Relationship Between Electrical Brain Responses to Motor Imagery and Motor Impairment in Stroke

Vera Kaiser, MSc*; Ian Daly, PhD*; Floriana Pichiorri, MD; Donatella Mattia, PhD; Gernot R. Müller-Putz, PhD; Christa Neuper, PhD

Background and Purpose—New strategies like motor imagery based brain–computer interfaces, which use brain signals such as event-related desynchronization (ERD) or event-related synchronization (ERS) for motor rehabilitation after a stroke, are undergoing investigation. However, little is known about the relationship between ERD and ERS patterns and the degree of stroke impairment. The aim of this work was to clarify this relationship.

Methods—EEG during motor imagery and execution were measured in 29 patients with first-ever monolateral stroke causing any degree of motor deficit in the upper limb. The strength and laterality of the ERD or ERS patterns were correlated with the scores of the European Stroke Scale, the Medical Research Council, and the Modified Ashworth Scale.

Results—Mean age of the patients was 58±15 years; mean time from the incident was 4±4 months. Stroke lesions were cortical (n=8), subcortical (n=11), or mixed (n=10), attributable to either an ischemic event (n=26) or a hemorrhage (n=3), affecting the right (n=16) or left (n=13) hemisphere. Higher impairment was related to stronger ERD in the unaffected hemisphere and higher spasticity was related to stronger ERD in the affected hemisphere. Both were related to a relatively stronger ERS in the affected hemisphere.

Conclusion—The results of this study may have implications for the design of potential poststroke rehabilitation interventions based on brain–computer interface technologies that use neurophysiological signals like ERD or ERS as neural substrates for the mutual interaction between brain and machine and, ultimately, help stroke patients to regain motor control. (Stroke. 2012;43:2735-2740.)

Key Words: event-related desynchronization ■ event-related synchronization ■ motor impairment ■ rehabilitation ■ spasticity ■ stroke recovery

After a stroke, the activation patterns of the brain are altered and change spontaneously in the first months after the incident. For hemiparetic strokes, a reduced excitability of the ipsilesional motor cortex can be observed soon after the incident, reflected in a smaller size of the motor representation area of the affected limb, increased excitability threshold, and reduced amplitude and prolonged latency of motor-evoked potentials.1,2 The brain tries to compensate by shifting the activation to nonprimary motor areas and by shifting activity and functional connectivity to the contralateral hemisphere.3-5

In the first year after the incident, these altered activation patterns can revert to normal again, with normalization of reduced excitability and increasing size of the cortical representation of motor function. The extent of recovery of motor function is related to the extent of the normalization of activation patterns and depends on the localization of the lesion, new interactions of remaining cerebral structures, age of the patient, and state of the brain before stroke.2,6,7 Several studies indicate that motor imagery (MI) has a positive effect on motor rehabilitation after stroke.8 However, there are some drawbacks with the current application of this therapy. First, the therapists have no feedback about patient compliance, making it difficult to control if patients really perform kinesthetic MI and therefore activate the motor networks of their brains.9 Visual MI is mediated through a different neural system than kinesthetic MI.10 Therefore, monitoring would be beneficial for the therapists to be able to guide the patients to change MI strategy if necessary. Second, the patients may find MI difficult to perform without any feedback. Feedback is important for learning and, in the context of motor learning, sensory feedback effects motor ability and reshapes sensorimotor integration.11

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A possible means for providing feedback and enhancing the effect of MI therapy on stroke rehabilitation is a brain–computer interface (BCI). In a BCI, mentally modulated brain signals are measured and converted to control signals for different applications, which give feedback to the user (Figure 1). A commonly used control paradigm in BCI is based on MI. MI produces a relative change in the level of electric activation in the somatosensory cortices. The spectral amplitude of ongoing EEG within the motor cortex decreases (event-related desynchronization [ERD]) during movement or MI, typically in the mu frequency rhythm (8–12 Hz) and the beta frequency band (13–30 Hz), and increases (event-related synchronization [ERS]) after termination of movement or MI. In stroke rehabilitation, BCI could offer a valuable tool to support training and practice, even in the absence of residual motor activity, and could encourage and guide brain plasticity to improve motor function. However, because stroke is associated with major changes in the activation patterns of motor cortical areas, the strength and the distribution of the ERD or ERS patterns might be altered.

