Frontal and parietal EEG alpha asymmetry: A large-scale investigation of short-term reliability on distinct EEG systems

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Abstract

EEG resting state alpha asymmetry is one of the most widely investigated forms of functional hemispheric asymmetries in both basic and clinical neuroscience. However, studies yield very inconsistent results. One crucial prerequisite to obtain reproducible results is the reliability of the index of interest. There is a body of research suggesting a moderate to good reliability of EEG resting state alpha asymmetry, but unfortunately sample sizes in these studies are typically small. This study presents the first large scale short-term reliability study of frontal and parietal EEG resting state alpha asymmetry. We used the Dortmund Vital Study data set containing 541 participants. In each participant, EEG resting state was recorded eight times, twice with their eyes opened, twice with their eyes closed, each on two different EEG systems. We found good reliability of EEG alpha power and alpha asymmetry on both systems. Interestingly, we found no reliable alpha asymmetry in frontomedial brain regions, one of the most investigate brain regions in alpha asymmetry research. Furthermore, we investigated the link between EEG alpha asymmetry and handedness, since previous studies showed that right-handedness is associated with higher rightward alpha asymmetry. Our results only partly replicate this association. In conclusion, our results suggest that while EEG alpha asymmetry is an overall reliable measure, frontal alpha asymmetry should be assessed by using multiple electrode pairs. Furthermore, the question of EEG alpha asymmetry's association with handedness remains unsettled and needs further investigation.

1. Introduction

For decades, researchers have investigated frontal EEG alpha band (8–13 Hz) asymmetry and its role in psychopathology, motivation, and personality (Allen et al. 2018; Davidson et al. 1979; Gable et al. 2018; Harmon-Jones and Gable 2018; Reznik and Allen 2018). Using the search term "alpha asymmetry" on the scientific search engine PubMed yields almost 2000 hits (February 2021), reflecting the large body of literature that has accumulated on this specific form of hemispheric asymmetries.

Alpha has been proposed to have an inverse relationship with brain activity (Pfurtscheller et al. 1996). Thus, relatively higher right to left alpha power has commonly been interpreted as relatively higher left to right activity, and vice versa (Reznik and Allen 2018). To determine the extent of individual EEG alpha asymmetry, a laterality quotient (LQ) is calculated by subtracting left alpha power from right alpha power (ln[R] – ln[L]) (Reznik and Allen 2018). This way, positive LQ values represent higher relative right alpha power (left activity) while negative LQ values represent higher relative left alpha power (right activity). The amount of EEG alpha activity in the brain is influenced by the eye-status of the participant. In healthy subjects, EEG alpha activity is more pronounced when eyes are closed than when eyes are open (Barry et al. 2007). This decrease in alpha activity is thought to represent an increased activity of the visual system that is activated once eyes are opened and visual information is processed (Barry et al. 2007).

Frontal EEG alpha asymmetry has been associated with various forms of psychopathology, developmental disorders, as well as with interindividual variation in affective style and personality parameters (Reznik and Allen 2018). A vast body of research has associated major depression disorder

(MDD) (Allen et al. 2018) with increased left alpha asymmetry during rest (Debener et al. 2000; Metzger et al. 2004; Stewart et al. 2010) as well as during emotional tasks (Stewart et al. 2011, 2014). These effects can also be found in people with genetic risks for affective disorders (Christou et al. 2016) or remitted MDD (Stewart et al. 2010). Alpha asymmetry may also be linked to responding to antidepressants like serotonin reuptake inhibitors (Bruder et al. 2008) or the risk of affective disorders for children of depressed parents (Bruder et al. 2005). Alpha asymmetry may additionally be altered in people with attention deficit hyperactivity disorder (ADHD) (Alperin et al. 2019; Hale et al. 2009) or post-traumatic stress disorder (PTSD) (Meyer et al. 2015; Meyer et al. 2018).

The reason why frontal alpha asymmetry may be altered in affective and executive disorders could be the frontal lobes' role in motivational and affective traits in general (Davidson 1998). An especially important part of our personality is how we manage and regulate approach and withdrawal towards or away from stimuli (Gable et al. 2018). Approach-related behavior seems to be linked to higher left frontal activity while withdrawal-related behavior is linked to higher right in frontal activity (Coan and Allen 2003; Grimshaw and Carmel 2014; Harmon-Jones and Allen 1997; Koslov et al. 2011; Sutton and Davidson 1997). Frontal asymmetries have also been linked to positive affect and wellbeing (Papousek et al. 2019; Sutton and Davidson 2000; Urry et al. 2004; Wheeler et al. 1993), emotion regulation (Jackson et al. 2003; Papousek et al. 2012), stress regulation (Lewis et al. 2007; Quaedflieg et al. 2015; Zhang et al. 2018), and reward responsiveness (Pizzagalli et al. 2005). Thus, decreased left sided frontal activity in MDD and PTSD may reflect a tendency towards withdrawal-related behavior and negative affect, while increased left sided frontal activity in ADHD may reflect a tendency towards high approach-related behavior (Meyer et al. 2018; van der Vinne et al. 2017). Furthermore, a recent study found that frontal alpha asymmetries in socially avoidant mothers during emotion inducing conditions are able to predict their child's frontal asymmetry pattern (Krzeczkowski et al. 2020). Thus, individual differences in frontal asymmetry patterns may represent a neural mechanism through which withdrawal tendencies are passed onto the next generation. Overall, altered frontal hemispheric asymmetry may be linked to vulnerability for psychopathology and not to any disorders themselves (Ocklenburg et al. 2019).

Additionally, alpha asymmetries have been associated with another important measure of laterality: handedness. Handedness is an often used proxy for cerebral lateralization and can be assessed using questionnaires or tasks (Ocklenburg and Güntürkün 2018). A recent meta-analysis with over two million subjects showed that 81.9–90.7% of the population is right-handed, depending on the measurement of handedness (Papadatou-Pastou et al. 2020). However, research concerning the association of handedness and neurophysiological forms of asymmetry is relatively rare. A study by Ocklenburg et al. (2019) used a questionnaire to measure handedness as investigate its relationship to EEG alpha asymmetry at rest. They found that stronger right-handedness predicted greater rightward alpha asymmetry, or greater left activity. Similarly, a study by Packheiser et al. (2020) used a mobile EEG to measure alpha asymmetry while their participants performed manual tasks. In accordance with Ocklenburg et al. (2019) they found that right-handed subjects showed higher rightward alpha asymmetry during manual tasks, while left-handed subjects showed higher leftward alpha asymmetry during manual tasks. Thus, EEG alpha asymmetry appears to be correlated to behavioral laterality measures and can

distinguish between right- and left-handers. Furthermore, alpha asymmetry seems to be associated with both hand preference as measured by a questionnaire and actual manual performance.

