stepwise multivariate linear regression analysis (Draper and Smith 1981) with a leave-one-out replication was applied to determine which of the extracted EEG features correlated best with P300

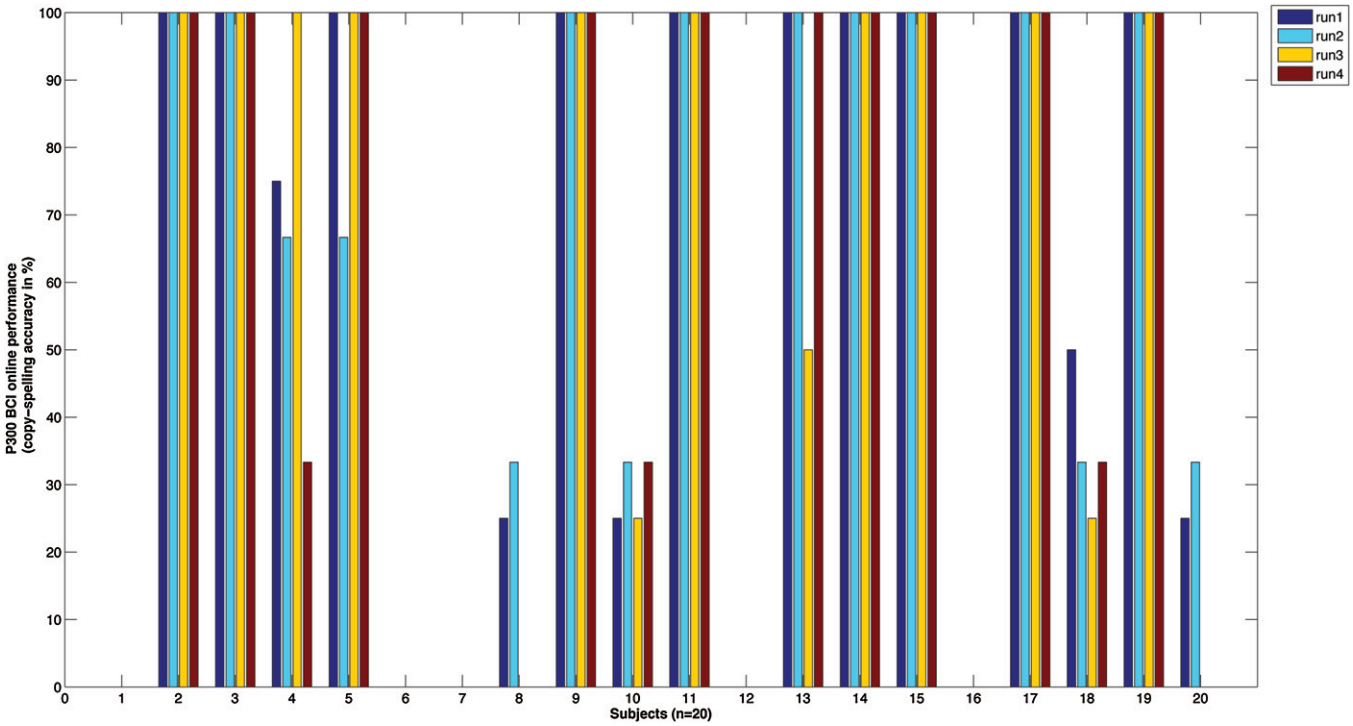

Figure 2. P300 BCI online performance of 20 ALS subjects (four testing runs per subject: runs 1–4). 48.75% of runs achieved 100% online accuracy; 30% of runs had online accuracy of 0%.

BCI performance. The stepwise algorithm adds and removes features in steps until the optimum model is reached. Only features significantly improving ($p < 0.05$) the model's ability to predict P300 BCI performance were retained in the model. Four prediction models of P300 BCI performance (i.e. accuracy) were developed from the four different possible combinations of three of the four feature groups (i.e. the training sets). Cross-validation was performed to deal with the possible problem caused by multiple test procedures during model selection (Simon 1994, Tukey 1977). The generalization of each model was tested by applying it to the group that had not been included in the combination used to develop the model (i.e. the validation set). The predicted accuracy for the validation set was calculated and then compared to its actual online accuracy. The model yielding the most reliable prediction of P300 BCI performance was selected. To verify the robustness of the selected prediction model, we repeated the above model training and validation procedures with regular linear regression analyses, using only EEG features retained in the selected model.