ERD and ERS patterns in stroke patients have only been investigated in a small number of studies. Gerloff et al found enhanced contralesional activity (stronger ERD) in the beta frequency range of 13 to 30 Hz during preparation and execution of movement in chronic stroke patients. Nevertheless, the fact that activation patterns of the brain are related to motor performance after stroke is a prerequisite for BCI supported stroke rehabilitation. The relationship between those patterns and the degree of stroke impairment has to be taken into account in the development of BCI-based strategies for stroke rehabilitation. However, little is currently known about the relationship between strengths of ERD and ERS patterns, during movements or MI, and stroke severity.

The aim of the present study was to investigate if there is a relationship between the intensity of ERD or ERS patterns and severity of motor impairment after stroke. Previous literature concerning brain activation patterns in stroke patients has reported results measured with functional magnetic resonance imaging. With regard to these results, we expect that similar relationships are also reflected, to a certain extent, in the ERD and ERS patterns.

Figure 1. Schematic of a brain–computer interface.

**Patients**

Twenty-nine stroke patients (14 females) were consecutively enrolled from a rehabilitation hospital ward (Fondazione Santa Lucia, Rome, Italy). Inclusion criteria were: adults (older than 18 years); first-ever monolateral stroke causing any degree of motor deficit in the upper limb; ability to understand the task; and stability of clinical conditions. The exclusion criteria were presence of any medical condition other than stroke affecting motor ability in the upper limb and anything preventing proper EEG recording. All patients gave informed consent. The study was approved by the local ethical committee of Fondazione Santa Lucia and was performed according to the declaration of Helsinki.

An expert physician, blinded regarding the study, evaluated all patients. The European Stroke Scale (ESS) was used to assess the severity of the impairment, ranging from 0 (most affected) to 100 (least affected). The Medical Research Council (MRC) scale for muscle strength (upper limb section) was used to assess residual strength, evaluating the strength of 8 segments per arm and ranging from 0 (absence of visible muscular contraction) to 5 (normal muscular contraction against full resistance) for each segment (healthy people score 80; hemiplegic patients score 40). Finally, the Modified Ashworth Scale (MAS) was used to assess spasticity (upper limb section), evaluating muscular tone to passive movements in 3 upper limb joints (shoulder, elbow, and wrist) and ranging from 0 (normal muscular tone) to 5 (passive movement impossible).出席

**Data Recording**

During the recording session, the patient was comfortably seated in an armchair placed in a dimly lit room with upper limbs visible on a desk, with the dorsopalmar axis parallel to the surface of the desk. A computer screen was positioned on the desk in front of the patient to provide visual cues. EEG was collected from 61 standard positions (according to the extended 10–20 International System) band pass filtered between 0.1 and 70 Hz, digitized at 200 Hz, and amplified by a commercial EEG system. The session was divided into runs, with 30 trials for each run. Each trial was temporally determined by a cursor appearing in the low center of the screen and moving toward the top at a constant velocity on a straight trajectory.

The total trial duration was 9 seconds and the intertrial interval was 1.5 seconds (Figure 2). During rest trials, the patient was asked to watch the cursors trajectory. During motor task trials, a green rectangle (occupying the last 4 seconds of cursor trajectory) appeared at the top of the screen. The patient was asked to start performing the cued motor task when the cursor reached the green rectangle and to continue until the end of the trajectory. The command sequence was randomized (15 rest and 15 motor trials per run). Patients were asked to either execute or imagine simple movements (grasping and complete finger extension) with the affected and unaffected hand in separate runs. Each run was dedicated to a different motor task; the run sequence was randomized across patients. Depending on the severity of the motor deficit in the affected upper limb, patients were...
asked to execute the full movement or to just attempt it; in severely affected (plegic) patients, motor execution (ME) with the affected hand was not performed.