However, not all results concerning alpha asymmetry effects on psychopathology and personality yield the same results and there are considerably inconsistencies between studies (Bruder et al. 1997; Jesulola et al. 2015; Nusslock et al. 2015; van der Vinne et al. 2017). For instance, a meta-analysis investigating the relationship between frontal alpha asymmetry and MDD found no significant link between the two (van der Vinne et al. 2017), indicating that the relationship between alpha asymmetry and depression is not as reliable as previously thought. Several methodological issues have been suggested as possible reasons for these inconsistencies, like duration of the EEG recordings, operationalization of diagnosis and symptoms or age (Thibodeau et al. 2006). Furthermore, it has been noticed that alpha asymmetries during emotionally demanding situations or tasks may be a much better indicator for affective disorders than alpha asymmetries during rest (Coan et al. 2006; Stewart et al. 2014) and that some symptom clusters may be better suited for prediction than others (Nusslock et al. 2015).

One essential prerequisite for replicable results is the reliability of EEG alpha asymmetry. For a long time alpha asymmetries have been regarded as a trait-like quality (Hagemann et al. 2002) that should not change considerably over time. Several studies have investigated test-retest reliability of alpha asymmetry on different sites over different periods of time, yielding moderate to good results, comparable to other laterality measures (Voyer 1998). In healthy samples, midfrontal EEG alpha asymmetry reliability three weeks apart yielded correlation coefficients between 0.53 and 0.66 (Davidson et al. 1992), frontal alpha asymmetry 1 month apart yielded a correlation coefficient of 0.57 (Winegust et al. 2014) and parietal alpha asymmetry 12 years apart yielded correlation coefficients of 0.57 (Tenke et al. 2018). Retest-reliability in depressed samples of frontal alpha 3 months apart yielded a correlation coefficient of 0.61 (Gold et al. 2013), different site alpha 8–16 weeks apart yielded correlation coefficients between 0.33 and 0.85 (Allen et al. 2004). A study investigating a mixed sample found correlation coefficients between 0.54 and 0.60 for frontolateral, frontomedial and parietal alpha asymmetries and no differences in test-retest reliability between depressed and non-depressed subjects (Vuga et al. 2006). Interestingly, a recent study investigated healthy subjects during an emotional face processing task one week apart. They found considerable reliability differences between recording sites (Koller-Schlaud et al. 2020). While frontolateral and parietomedial sites yielded acceptable reliability ($r = 0.63–0.73$), frontomedial and parietolateral sites yielded lower reliability ($r = 0.30–0.45$). Considering these effect sizes, it appear plausible that EEG alpha asymmetry is not entirely a trait-like quality but may be influenced by state-dependent variables as well (Hagemann et al. 2002; Peterson and Harmon-Jones 2009).

In this regard, it should be noted that the study of Koller-Schlaud et al. (2020) had a rather small sample size ($n = 23$). This may also be a critical point of the other mentioned studies investigating reliability of EEG alpha asymmetry, which's sample sizes range from 10 (Winegust et al. 2014) to 99 (Vuga et al. 2006). This may be especially critical considering the present critique concerning small sample sizes and effect sizes in the light of replication crisis, which is an important topic concerning all of neuroscience

(Button et al. 2013) and laterality-research (Brederoo et al. 2019; Brysbaert 2019; Ocklenburg et al. 2020). Another important point is that none of the above-mentioned studies has systematically investigated the reliability of alpha asymmetries between eyes-open and eyes-closed recordings. The studies investigating resting state EEG have either used an eyes-open and eyes-closed mixed design, calculating the mean over the whole recording (Davidson et al. 1992; Winegust et al. 2014) or investigated reliability within eyes-closed and eyes-open recordings but not between them (Tenke et al. 2018; Vuga et al. 2006). Thus, the reliability of EEG asymmetry between different eye-status conditions remains uninvestigated.

The aim of the present study was to investigate the short-term reliability of frontal and parietal alpha asymmetries and to test whether previous results can be replicated in a large sample of 541 healthy adults. In each participant, EEG resting state was recorded eight times, four times each on two different EEG systems. On each of the two systems, EEG resting state was recorded two times while the participant had their eyes open and two times while they had their eyes closed. Compared to previous reliability studies on EEG resting state asymmetries, our study has a substantially larger sample sizes, enabling a much more robust statement concerning the short-term reliability of EEG asymmetry measures. Considering EEG asymmetry's immense popularity in clinical as well as basic research, insight into its reliability is crucial.

Taken together, we first aimed to replicate overall leftward frontal alpha asymmetry(van der Vinne et al. 2017; Winegust et al. 2014) and rightward parietal alpha asymmetry in healthy subjects (Ocklenburg et al. 2019). Second, we aimed to replicate alpha asymmetry's association with handedness as reported by previous studies (Ocklenburg et al. 2019; Packheiser et al. 2020), with stronger right-handedness predicting greater rightward alpha asymmetry. Third, we wanted to investigate overall reliability of alpha power and alpha asymmetry on two distinct EEG systems. Fourth, we want to investigate, if reliability of alpha power is different between hemispheres or frontal and parietal brain regions as reported byKoller-Schlaud et al. (2020). Fifth, we want to investigate the effect of eye-status on alpha power and on alpha asymmetry and if this effect differs between hemispheres or brain regions. Lastly, we want to further investigate the effect of eye-status on reliability. We hypothesize, that there should be a decrease in reliability when comparing two recordings with different eye-status in contrast to two recordings with the same eye-status.

2. Methods

2.1. Participants

Data was obtained from the Dortmund Vital Study, an ongoing large-sample cohort study on the development of cognitive functions over a wide age range, carried out by the Leibniz Research Centre for Working Environment and Human Factors at the Technical University Dortmund (IfADo). The participants were recruited from local colleges, companies, and public institutions, and through advertisements in newspapers and public media. Data of a total of 583 participants were available. After controlling for outliers and excluding all participants that did not have any EEG data (see 2.4), the number of

participants analyzed was 541 (331 females, 503 right-handers). They ranged from 20 to 70 years of age (M = 44.71, SD = 14.07).

All participants gave their written informed consent before any study protocol was commenced. The study conformed to the Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the local Ethical Committee of IfADo.

2.2. Behavioral measures

The participants hand preference was measured using the Edinburgh Handedness Inventory (EHI) (Oldfield 1971). In this questionnaire participants are asked to answer 10 items regarding several everyday tasks – like writing or throwing – and which hand they are using for this task. The lateralization quotient (LQ) was measured using the following formula LQ [(R-L)/(R + L)]*100, with R being the sum of right-hand responses and L being the sum of left-hand responses. Hand performance was measured using the Pegboard Test (Francks et al. 2002). In this task participants sit in front of a board with ten holes on the side of the board nearest and furthest away from the participant. On one side the holes are filled with little sticks that the participants have to move from this side of the board to the other as fast as possible, using only their right or their left hand. Pegboard lateralization quotient (PegQ) was calculated using the following formula PegQ = [2 x (L-R)/(L + R)], with R being the average time the participant needed to complete the task with their right hand and L being the average time the participant needed to complete the task with their left hand. Participants completed the EHI at home (together with other questionnaires), the Pegboard test was carried out at the first recording day before the EEG testing started.