The data displayed both within- and between-subject variances (i.e. a mixed-effect model). The statistical procedure of within-subject centering (van de Pol and Wright 2009) was performed to separate the two sources of variance. The relationship between the selected EEG features and P300 BCI performance was then examined with bivariate models (i.e. Pearson's r) in both fixed-effect (within- and between-subject effects) and mixed-effect models. These analyses also assessed the topographic specificity of the selected features.

All offline EEG analysis was performed by software developed in the MATLAB (The Mathworks, Natick, MA) environment. All statistical procedures were performed using the Statistical Package for the Social Sciences, Version 10 (Chicago, IL).

Results

The performance of P300 BCI operation was assessed in terms of the online accuracies of individual testing runs. Online accuracy was defined as the per cent of accurate classification (i.e. per cent of letters correctly selected) in a single run. Figure 2 shows the online performance (per cent correct) of all 20 subjects (80 runs in total). About half of the runs (48.75%) achieved 100% accuracy, while 30% of the runs resulted in 0% accuracy. Chance accuracy was 2.8%. Table 2 shows the average peak-to-peak amplitude of target ERP at Cz of all 20 subjects, during online testing phase.

As described in methods, four prediction models of P300 BCI performance were developed from different combinations of training groups, using stepwise multivariate linear regression analyses. With a leave-one-out approach, each model was tested by its validation set, the group left out during model training. Significant correlations ($p < 0.05$) between the predicted and actual online accuracies for the validation set were found in all four models. As table 3 shows, model 1 produced the most reliable prediction ($R^2 = 0.55$, $p < 0.001$) among all the prediction models. It was also the simplest model with the fewest degrees of freedom.

To verify the robustness of the selected prediction model (i.e. model 1 in table 3), regular linear regression analyses using the five selected EEG features (TRMS at Fz, Cz, and P3; TnPeak at Pz; and Theta at PO7) from model 1 were performed with a leave-one-out replication using each

Table 2. Average peak-to-peak amplitude of target ERP at Cz during testing phase ($n = 20$ subjects; testing runs = 4; characters = 14).

	Average peak-to-peak amplitude
Subject 1	5.53 (1.34)
Subject 2	16.76 (2.69)
Subject 3	10.74 (1.93)
Subject 4	5.38 (1.50)
Subject 5	6.55 (0.35)
Subject 6	4.48 (0.90)
Subject 7	6.76 (1.37)
Subject 8	8.03 (0.74)
Subject 9	5.98 (1.63)
Subject 10	11.74 (0.97)
Subject 11	6.51 (0.88)
Subject 12	2.73 (0.49)
Subject 13	10.14 (0.93)
Subject 14	16.64 (2.45)
Subject 15	8.21 (0.55)
Subject 16	3.45 (0.24)
Subject 17	5.10 (1.43)
Subject 18	6.84 (0.60)
Subject 19	7.70 (1.26)
Subject 20	4.83 (0.39)

Standard deviations are included in parentheses.

of the four training sets (table 4). Significant correlations ($p < 0.001$) between the predicted and actual accuracies were found for all four training sets. As comparison of the results in tables 3 and 4 indicates, prediction models developed with the five selected EEG features yielded higher performance levels. This confirmed the robustness of the selected prediction model. In sum, for people with ALS, P300 BCI performance can be predicted by the following equation:

$$\begin{aligned}\text{Accuracy} = {} & \beta_{\text{TRMS(Fz)}} \cdot \text{TRMS(Fz)} + \beta_{\text{TRMS(Cz)}} \\ & \cdot \text{TRMS(Cz)} + \beta_{\text{TRMS(P3)}} \cdot \text{TRMS(P3)} + \beta_{\text{TnPeak(Pz)}} \\ & \cdot \text{TnPeak(Pz)} + \beta_{\text{Theta(PO7)}} \cdot \text{Theta(PO7)} + b,\end{aligned}$$

where β is the weight of the corresponding EEG feature and b is a constant.

Figure 3 illustrates individual relationships of the selected EEG features with P300 BCI performance; TRMS at Fz, Cz and P3 are positively correlated with performance, while both Theta at PO7 and TnPeak at Pz are negatively correlated with performance.