Analysis
To assure blinding, data analysis was performed by researchers who were not involved in the assessment of the stroke impairment scales. Before analysis, artifacts were removed from the data. To be able to clean and use trials containing only a small amount of artifact contamination in further analysis steps, the second-order blind identification component analysis–based26 approach was used. To verify only clean EEG trials were used for analysis, trials were visually inspected and removed if necessary.

ERD and ERS strength values in the EEG were estimated as the change in band power in the frequency band of the μ rhythm (8–13 Hz) recorded on channels positioned over the left (C3) and right (C4) motor cortices in 2 to 6 seconds relative to a baseline (~1.5 to 0 seconds). Times are relative to the cue presentation and are chosen to encompass the observed movement period performed by the subjects in the ME condition. ERD or ERS strength was calculated from the summation of relative changes in band power on each channel in the specified time–frequency ranges.

For assessing hemispheric asymmetries of the ERD and ERS patterns, a laterality coefficient (LC) was calculated according to equation 1:

\[
LC = \frac{C-I}{C+I},
\]

where C denotes the ERD and ERS values of the hemisphere contralateral to the moved hand and I denotes the values ipsilateral to the moved hand. This method was chosen because it allows the most straightforward interpretation of hemispheric asymmetries.\(^27\) A positive or negative LC indicates higher or lower values in the hemisphere contralateral to the moved hand.

Stepwise regressions were calculated with the stroke impairment scores of ESS, MRC, and MAS as predictors and either ERD, ERS, or LC for ME and MI of the affected and unaffected hand as criterion. This allows the identification of the specific type of impairment measure that has the greatest relationship with the magnitude or laterality of the ERD or ERS.

Six different criterions are tested against the nonindependent predictors, thus requiring correction for multiple comparisons. Using Bonferroni correction, the alpha significance level is divided by 6; however, it may be argued that Bonferroni correction is overly conservative.\(^28\) Therefore, probability values are reported for all tests.

Results
Patients
Mean age was 58±15 years; mean time from the incident was 4±4 months. Stroke lesions were cortical (n=8), subcortical (n=11), or mixed (n=10), either because of an ischemic event (n=26) or a hemorrhage (n=3) affecting the right (n=16) or left (n=13) hemisphere. The mean ESS score was 69±13, the mean MRC score was 57±13, and the mean MAS score was 4±3. Tasks execution was not uniform across patients because of individual compliance with the overall duration of the recording session. Of the 29 patients, 17 performed ME and 27 performed MI with their affected hand, and 22 performed ME and 25 performed MI with their unaffected hand.

Motor Execution
For movement of the unaffected hand, no significant correlation or regression was found. For movement of the affected hand, the LC for ERS showed a significant negative correlation and stepwise regression with the scores of the MRC (correlation:

\[
R = -0.51; P = 0.037; \text{regression: } B = -0.24; P = 0.037.
\]

During movement of the affected hand, patients with higher MRC values, indicating less impairment, showed relatively higher contralesional ERS during movement of the affected hand, whereas patients with higher impairment showed relatively higher ipsilesional ERS (Figure 3A). For ERD, no significant effects were found.

Motor Imagery
No significant correlation or regression was found for MI of the unaffected hand. For MI of the affected hand, there was a significant positive correlation and regression between ERD of the contralesional hemisphere and ESS scores (correlation: \(R = 0.41; P = 0.036; \text{regression: } B = 142.31; P = 0.036\)). During MI of the affected hand, patients with less impairment (higher ESS scores) showed weaker contralesional ERD, whereas patients with higher impairments showed stronger contralesional ERD (Figure 4A).