2.3. Procedure, EEG recording and preprocessing

The ongoing Dortmund Vital Study includes a series of EEG-based mental tasks in which different cognitive functions are tested. These tasks are performed in two test blocks, each lasting about two hours. The two test blocks take place on two different days on two different EEG systems. The time period between day 1 and day 2 varies and was 56.74 days on average (SD 86.89; range 1–906) for the cohort analyzed in the present study. Before and after completion of each test block, the resting-state EEG is measured (session 1 and session 2) with eyes open and closed for two minutes each.

EEG was recorded using a 64 channel actiCap system (Brain Products GmbH; Munich, Germany) with 1000 Hz sampling rate on day 1, and a 32 channel BioSemi system (BioSemi B.V.; Amsterdam, The Netherlands) with a 2048 Hz sampling rate on day 2. Electrodes were placed according to the international 10–20 system. Impedances were kept below 10 kΩ. EEG signal processing was performed in Matlab 2018b (The MathWorks Inc., Natick, Massachusetts) using functions of the EEGLab toolbox (Delorme and Makeig, 2004). The signal was band-pass filtered (1–30 Hz) before corrupted channels were identified and removed based on kurtosis and probability criteria. Subsequently the data was re-referenced to the average of all electrodes, segmented into 2 second epochs. Corrupted epochs were automatically identified and removed. On average, 94.1 % (SD = 4.6) of epochs were retained for EEG system 1 and 96.1 % (SD = 4.1) for EEG system 2. Epochs were extracted with 50% overlap using a

Hamming window and a Fast Fourier Transform was applied to determine Alpha band (8–13 Hz) power separately for eyes-open and eyes-closed conditions within each session and day.

2.4. Statistical Analysis

All calculations were conducted in RStudio (1.4.1103) using R 4.0.3 (2020-10-10). First, we excluded 16 subjects that did not have any EEG data. Furthermore, we identified outliers of alpha power values. Outliers were indicated by deviating at least three standard deviations from the mean. We had to exclude 26 more subjects, which left us with 541 subjects in total.

First, we examined the distribution of handedness (see 3.1) and the distribution of EEG alpha asymmetry (see 3.2). Here we used Bonferroni-corrected t-test against zero to determine if EEG alpha asymmetry was significantly different from zero.

Second, we calculated intra-class correlation (ICC) of all four recording per electrodes and EEG system (see 3.3), as ICC is a more accurate measurement of reliability than simple correlation coefficients (Koo and Li 2016; Winegust et al. 2014). Following guidelines for choosing the appropriate model of ICC and previous research using ICC for test-retest reliability of EEG data, we used an ICC(3,1) two-way mixed effect model (Koo and Li 2016; van der Velde et al. 2019). To further investigate the effect of eye-status on reliability, we created heatmaps of alpha power reliability for the left (F3, F7, P3, P7) and the right (F4, F8, P4, P8) electrodes for both EEG systems.

Third, we conducted two 2x2 repeated measure ANOVAs, with the dependent variable being EEG alpha power and the independent variables being eye-status (eyes-open, eyes-closed) and hemisphere (left, right) (see 3.4). After omitting all subjects with one or more missing values, these analyses were performed with 388 subjects.

Fourth, we calculated ICC for alpha asymmetry (see 3.5). Additionally, we created heatmaps of alpha asymmetry reliability for all electrode pairs (F3/F4, F7/F8, P3/P4, P7/P8) for both EEG systems. The EEG alpha AIs (Asymmetry Indices) were determined using the standard formula (ln[right electrode] – ln[left electrode]) (Reznik and Allen 2018). Positive AIs therefore reflect higher relative EEG Alpha power in the right hemisphere, and negative AIs reflect higher relative EEG Alpha power in the left hemisphere.

Fifth, we conducted two 4x2 ANOVA to investigate the effect of electrode pair (F3/F4, F7/F8, P3/P4, P7/P8) and eye-state (eyes-open, eyes-closed) on EEG alpha asymmetry in both EEG systems. Finally, we correlated EEG alpha asymmetry and handedness. Since the majority of alpha power recordings was not normally distributed (Kolgomorov-Smirnov-Tests, $p < 0.001$) we used Spearman's rank correlation coefficients for all aforementioned bivariate correlations. Even though the non-normality of our data violated one of the assumptions of ANOVA, we have decided to carry out our analysis due to our large sample size and F-test's general robustness under departures from normality (Pearson 1931; Schmider et al. 2010).

3. Results

3.1 Distribution of hand preference and hand skill data

Figure 1 shows the distribution of LQs measured via EHI and Pegboard test. The EHI LQ distribution shows a typical J-shape (M = 73.54, SD = 43.33), while the PegQ distribution shows a typical bell-shape (M = 0.06, SD = 0.09). The mean EHI LQ was significantly different from zero and indicated an overall rightward preference ($t_{(538)}$= 39.4, p < .001). Its range was between – 100 and 100. Overall, there were 35 subjects with an LQ lower than zero (indicating left-handedness) and 503 subjects with an LQ higher than zero (indicating right-handedness). There was one subject with an LQ of 0 (indicating ambidexterity). The mean PegQ indicated a significant rightward preference as well ($t_{(541)}$=15.31, p < .001), although less pronounced than for the EHI LQ.

3.2 Distribution of EEG alpha asymmetry data

Figure 2 shows the distribution of EEG alpha asymmetry in the eight different recordings per electrode pair (system 1 vs. system 2, session 1 vs. session 2, eyes-open vs. eyes-closed). For a first assessment of the data, we used Bonferroni-corrected t-tests against zero to determine whether there was a significant leftward or rightward alpha asymmetry for a specific electrode pair in each condition.

For alpha asymmetry of electrode pair F3/F4 only one measurement's mean was significantly unequal from zero ($t_{(525)}$ = -3.49, p = .018), namely the session 2 eyes-open recording with system 1 (M = -0.013, SD = 0.086). In contrast, for the electrode pairs F7/F8, P3/P4 and P7/P8 all recordings' means were unequal from zero, p ≤ .008, except for P7/P8's session 1 eyes-open recording with system 1 ($t_{(519)}$ = 1.67, p = 1, M = 0.012, SD = 0.16). Furthermore, frontal electrodes on average showed a leftward alpha power asymmetry (M = -0.022; range -0.338 to 0.145, SD = 0.06), while parietal electrodes showed a rightward alpha power asymmetry (M = 0.078; range -0.308 to 0.575, SD = 0.128).