The topographic specificity of TRMS, TnPeak, and Theta in predicting P300 BCI performance was evaluated (table 5). Significant correlations were found for: TRMS at Fz, Cz, P3, Pz, and P4 ($p < 0.01$); TnPeak at Fz, Cz, P3, Pz, and P4 ($p < 0.05$); and Theta at all electrode locations (Fz, Cz, P3, Pz, P4, PO7, Oz, PO8) ($p < 0.001$).

The strongest correlation between P300 BCI performance and EEG Theta frequency power was found at PO7 ($R = -0.446$, $p < 0.001$). One possibility is that the parietal-occipital Theta represents user visual evoked responses to the 4 Hz visual stimulus (i.e. a group of items flashes every 250 ms). To evaluate this possibility, the power spectrum distributions between 4 and 8 Hz at PO7 in low accuracy runs (accuracy = 0–33%; $n = 36$) and high accuracy runs (accuracy = 100%; $n = 39$) were examined separately. The interval of frequency bins in the power spectrum was 1 Hz. As figure 4 illustrates, the distribution of power between 4 and 8 Hz was flat in high accuracy runs. In low accuracy runs, a significantly higher ($p < 0.001$) spectral power was found for all single frequency bins when compared to that in high accuracy runs. Moreover, spectral power at 4 Hz was less than that at 5, 6, 7, or 8 Hz. Thus, it appears that the 4 Hz visual stimulus did not account for the theta power effects at PO7.

After within-subject centering, the within- and between-subject effects of each of the three strong predictors (TRMS, TnPeak and Theta) were examined separately. As shown in figures 5(a)–(c), the significant correlations of the three predictors with P300 BCI performance found in the mixed-effect model reflected mainly a between-subject effect ($p < 0.05$). No significant within-subject correlations were found for these three predictors.

Discussion

This study identified three predictors of P300 BCI performance in people severely disabled by ALS. They are: (1) root-mean-square amplitude (TRMS); (2) negative peak (TnPeak) of the target ERP at Fz, Cz, P3, Pz, and P4; and (3) Theta frequency power (Theta) at Fz, Cz, P3, Pz, P4, PO7, Oz, and PO8. Each of these EEG features was significantly correlated with the online accuracy of P300 BCI. A statistical prediction model that used a subset of these features accounted for >60% of the variance in P300 BCI online performance ($p < 0.001$, mean $R^2 = 0.6175$).

As independent features, TRMS at Fz ($R = 0.331$, $p < 0.01$), Cz ($R = 0.483$, $p < 0.001$) and P3 ($R = 0.241$, $p < 0.01$) were positively correlated with P300 BCI performance (figure 3). Thus we can expect that performance (i.e. classification accuracy) will increase as TRMS at these three electrode locations increases. However, we found negative beta weights for TRMS at Fz and P3 in the regression equations of the prediction models (table 4). This difference between the signs of bivariate correlation coefficients and multivariate regression weights suggested that TRMS at Fz and P3 were operating as suppressor variables in the statistical prediction model (Cohen *et al* 2003). We speculated that the primary effect of TRMS at Fz and P3 was suppression of the error variance of TRMS at Cz (i.e. by reducing spatial noise). In general, TRMS at Fz, Cz, P3, Pz, and P4 were each significantly correlated ($p < 0.05$) with P300 BCI performance.

As separate ERP amplitude measures, TnPeak at Fz, Cz, P3, Pz, and P4 were significantly correlated ($p < 0.05$) with P300 BCI performance (table 5). These features shared electrode locations with the TRMS features that also correlated with P300 BCI performance. Previous studies have reported the importance of a negative peak at parietal electrodes (Hoffmann *et al* 2008), particularly Pz (Dal Seno *et al* 2008), in P300-based BCI classification accuracy. In agreement with these previous findings, in this study, TnPeak at Pz was selected by the stepwise algorithm as one of the features in the prediction model of P300 BCI performance.