In addition, a significant negative correlation was found between ERD of the ipsilesional hemisphere and MAS scores (\(R = -0.52; P = 0.027\)). Patients with lower spasticity showed weaker ERD in the ipsilesional hemisphere during MI of the affected hand, whereas patients with higher spasticity showed stronger ERD in the ipsilesional hemisphere (Figure 4B).
MI. During MI of the affected hand, patients with higher impairment showed higher ERD in the contralesional hemisphere as compared with patients with less impairment. This result is in line with previous findings in functional magnetic resonance imaging studies\(^5\) and EEG coherence studies.\(^4\) Additionally, this higher contralesional activation is associated with poor recovery and higher degrees of stroke impairment.\(^2,7\)

In addition, a significant relationship was identified between ipsilesional ERD during MI of the affected hand and the degree of spasticity. Stronger ERD was associated with higher spasticity. To our knowledge, this has not been found previously. A possible explanation for this effect is an overdrive of the motor system in patients with a higher degree of spasticity. This might cause a higher reactivity, reflected in a stronger ERD. Support for this explanation comes from a study with patients with hereditary spastic paraparesis. Koritnik et al\(^29\) found increased functional magnetic resonance imaging activation during finger tapping in patients compared with healthy controls. Another explanation might be that movement of a more spastic arm requires higher effort, which is related to higher activation and recruitment of additional brain areas.\(^30\) However, our finding should be considered if ERD is used in a BCI application for stroke rehabilitation. It is highly recommended to clinically monitor spasticity during the course of training, eg, with electromyography, and ensure that spasticity is not reinforced.

For the LC of ERS during ME and MI of the affected hand, a significant relationship with the degree of impairment (ME) and spasticity (MI) exhibited by patients was identified. Higher spasticity and impairment were associated with a relatively stronger ipsilesional ERS. ERS can be interpreted as deactivty or active inhibition of the underlying cortical areas,\(^31–33\) meaning higher spasticity and impairment are related to a deactivation of the affected hemisphere. In patients with higher motor impairment, in terms of muscle strength, this deactivation might be interpreted as active inhibition caused by the contralesional hemisphere, which showed higher activation (ERD) in these patients.

One might wonder why most of the results were found for MI but not for ME. Only 17 of 29 patients were able to perform ME. Because of this smaller sample, the range of impairment and range of spasticity were reduced because highly impaired patients were missing. This might explain the difference in the results.

The relationship between strength of ERD or ERS patterns and stroke impairment was only evident during ME and MI of the affected hand. For the unaffected hand, no significant correlations were observed, indicating that this relationship is really something specific to the affected side.

<table>
<thead>
<tr>
<th>Affected Hemisphere (AH)</th>
<th>Impairment</th>
<th>Spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>high</td>
<td>low</td>
</tr>
<tr>
<td></td>
<td>n.sign.</td>
<td>strong ERD &gt; weak ERD</td>
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<tr>
<td>Unaffected Hemisphere (UH)</td>
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<td></td>
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<tr>
<td></td>
<td>strong ERD &gt; weak ERD</td>
<td>n.sign.</td>
</tr>
<tr>
<td>Laterality Coefficient</td>
<td></td>
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<tr>
<td>ERS*</td>
<td>AH &gt; UH</td>
<td>UH &gt; AH</td>
</tr>
<tr>
<td>ERS</td>
<td>AH &gt; UH</td>
<td>UH &gt; AH</td>
</tr>
<tr>
<td>ERS*</td>
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</tbody>
</table>

Figure 5. Summary of the correlation and regression analysis for motor execution (ME)/motor imagery (MI) of affected hand with stroke impairment severity scores. *Results for ME are marked with an asterisk. All other results are for MI.
It might be noted that the population are relatively young. The population was enrolled in a rehabilitation center, to which the patients were admitted after their first stroke event, and no control for age was made. Additionally, the incidence rate for stroke is increasing in younger people and, therefore, the resulting population sample, although not completely representative of the larger stroke population, is sufficient for the aims of this study.