3.3 Reliability of alpha power

Table 1 shows ICC of EEG alpha power for all electrodes and both EEG systems. Depending on classification criteria, ICC of alpha power can be considered good to very good (Cicchetti 1994; Koo and Li 2016). For system 1 (Brain Products) ICC from 0.7 to 0.75 for left-sided electrodes (M = 0.72), while it ranges from 0.69 to 0.76 (M = 0.71) for right electrodes. ICC for system 2 (BioSemi) is similar, ranging from 0.79 to 0.82 (M = 0.77) for left electrodes and 0.73 to 0.81 (M = 0.77) for right electrodes.

Table 1: ICC of EEG alpha power for left (F3, F7, P3, P7) and right (F4, F8, P4, P8) electrodes for EEG system 1 (Brain Products) and EEG system 2 (BioSemi), respectively.

	System 1	System 2
F3	0.72 ***	0.79 ***
F7	0.75 ***	0.82 ***
P3	0.71 ***	0.78 ***
P7	0.69***	0.75 ***
F4	0.72 ***	0.78 ***
F8	0.76 ***	0.81 ***
P4	0.69 ***	0.78 ***
P8	0.67 ***	0.73 ***

∗∗∗p < .001

Figure 3 shows the heatmaps of Spearman's rank correlation coefficients ρ between electrodes on the two different EEG systems, respectively. All correlation coefficients reach corrected alpha threshold of p = 0.00125. For the first EEG system (Brain Products), electrodes show Spearman's ρ between 0.7 and 0.94, $p < .001$. For the second EEG System (BioSemi) electrodes show Spearman's ρ between 0.74 and 0.95, $p < .001$. Results indicate that correlation between two same eye-status recordings is in general higher (0.91 – 0.94) than correlation between two different eye-status recordings (0.7 – 0.86).

3.4 Effect of eye-status and hemisphere on EEG alpha power

To investigate the effect of eye-status on EEG alpha power we conducted two 2x2 repeated measure ANOVAs for both EEG systems. The independent variables were eye-status (eyes-closed vs. eyes-open) and hemisphere (left vs. right).

System 1: Brain Products

The fist ANOVA – using EEG alpha power recorded with the Brain Products system – revealed a main effect of eye-status, $F_{(1,387)} = 418.84$, $p < .001$, $\eta_p^2 = 0.52$. Alpha power in the closed eye condition was higher ($M = 0.84$, $SD = 0.41$) than in the eyes-open condition ($M = 0.55$, $SD = 0.20$). There was a main effect of hemisphere as well, $F_{(1,387)} = 78.35$, $p < .001$, $\eta_p^2 = 0.17$. Alpha power was higher in the right hemisphere ($M = 0.71$, $SD = 0.31$) than in the left hemisphere ($M = 0.68$, $SD = 0.28$). Additionally, the interaction between eye-status and hemisphere reached significance, $F_{(1,387)} = 180.6$, $p < .001$, $\eta_p^2 = 0.32$. Bonferroni-corrected post-hoc t-tests revealed that while alpha power was higher in the right ($M = 0.87$, $SD = 0.43$) than in the left ($M = 0.81$, $SD = 0.4$) hemisphere in the eyes-closed condition, $p < .001$, this effect

was not present between right (M = 0.55, SD = 0.21) and left (M = 0.55, SD = 0.2) hemisphere in the eyes-open condition, p = 0.39.

System 2: BioSemi

The second ANOVA – using EEG alpha power recorded with the BioSemi system – also revealed a main effect of eye-status, $F_{(1,387)}$ = 498.64, p < .001, η_p^2 = 0.56. Just as in system 1, EEG alpha power was higher in the eyes-closed condition (M = 0.92, SD = 0.45) than in the eyes-open condition (M = 0.62, SD = 0.27). There was also a main effect of hemisphere, $F_{(1,387)}$ = 81.01, p < .001, η_p^2 = 0.17. Again, alpha power was higher in the right hemisphere (M = 0.79, SD = 0.36) than in the left hemisphere (M = 0.75, SD = 0.34). In the eyes-closed condition, the alpha power was higher in the right (M = 0.95, SD = 0.47) than in the left (M = 0.89, SD = 0.44) hemisphere, p < .001. This difference between right (M = 0.63, SD = 0.28) and left (M = 0.61, SD = 0.28) hemisphere was also present in the eyes-open condition, albeit smaller, p < .001.

3.5 Reliability of EEG resting state alpha asymmetry

Table 2 shows ICC of EEG alpha asymmetry power for all electrode pairs and both EEG systems. ICC of recordings conducted with system 1 (Brain Products) range from 0.5 to 0.65 (M = 0.58), ICC of recording conducted with system 2 (BioSemi) range from 0.56 to 0.7 (M = 0.63). Overall, ICC can be considered average to good (Cicchetti 1994; Koo and Li 2016).

Table 2: ICC of EEG alpha asymmetry for all electrode pairs (F3/F4, F7/F8, P3/P4, P7/P8) for EEG system 1 (Brain Products) and EEG system 2 (BioSemi), respectively.

	System 1	System 2
F3/F4	0.5 ***	0.56 ***
F7/F8	0.57 ***	0.6 ***
P3/P4	0.61 ***	0.66 ***
P7/P8	0.65 ***	0.69 ***

***p < .001

Figure 4 shows correlation heatmaps of the EEG resting state alpha power asymmetries from the eight recordings per electrode pair (session 1 vs. session 2, eyes-open vs. eyes-closed) for both EEG systems using Spearman's rank correlation. All correlation coefficients reach corrected alpha threshold of p = 0.00125. For both systems, electrode pair F3/F4 shows correlation coefficients between 0.4 and 0.71, F7/F8 shows coefficients between 0.55 and 0.83, P3/P4 shows correlation coefficients between 0.48 and 0.83 and P7/P8 shows correlation coefficients between 0.55 and 0.87. The heatmap shows that

correlation between two same eye-status recordings (0.64 – 0.87) are much higher than correlation between two different eye-status recordings (0.4 – 0.68).

3.6 Effects of electrode pair and eye-status on alpha asymmetry

To further investigate differences in EEG alpha asymmetry between electrode pairs and different eye-status condition, we conducted two 4x2 repeated measure ANOVA for both EEG systems. The independent variables were electrode pair (F3/F4, F7/F8, P3/P4, P7/P8) and eye-status (eyes-closed, eyes-open).

System 1 (Brain Products)

Mauchly's test for sphericity showed that the assumption of sphericity had been violated for the main effect of electrode (W = 0.5, p < .001) and the interaction of electrode pair and eye-status (W = 0.38, p < .001). Thus, degrees of freedom and p-values of these effects have been Greenhouse-Geisser corrected.