Table 5 shows that theta frequency power (Theta) at all electrode locations used for online classification (Fz, Cz,

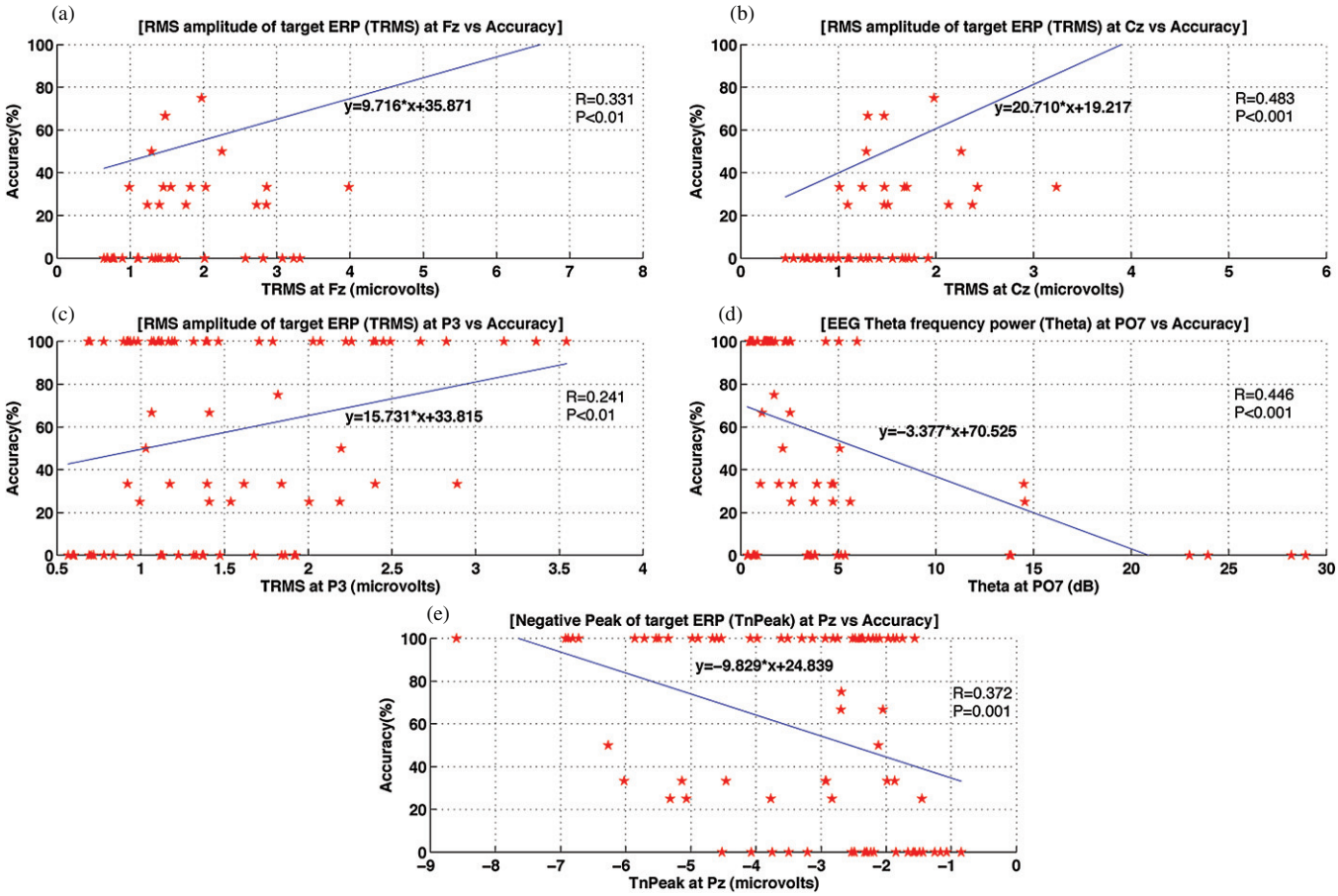

Figure 3. Relationships between selected EEG features and P300 BCI online performance (% accuracy). (a) RMS amplitude of target ERP at Fz. (b) RMS amplitude of target ERP at Cz. (c) RMS amplitude of target ERP at P3. (d) EEG theta frequency power at PO7. (e) Negative peak amplitude of target ERP at Pz.

Table 3. Stepwise multivariate linear regression analyses: statistical prediction models for P300 BCI performance and validation results.