It is important to also consider a few associated caveats. First, the identified correlations must be considered against the caveat that multiple comparison correction may be required, reducing significance levels. However, given an assumption of independence of the measures, ESS, MAS, and MRC, a number of statistically significant ($P<0.05$) correlations were found. The results provide strong support for a link between the degree of stroke impairment and ERD or ERS strength. Second, the sample size was only 29 patients. A sample size of 29 stroke patients is large when compared with the sample sizes used in many BCI studies, which typically focus on single patients or small groups of subjects. The population was enrolled in a rehabilitation center, to which the patients were admitted after their first stroke event, and no control for age was made. Additionally, the incidence rate for stroke is increasing in younger people and, therefore, the resulting population sample, although not completely representative of the larger stroke population, is sufficient for the aims of this study.

Our results are applicable to BCI for stroke rehabilitation. For example BCI could encourage changes in the strength of the ERD or ERS response by providing appropriate feedback. High degrees of impairment have been shown to be associated with a strong ERD on the contralesional hemisphere and BCI could be designed to encourage a decrease in the strength of this contralesional ERD response. This may, subsequently, encourage neuroplasticity-related changes that are beneficial to the patient in terms of increasing motor control and/or decreasing spasticity. The identification of significant correlations between the degree of upper limb stroke impairment and the ERD or ERS strength is encouraging. It suggests the idea of using ERD or ERS in the assessment of stroke impairment and that the use of BCI training may have links to the degree of control that may be exerted over a limb. Hence, pursuing BCI training for stroke rehabilitation is encouraged.

Source of Funding

This work is supported by the European ICT Programme Project FP7-224631. This article only reflects the authors’ views and funding agencies are not liable for any use that may be made of the information contained herein.

Disclosures

None.

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Stroke. 2012;43:2735-2740; originally published online August 14, 2012;
doi: 10.1161/STROKEAHA.112.665489

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S1 Table 1. Correlation coefficients and p-values for correlations between ERD/ERS and ESS, MRC and MAS for motor execution. Correlations with p < .05 are written in red and bold.

<table>
<thead>
<tr>
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<th>Motor execution (ME)</th>
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<tr>
<td></td>
<td>affected hemisphere</td>
</tr>
<tr>
<td>ERD * ESS</td>
<td>R = -0.06; p = 0.82</td>
</tr>
<tr>
<td>ERD * MRC</td>
<td>R = -0.28; p = 0.30</td>
</tr>
<tr>
<td>ERD * MAS</td>
<td>R = -0.08; p = 0.82</td>
</tr>
<tr>
<td>ERS * ESS</td>
<td>R = -0.38; p = 0.15</td>
</tr>
<tr>
<td>ERS * MRC</td>
<td>R = -0.19; p = 0.47</td>
</tr>
<tr>
<td>ERS * MAS</td>
<td>R = -0.07; p = 0.85</td>
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<tr>
<td></td>
<td>Motor execution (ME)</td>
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<td></td>
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<td>affected</td>
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<tr>
<td>hemisphere</td>
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<tr>
<td>ERD * ESS</td>
<td>B = -10.08 ; p = .91</td>
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<tr>
<td>ERD * MRC</td>
<td>B = -53.88; p = .53</td>
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<tr>
<td>ERD * MAS</td>
<td>B = 85.80; p = .32</td>
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<tr>
<td>ERS * ESS</td>
<td>B = 1.79; p = .98</td>
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<tr>
<td>ERS * MRC</td>
<td>B = 19.51; p = .77</td>
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<tr>
<td>ERS * MAS</td>
<td>B = 13.01; p = .84</td>
</tr>
</tbody>
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S2 Table 2. Regression coefficients (B) and p-values for Stepwise regression between ERD/ERS and ESS, MRC and MAS for motor execution. Regressions with p < .05 are written in red and bold.
S3 Table 3. Correlation coefficients and p-values for correlations between ERD/ERS and ESS, MRC and MAS for motor imagery. Correlations with p < .05 are written in red and bold.