There was a main effect of electrode, $F_{(2.122,821.063)} = 113.87$, $p < .001$, $\eta_p^2 = 0.23$. Bonferroni-corrected t-tests revealed that all electrode pairs differed from each other, p < .001, except electrode pairs P7/P8 and P3/P4, p = 0.74. While both frontal electrode pairs showed leftward alpha asymmetry, this leftward asymmetry was larger in the F7/F8 pair (*M* = -0.05, *SD* = 0.1) than the F3/F4 pair (*M* = -0.01, *SD* = 0.01). Parietal electrode pairs P3/P4 (*M* = 0.07, *SD* = 0.13) and P7/P8 (*M* = 0.08, *SD* = 0.16) showed rightward alpha asymmetry.

There was also a main effect of eye-status, $F_{(1,387)} = 191.89$, $p < .001$, $\eta_p^2 = 0.33$. In the eyes-closed condition there was a rightward alpha asymmetry (*M* = 0.05, *SD* = 0.08) while the eyes-open condition's mean was close to zero (*M* = -0.004, *SD* = 0.07). Furthermore, the interaction between electrode pair and eye-status reached significance, $F_{(1.893,732.677)} = 63.76$, $p < .001$, $\eta_p^2 = 0.14$. Bonferroni-corrected post-hoc t-test revealed that in the F7/F8 electrode pair leftward alpha asymmetry was larger in the eyes-open (*M* = -0.06, *SD* = 0.12) than in the eyes-closed (*M* = -0.04, *SD* = 0.09) condition, p < .001. However, this difference was not present in the second frontal electrode pair F3/F4 (eyes closed: *M* = -0.006, *SD* = 0.07; eyes-open: *M* = -0.01, *SD* = 0.09), p = 0.1. On the other hand, in parietal electrode pairs P3/P4 and P7/P8, rightward alpha-asymmetry was larger in the eyes-closed condition (P3/P4: *M* = 0.1, *SD* = 0.17; P7/P8: *M* = 0.13, *SD* = 0.22) than in the eyes-open condition (P3/P4: *M* = 0.04, *SD* = 0.11; P7/P8: *M* = 0.02, *SD* = 0.14).

System 2 (BioSemi)

Mauchly's test for sphericity showed that the assumption of sphericity had been violated for the main effect of electrode (W = 0.4, p < .001) and the interaction of electrode pair and eye-status (W = 0.27, p < .001). Thus, degrees of freedom and p-values of these effects have been Greenhouse-Geisser corrected.

There was a main effect of electrode, $F_{(1.888,730.838)} = 85.07$, $p < .001$, $\eta_p^2 = 0.18$. Bonferroni-corrected t-tests revealed that all electrode pairs differed from each other, p < .001. F7/F8 shows leftward alpha asymmetry (*M* = -0.03, *SD* = 0.09) while F3/F4's mean was close to zero (*M* = 0.007, *SD* = 0.06). Parietal electrode pairs P3/P4 (*M* = 0.06, *SD* = 0.16) and P7/P8 (*M* = 0.11, *SD* = 0.19) showed rightward alpha asymmetry, with P7/P8 showing a larger one.

There was also a main effect of eye-status, $F_{(1,387)} = 71.86$, $p < .001$, $\eta_p^2 = 0.16$. Rightward alpha asymmetry was larger in the eyes-closed condition (*M* = 0.05, *SD* = 0.09) than in the eyes-open condition (*M* = 0.02, *SD* = 0.08). Furthermore, the interaction between electrode pair and eye-status reached significance, $F_{(1.888,730.838)} = 45.25$, $p < .001$, $\eta_p^2 = 0.10$. Bonferroni-corrected post-hoc t-test revealed that in the F7/F8 electrode pair leftward alpha asymmetry was larger in the eyes-open (*M* = -0.03, *SD* = 0.11) than in the eyes-closed (*M* = -0.02, *SD* = 0.08) condition, p = .042. However, this difference was not present in the second frontal electrode pair F3/F4 (eyes closed: *M* = -0.005, *SD* = 0.07; eyes-open: *M* = -0.009, *SD* = 0.08), p = 0.15. On the other hand, in parietal electrode pairs P3/P4 and P7/P8, rightward alpha-asymmetry was larger in the eyes-closed condition (P3/P4: *M* = 0.07, *SD* = 0.18; P7/P8: *M* = 0.15, *SD* = 0.24) than in the eyes-open condition (P3/P4: *M* = 0.04, *SD* = 0.16; P7/P8: *M* = 0.07, *SD* = 0.17).

Taken together, EEG alpha power shows good to very good reliability while EEG alpha asymmetry shows average to good reliability. There is a frontal leftward alpha asymmetry and a parietal rightward asymmetry. These tendencies, however, seem to be weaker in the electrode pairs F3/F4 and P3/P4 than F7/F8 and P7/P8. The parietal rightward alpha asymmetry is larger in the eyes-closed condition than in the eyes-open condition. The frontal leftward alpha asymmetry is stronger in the open-eye condition in electrode pair F7/F8, however there is no difference between eyes-closed and eyes-open condition in electrode pair F3/F4.

3.7 Association between handedness and EEG resting state alpha asymmetry

Figure 5 shows the Spearman's rank correlation heatmaps of the behavioral handedness indexes and alpha power asymmetry averaged across electrode pairs for both EEG systems. Figure 5 shows nominal significance, the corrected alpha threshold is p < .0025. Correlation of the two behavioral handedness indexes show a medium effect (ρ = 0.31, *p* < .001). Of the correlations between handedness measures and EEG conditions the correlation between PegQ and electrode pair, F3/F4 on system 1 (ρ = 0.12, *p* = .008) reached nominal significance, indicating that a stronger right-sided hand performance was associated with a stronger rightward alpha asymmetry in F3/F4. Unexpectedly, there was a nominally significant negative correlation between PegQ and P3/P4 alpha asymmetry on system 1 (ρ = -0.09, p = .036), indicating that a stronger right-sided hand performance is associated with left-ward alpha asymmetry in P3/P4. The correlation between the same variables did not reach significance using the second EEG system. While both correlations are significant on a nominal level, they do not meet the corrected alpha threshold.

Additionally, we calculated Spearman's rank correlation between the absolute LQ value (that is, the index for strength of handedness independent of direction) and EEG alpha asymmetry. The correlation coefficients are between ρ = -0.049 and r = 0.01, none reached significance, p = 0.9 – 0.29.