Prediction models (stepwise multivariate linear regression)				
	Model 1	Model 2	Model 3	Model 4
Training set	Groups 2, 3, and 4 ($n = 60$)	Groups 1, 3, and 4 ($n = 60$)	Groups 1, 2, and 4 ($n = 60$)	Groups 1, 2, and 3 ($n = 60$)
Regression equation: *predictors, corresponding beta weights (β) and constant (b)*	Constant 43.49 TRMS(Fz) −21.24 TRMS(Cz) +76.83 TRMS(P3) −81.71 Theta(PO7) −2.08 TnPeak(Pz) −14.35	Constant 29.18 TRMS(Cz) +94.75 TRMS(P3) −62.58 TnPeak(Fz) +14.07 TnPeak(Pz) −14.04 TnLat(Fz) +0.04 TPeak(Pz) −13.62 NTpLat(PO7) +0.04 TpLat(P3) −0.05 Theta(PO7) −1.82	Constant 25.17 TRMS(Fz) −27.98 TRMS(Cz) +83.71 TRMS(P3) −91.36 TnPeak(P3) −18.11 TnLat(P4) +0.05 Theta(PO7) −2.04	Constant −8.39 TRMS(Fz) −21.03 TRMS(Cz) +64.58 TRMS(P3) −30.70 NTpLat(Fz) +0.06 NTpLat(P3) +0.05 Theta(PO7) −1.69
		Validation		
Validation set	Group 1 ($n = 20$)	Group 2 ($n = 20$)	Group 3 ($n = 20$)	Group 4 ($n = 20$)
Significance	$p < 0.001$	$p < 0.05$	$p < 0.05$	$p < 0.05$
Correlation	$R^2 = 0.55$	$R^2 = 0.36$	$R^2 = 0.41$	$R^2 = 0.39$

EEG features selected by the stepwise algorithm in each model.
Model 1—root-mean-square amplitude of target ERP (TRMS) at Fz, Cz, and P3, negative peak amplitude of target ERP (TnPeak) at Pz, and EEG theta frequency power (Theta) at PO7.
Model 2—TRMS at Cz, and P3, TnPeak at Fz and Pz, negative peak latency of target ERP (TnLat) at Fz, positive peak amplitude of target ERP (TPeak) at Pz, positive peak latency of non-target ERP (NTpLat) at PO7, positive peak latency of target ERP (TpLat) at P3, and Theta at PO7.
Model 3—TRMS at Fz, Cz, and P3, TnPeak at P3, TnLat at P4, and Theta at PO7.
Model 4—TRMS at Fz, Cz, and P3, NTpLat at Fz and P3, and Theta at PO7.