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<tr>
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<td></td>
<td>affected hand</td>
<td>affected hemisphere</td>
<td>laterality coefficient</td>
<td>unaffected hand</td>
<td>unaffected hemisphere</td>
<td>laterality coefficient</td>
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<tr>
<td>ERD * ESS</td>
<td>R = 0.33; p = .09</td>
<td>R = <strong>0.41; p = .04</strong></td>
<td>R = -0.22; p = .28</td>
<td>R = 0.09; p = .66</td>
<td>R = 0.09; p = .68</td>
<td>R = 0.01; p = .97</td>
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<tr>
<td>ERD * MRC</td>
<td>R = 0.35; p = .07</td>
<td>R = 0.27; p = .17</td>
<td>R = -0.06; p = .78</td>
<td>R = -0.06; p = .79</td>
<td>R = -0.07; p = .73</td>
<td>R = -0.03; p = .89</td>
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<tr>
<td>ERD * MAS</td>
<td>R = <strong>-0.52; p = .03</strong></td>
<td>R = -0.18; p = .48</td>
<td>R = -0.07; p = .74</td>
<td>R = 18; p = .51</td>
<td>R = 0.12; p = .67</td>
<td>R = -0.15; p = .46</td>
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<td>ERS * ESS</td>
<td>R = 0.19; p = .35</td>
<td>R = 0.28; p = .16</td>
<td>R = -0.12; p = .56</td>
<td>R = 0.03; p = .88</td>
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<td>ERS * MRC</td>
<td>R = 0.21; p = .28</td>
<td>R = 0.28; p = .16</td>
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<td>R = -0.08; p = .73</td>
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<td>ERS * MAS</td>
<td>R = -0.34; p = .16</td>
<td>R = -0.15; p = .54</td>
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<tr>
<td></td>
<td>affected hemisphere</td>
<td>B = 122.14; p = .09</td>
<td>B = -0.12; p = .28</td>
<td>B = 41.16; p = .66</td>
<td>B = 46.29; p = .68</td>
<td>B = 0.004; p = .97</td>
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<tr>
<td>ERD * ESS</td>
<td>B = 142.31; p = .04</td>
<td>B = -145.47; p = .31</td>
<td>B = -25.06; p = .79</td>
<td>B = -38.63; p = .73</td>
<td>B = -0.02; p = .89</td>
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<td>ERD * MRC</td>
<td>B = 130.68; p = .07</td>
<td>B = -0.03; p = .78</td>
<td>B = -25.06; p = .79</td>
<td>B = -38.63; p = .73</td>
<td>B = -0.02; p = .89</td>
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<td>ERD * MAS</td>
<td>B = -106.32; p = .14</td>
<td>B = -0.04; p = .74</td>
<td>B = 67.39; p = .47</td>
<td>B = 78.54; p = .49</td>
<td>B = -0.09; p = .46</td>
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<tr>
<td>ERS * ESS</td>
<td>B = 193.90; p = .35</td>
<td>B = 0.05; p = .65</td>
<td>B = 45.29; p = .88</td>
<td>B = -54.83; p = .79</td>
<td>B = -0.02; p = .88</td>
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<td>ERS * MRC</td>
<td>B = 220.34; p = .28</td>
<td>B = 0.01; p = .95</td>
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<td>ERS * MAS</td>
<td>B = -222.55; p = .28</td>
<td>B = -88.26; p = .30</td>
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<td>B = -376.16; p = .06</td>
<td>B = 0.16; p = .10</td>
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</table>

S4 Table 4. Regression coefficients (B) and p-values for Stepwise regression between ERD/ERS and ESS, MRC and MAS for motor imagery. Regressions with p < .05 are written in red and bold.