4. Discussion

EEG alpha asymmetry is one of the most widely investigated forms of hemispheric asymmetries (Reznik and Allen 2018). It has been suggested to be a stable trait that has stable long-term associations with motivational and personality traits, but also with psychopathology like MDD (Bruder et al. 1997; Bruder et al. 2008; Jesulola et al. 2015; Stewart et al. 2014). In contrast to this widely-cited idea, a recent meta-analysis did not find a strong relationship between frontal alpha asymmetry and MDD (van der Vinne et al. 2017). One crucial requirement for replicability of associations between EEG alpha asymmetries and cognitive or clinical variables is a high reliability of the alpha asymmetry LQ. While a body of previous EEG research on alpha asymmetry reliability exists, most studies rely on rather small sample sizes. The aim of the present study was to test the reliability of frontal and parietal alpha asymmetry in a larger dataset, comprising a total of 541 participants with four different EEG recordings on two EEG systems. This allowed us to assess reliability of EEG alpha asymmetry between different sessions within one day and recordings with eyes either closed or open. Since all subjects were tested twice with two different EEG systems we could also investigate if reliability is stable across distinct systems. Furthermore, we aimed to replicate results from previous research concerning overall direction of EEG alpha asymmetry as well as its connection to handedness.

We were able to replicate the overall leftward alpha asymmetry in frontal sites and the overall rightward alpha asymmetry in parietal sites. However, only one of eight recordings on the frontomedial (F3/F4) site revealed a significant leftward asymmetry, while all recordings on the frontolateral (F7/F8) site revealed significant leftward asymmetry. This is in line with findings by Ocklenburg et al. (2019), who also found no significant alpha asymmetry for electrode pair F3/F4 while reporting significant asymmetry for electrode pairs F7/F8, P3/P4 and P7/P8. This is surprising, however, as frontomedial EEG alpha asymmetry has been used as main indicator for frontal asymmetry in a large body of research (Harmon-Jones and Allen 1997; Krzeczkowski et al. 2020; Quaedflieg et al. 2015; Wheeler et al. 1993). Ocklenburg et al. (2019) argued, that one of the reasons for the lack of frontomedial (F3/F4) asymmetry may be the specific setup on the EEG cap. However, in our study this effect is present in recordings from two different EEG caps, one 64 channel system and one 32 channel system. Thus, it is unlikely that EEG setup is the only reason for the lack of asymmetry on frontomedial (F3/F4) site. One important methodological take-home message from the present study therefore is that researchers should consider including multiple frontal electrode pairs in their analysis when investigating frontal asymmetries.

We could only partly replicate the link between strong right-handedness and alpha asymmetry as presented by Ocklenburg et al. (2019). We could show a nominally significant positive association between handedness performance as measured by the Pegboard test and frontomedial (F3/F4) leftward EEG alpha asymmetry. This finding is in line with Ocklenburg et al. (2019) and Packheiser et al. (2020) as

stronger right-handedness is related to stronger frontal rightward alpha asymmetry, or in other words, higher leftward brain activity. Surprisingly, there was a negative association between hand performance and parietomedial (P3/P4) alpha asymmetry, indicating that stronger right-handedness is associated with stronger leftward alpha asymmetry, or higher rightward brain activity. However, the correlations albeit significant were small and did not reach significance after correcting for multiple comparisons. Furthermore, these associations were only present when analyzing the recording from the Brain Products system, but not the BioSemi system. Frontolateral (F7/F8) and parietolateral (P7/P8) sites did not show any link to handedness performance in any EEG system. Even more surprising is the fact that handedness preference as measured by EHI – which was the handedness measure used by Ocklenburg et al. (2019) – did not show any link to EEG alpha asymmetry. This was the case for the absolute LQ, a value of handedness strength, and the relative LQ, a value for strength and direction. One reason for those inconsistencies may be the small number of left-handed participants in the present study. Only 36 (6,5%) of our 557 participants had an LQ indicative of left-handedness, which is a very low amount in comparison to 64 or 25% of 235 subjects in Ocklenburg et al. (2019) and 26 or 51% of 51 subjects in Packheiser et al. (2020). However, our results clearly show that the question concerning the association of handedness and EEG alpha asymmetry needs further investigation, especially concerning differences between its association with hand performance and hand preference.

We also investigated reliability of absolute EEG alpha power and EEG alpha asymmetry. For EEG alpha power, the ICC between the four recordings from the Brain Products system ranged between 0.67 and 0.76, ICC of the four recordings from the BioSemi system ranged slightly higher between 0.73 and 0.82. Thus, alpha power reliability can be rated as good to very good, depending on interpretation criteria (Cicchetti 1994; Koo and Li 2016). Reliability does not differ between the two different hemispheres. Our more detailed analysis using bivariate Spearman's rank correlation between all four recordings per electrode and EEG system (see Fig. 3) emphasize alpha's good reliability. This analysis also revealed that reliability between two recordings with the same eye-status show higher correlations (up to .95) than two recordings with different eye-status. This indicates that reliability decreased by using both recordings conducted when subjects had their eyes closed and when they had their eyes open.

For EEG alpha asymmetry, ICC of the four electrode pairs range from 0.5 to 0.65 for the Brain Products System and again slightly higher from 0.56 to 0.69 for the BioSemi System. They can be rated as average or good, depending on interpretation criteria (Cicchetti 1994; Koo and Li 2016). Interestingly, in both systems the frontomedial (F3/F4) electrode pair shows the lowest ICC, followed by frontolateral (F7/F8), parietomedial (P3/P4) and partietolateral (P7/P8) electrode pairs. This reduced reliability of frontal EEG asymmetry might be due to the lack of especially frontomedial (F3/F4) alpha asymmetry in our study. These results further harden our suggestions to not rely on frontomedial EEG alpha asymmetry alone, but to include other frontal sites as well. The more detailed bivariate correlation analysis showed that correlation is a lot higher between same eye-status recordings (up to .87) than different eye-status recordings. This indicates, again, that reliability is higher if recordings with the same eye-status are used.

One important factor to keep in mind when interpreting our results is that we calculated reliability of a difference score, which are thought to be less reliable than the scores they are calculated from (Caruso 2004; Cronbach and Furby 1970). It has even been a point of argument if difference scores can be reliable at all (Trafimow 2015). What can be said is that high reliability scores comparable to – for instance – absolute alpha power are not to be expected from studies investigating alpha asymmetry. So, when keeping this in mind our study suggests an overall good short-term reliability for EEG alpha asymmetry, independent of EEG system.

Another factor that influences EEG alpha power and alpha asymmetry is the eye-status of participants, meaning if their eyes are closed or opened during the recording. Alpha power is generally higher when eyes are closed than when they are open. This effect has been shown in previous research (Barry et al. 2007) and can be explained by the activity in the visual system which is more active when eyes are open and visual input has to be processed. Additionally, there is more alpha power – or less activity – in the right hemisphere than in the left hemisphere when eyes are kept closed. However, this difference between hemispheres disappears when the eyes are opened.