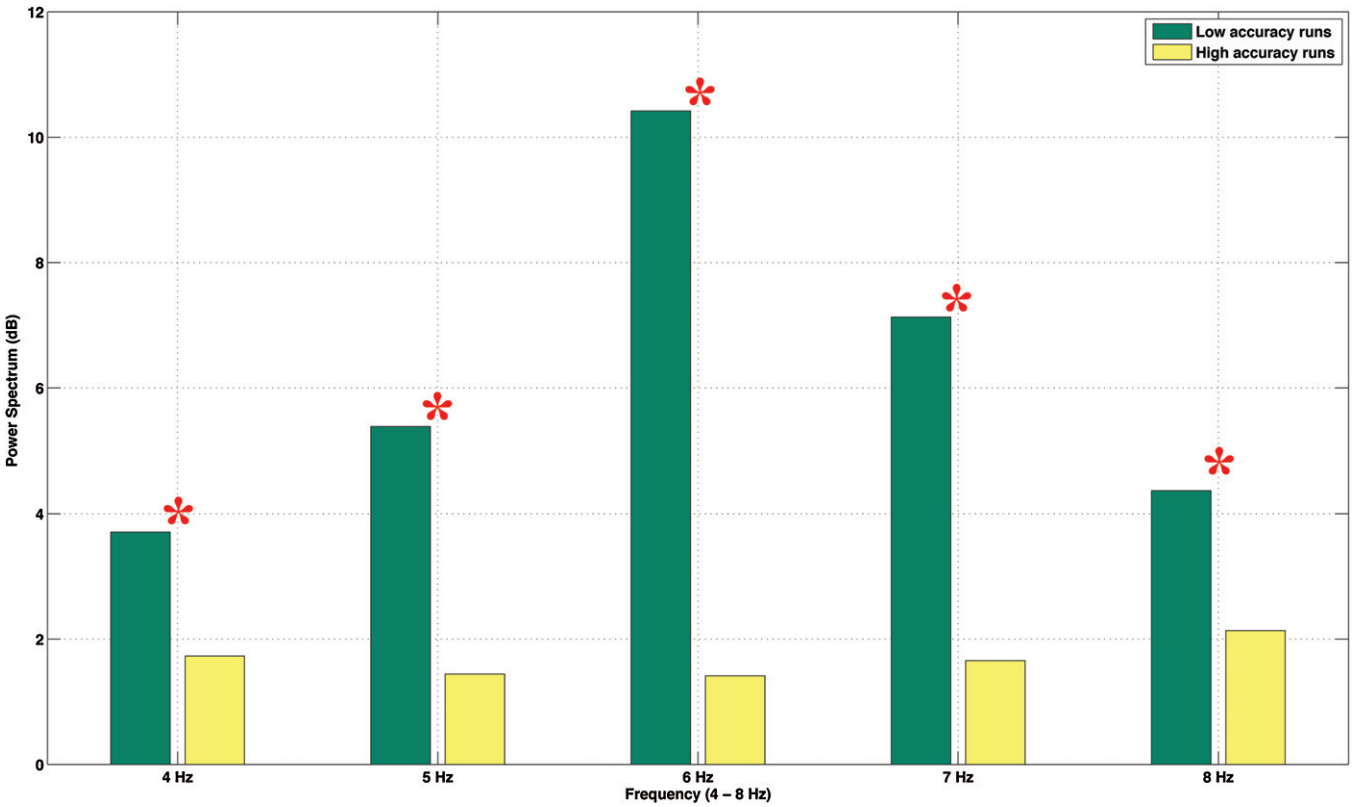

Figure 4. Average spectral power distribution (4–8 Hz) at PO7 in low and high accuracy runs. Low accuracy runs ($n = 36$; accuracy = 0–33%); high accuracy runs ($n = 39$; accuracy = 100%). Significantly higher spectral powers at 4–8 Hz ($p < 0.001$) were noticed in low accuracy runs. *Statistical significance at $p < 0.001$.

Table 4. Regular linear regression analyses: statistical prediction models for P300 BCI performance and validation results.

Prediction models (regular linear regression)								
Training set	Groups 2, 3, and ($n = 60$)		Groups 1, 3, and ($n = 60$)		Groups 1, 2, and ($n = 60$)		Groups 1, 2, and ($n = 60$)	
Regression equation: predictors, corresponding beta weights constant (b)	Constant	43.49	Constant	45.05	Constant	41.90	Constant	42.41
	TRMS(Fz)	−21.24	TRMS(Fz)	−24.21	TRMS(Fz)	−24.22	TRMS(Fz)	−19.80
	TRMS(Cz)	+76.83	TRMS(Cz)	+86.48	TRMS(Cz)	+76.56	TRMS(Cz)	+69.65
	TRMS(P3)	−81.71	TRMS(P3)	−84.50	TRMS(P3)	−72.47	TRMS(P3)	−59.47
	Theta(PO7)	−2.08	Theta(PO7)	−1.71	Theta(PO7)	−1.91	Theta(PO7)	−1.94
	TnPeak(Pz)	−14.35	TnPeak(Pz)	−11.91	TnPeak(Pz)	−13.16	TnPeak(Pz)	−8.24
Validation								
Validation set	Group 1 ($n = 20$)		Group 2 ($n = 20$)		Group 3 ($n = 20$)		Group 4 ($n = 20$)	
Significance	p <0.001		p <0.001		p <0.001		p <0.001	
Correlation	$R^2 = 0.55$		$R^2 = 0.60$		$R^2 = 0.57$		$R^2 = 0.75$	

Prediction models were developed by regular linear regression analyzes, using only the five EEG features from the best model found in prior statistical analyses (i.e. model 1 in table 2):
root-mean-square amplitude of target ERP (TRMS) at Fz, Cz, and P3, negative peak amplitude of target ERP (TnPEAK) at Pz, and Theta frequency power (Theta) at PO7.

P3, Pz, P4, PO7, PO8, Oz) is significantly correlated ($p < 0.001$) with P300 BCI performance. Theta power has been extensively studied. Theta oscillations are associated with various functions: task difficulty or complexity (Gevins *et al* 1997), error processing (Luu *et al* 2004); attention and/or arousal (Aftanas and Golocheikine 2001, Inanaga 1998); decision making (Jacobs *et al* 2006); memory recognition (Jacobs *et al* 2006); and memory load (Jacobs *et al* 2006, Jensen and Tesche 2002). In the present study we found that Theta increase was associated with decreased P300 BCI accuracy. This finding agrees with previous work showing a negative relationship between theta power and performance in cognitive and memory tasks (Hermens *et al* 2005, Klimesch 1999). Earlier studies have also reported increased theta power with drowsiness (Bittner *et al* 2000, Boksem *et al* 2005, De Gennaro *et al* 2007, Klimesch 1999). The higher Theta

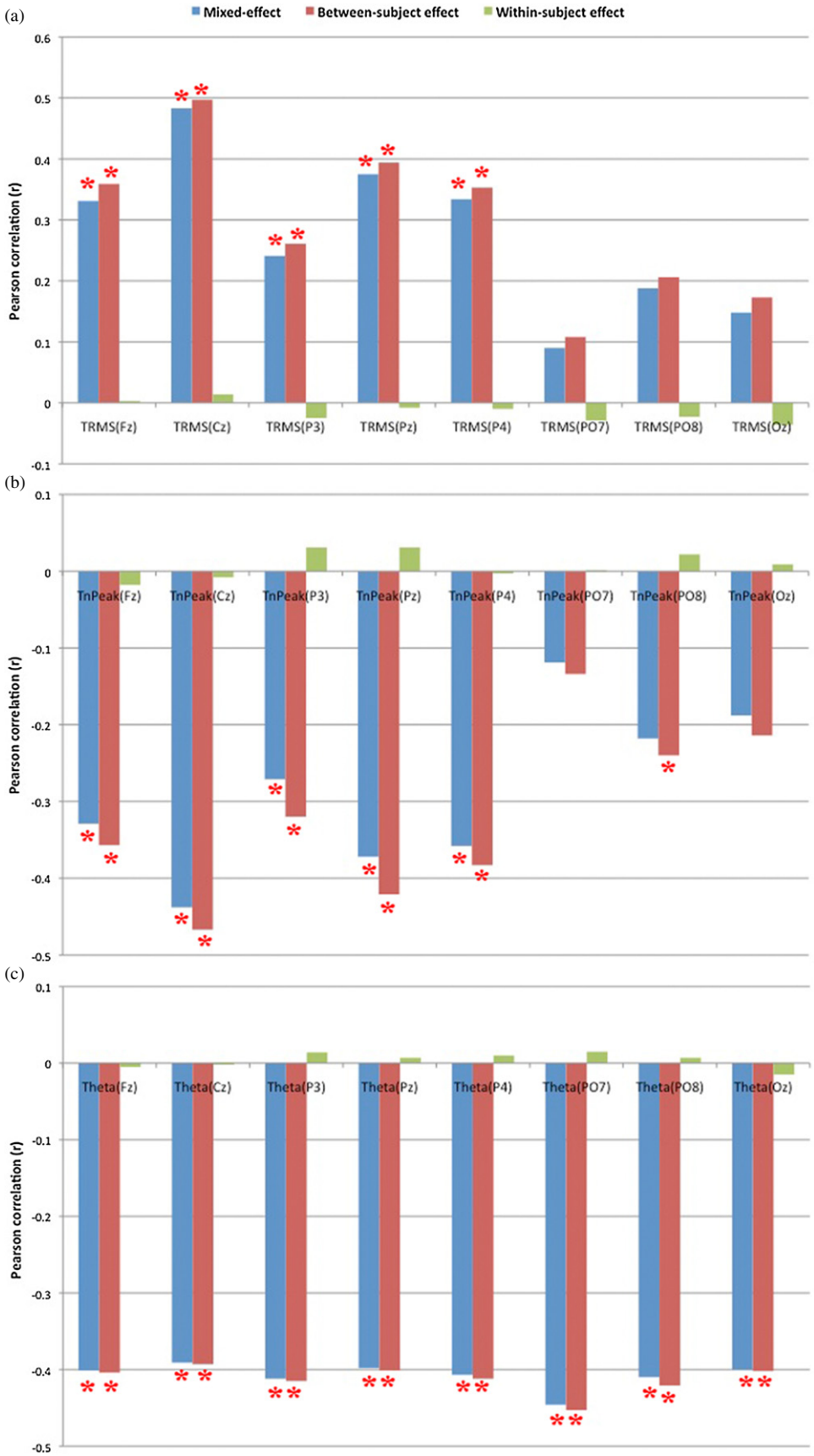

Figure 5. (a) Relationship between RMS amplitude of target ERP (TRMS) and P300 BCI performance: mixed-effect, within- and between-subject effects. (b) Relationship between negative peak amplitude of target ERP (TnPeak) and P300 BCI performance: mixed-effect, within- and between-subject effects. (c) Relationship between Theta power (Theta) and P300 BCI performance: mixed-effect, within- and between-subject effects. *Statistical significance at $p < 0.05$.

Table 5. Topographic specificity of (1) target ERP RMS amplitude (TMRS); (2) target ERP negative peak amplitude (TnPeak); and (3) EEG theta frequency power (Theta), in predicting P300 BCI performance.

EEG features	Location	Pearson's r	p
TRMS	Fz	0.331	$<0.01^*$
	Cz	0.483	$<0.001^*$
	P3	0.241	$<0.05^*$
	Pz	0.375	0.001^*
	P4	0.334	$<0.01^*$
	PO7	0.09	>0.05
	PO8	0.188	>0.05
	Oz	0.148	>0.05
TnPeak	Fz	−0.329	$<0.01^*$
	Cz	−0.438	$<0.001^*$
	P3	−0.271	$<0.05^*$
	Pz	−0.372	0.001^*
	P4	−0.358	0.001^*
	PO7	−0.119	>0.05
	PO8	−0.218	>0.05
	Oz	−0.188	>0.05
Theta	Fz	−0.401	$<0.001^*$
	Cz	−0.391	$<0.001^*$
	P3	−0.412	$<0.001^*$
	Pz	−0.398	$<0.001^*$
	P4	−0.407	$<0.001^*$
	PO7	−0.446	$<0.001^*$
	PO8	−0.410	$<0.001^*$
	Oz	−0.400	$<0.001^*$

Significant correlation with online accuracy of P300 BCI were found in:
(1) TRMS at Fz, Cz, P3, Pz, P4;
(2) TnPeak at Fz, Cz, P3, Pz, P4;