There is also an effect of eye-status on alpha asymmetry. Furthermore, the direction of this effect is dependent on recording site. Parietal rightward alpha asymmetry was larger in the eyes-closed condition than in the eyes-open condition. In contrast, there is a larger frontolateral leftward alpha asymmetry in the eyes-open condition than the eyes-closed condition. There was no difference in EEG alpha asymmetry between eyes-closed and eyes-open recordings in frontomedial electrode pair (F3/F4), which is unsurprising due to the general lack of asymmetry in this electrode location. These results indicate that the effect of eye-status on alpha asymmetry should be considered when designing an experiment.

As far as we know, our study presents the largest EEG alpha asymmetry reliability study so far. However, our study does not come without limitations. One thing to consider when applying our results to experimental studies is that we measured EEG alpha asymmetry during rest, not during an emotional task. According to the capability model (Coan et al. 2006), EEG alpha asymmetry during an emotion-inducing task is a much better predictor of motivational or psychopathological variables associated with frontal activity. It appears plausible that EEG alpha asymmetry during a specific task may be more reliable than sheer resting state alpha EEG. Another important thing to consider is that we only tested healthy participants, but that EEG alpha asymmetries are an index that are also often used in clinical populations. Even though a previous study has found no difference in alpha asymmetry reliability between healthy and depressed populations (Vuga et al. 2006), our results may not apply for clinical cohorts. Furthermore, our analysis concerns short-term reliability of recordings conducted on the same day and our results may not be applicable to long-term reliability of EEG alpha power and EEG alpha asymmetry.

5. Conclusion

This study presents the largest frontal and parietal EEG alpha asymmetry reliability study so far. We found a good reliability of EEG alpha power and EEG alpha asymmetry on both investigated EEG systems. Frontal EEG alpha asymmetry seems to be less stable than parietal EEG alpha asymmetry. Furthermore, the eye-status of participants, meaning if their eyes are closed or opened during the recording, have a considerable effect on EEG alpha power and EEG alpha asymmetry and can lower the reliability if not controlled for in the study design. The general lack and low reliability of frontomedial EEG alpha asymmetry may present a reason for inconsistent results in alpha asymmetry research. Further studies investigating the reliability in clinical cohorts as well as during emotion-inducing tasks are needed to evaluate and interpret the results of experimental studies.

Declarations

6.1 Funding

The Dortmund Vital Study is funded by IfADo.

6.2 Conflicts of interest

All authors disclose no actual or potential conflicts of interest including any financial, personal, or other relationships with other people or organizations that could inappropriately influence (bias) their work.

6.3 Availability of data and material

The data that support the findings of this study was not acquired by the corresponding author, but is part of the Dortmund Vital Study and was provided by IfADo. Data are however available from the authors upon reasonable request and with permission of IfADo.

6.4 Code Availability

Available on request.

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Figures

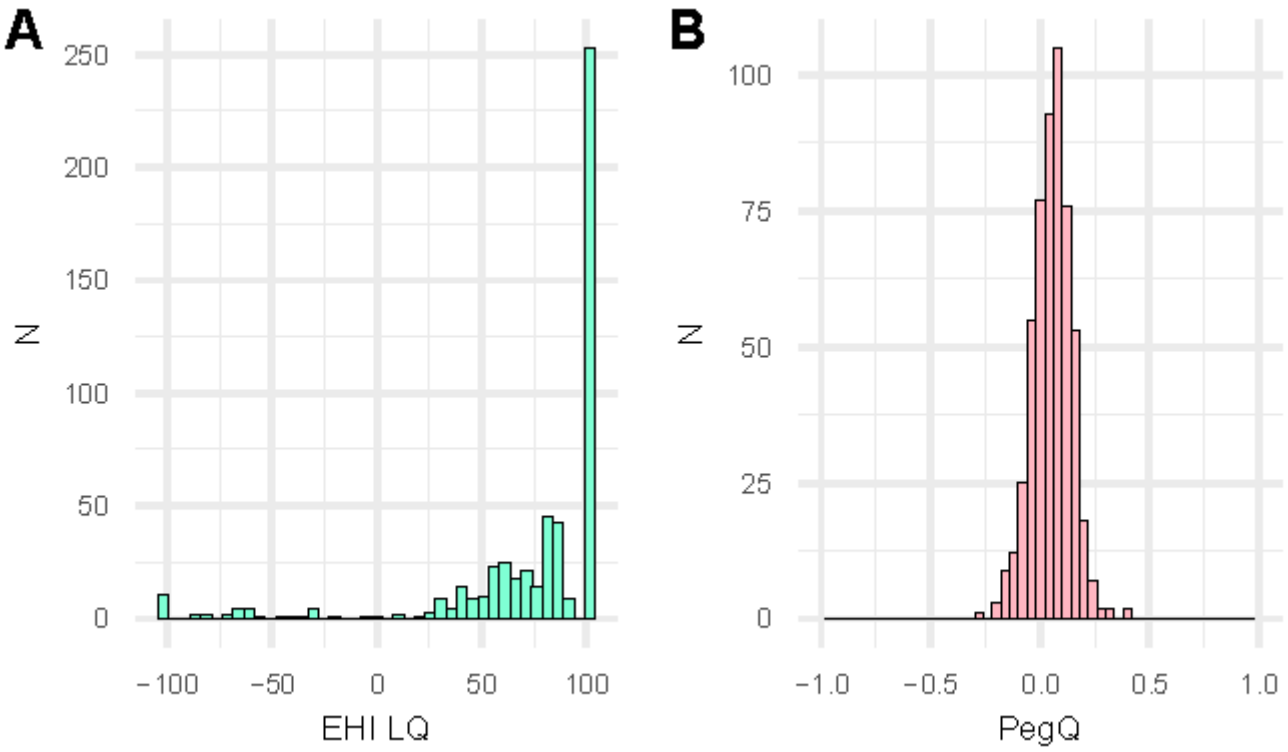

Figure 1

The distribution of handedness. A) number of participants (overall N=539) showing a certain laterality quotient (LQ) as measured by EHI. B) number of participants (overall N=540) showing a certain PegQ as measured by Pegboard test