(3) Theta at Fz, Cz, P3, Pz, P4, PO7, PO8, Oz.
*Statistical significance at p <0.05.

associated with poorer BCI performance in people with ALS could reflect decreased alertness during BCI operation. Further work is needed to clarify this relationship and its underlying mechanism.

This is to our knowledge the first study to identify EEG features that correlate with P300 BCI online performance. At the same time, the study has certain limitations. First, all possible EEG features were not evaluated. While EEG features that correlate with performance were certainly identified, it remains possible that other EEG features also correlate, or even account for additional variance. Second, while the study could readily detect between-subject effects, the relatively limited amount of data from each subject (i.e. one session) constrained its ability to detect within-subject effects. Studies that incorporate multiple sessions per subject are needed to identify EEG features that correlate with performance within individuals. Third, since all of the subjects had ALS, it is not clear to what extent the results will generalize to other populations.

By identifying EEG features that correlate with P300 BCI performance in people with ALS, this study may contribute in several ways to current efforts to provide P300-based BCIs to people with severe disabilities. This new knowledge could assist in identifying suitable candidates for long-term home use of P300 BCI systems. It could help recognize individuals for whom the system is likely to be effective as well as those for whom it is likely to be ineffective, and could thereby facilitate initial evaluations and reduce the risk of user frustration and disappointment. Furthermore, future investigation and experimentation into the within-subject effects of these identified EEG features is strongly recommended. P300 BCI performance might possibly be improved by optimizing one or more of these features (e.g. decreasing Theta power) through new stimulus presentation paradigms or new user training methods. Such improvements might substantially increase the capacity and reliability of P300 BCI systems for long-term home use by people with severe disabilities (Vaughan *et al* 2006).

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