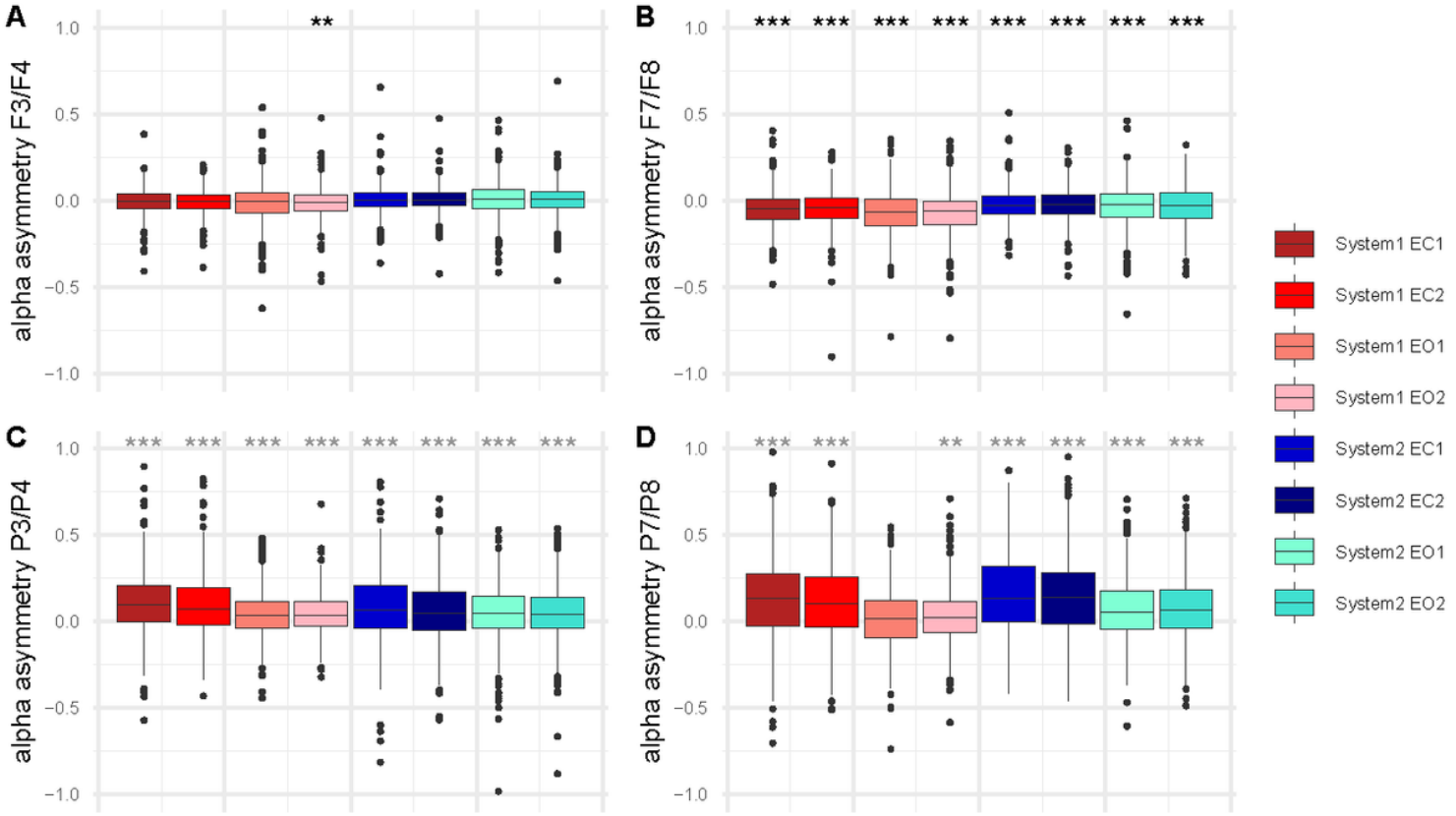

Figure 2

The Distribution of alpha asymmetry. The four panels show boxplots of the alpha asymmetry distribution of four electrode pairs over frontal (A: F3/F4; B: F7/F8) and parietal (C: P3/P4; D: P7/P8) scalp areas. Boxplots for each of our eight measurements per electrode pair are shown, separately for system 1 (Brain Products) and system 2 (BioSemi), with eyes open (EO) and eyes closed (EC), and for session 1 and 2. Dark horizontal lines within the boxplots mark the median. Lower and upper hinges correspond to the 25th and 75th percentile. Whiskers show the 95% confidence intervals. Black dots represent outliers. The asterisks above each boxplot show if this recording's mean is unequal to zero (* p<.05, ** p<.01, *** p<.001). Black asterisks indicate a mean significantly below zero, and gray asterisks indicate a mean significantly above zero

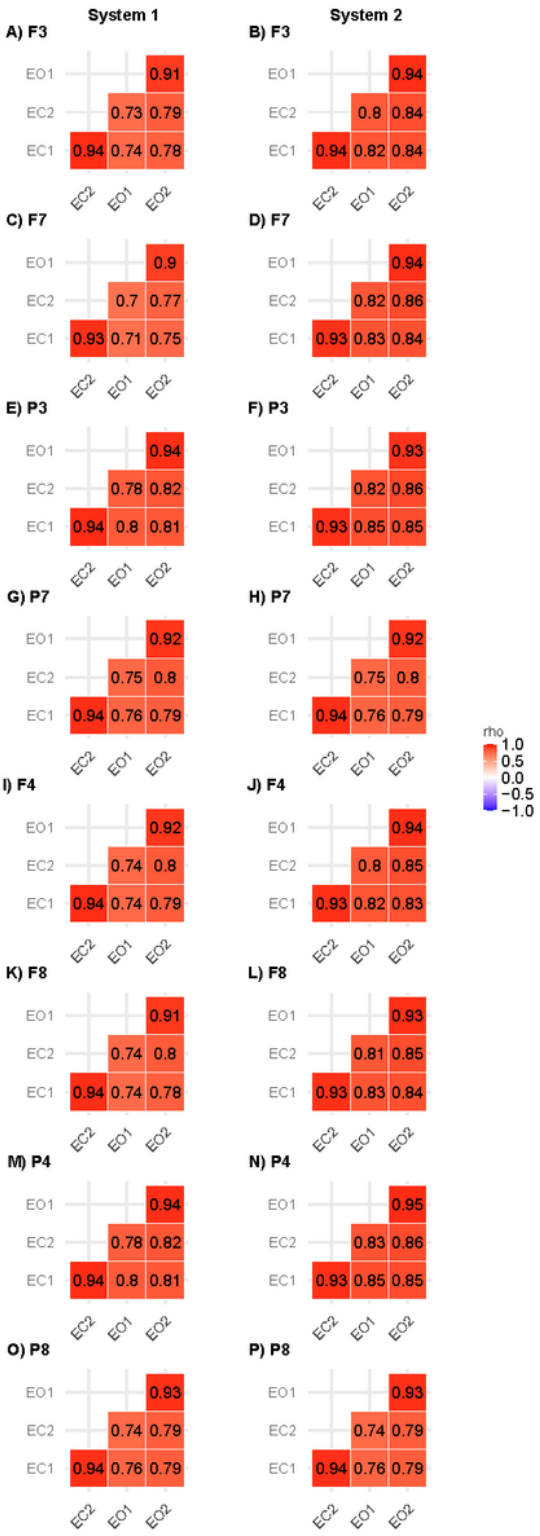

Figure 3

Spearman's rank correlation heatmap of EEG alpha per electrode. The panels show heatmaps of correlation coefficient ρ between the eight different measurements for the eight electrodes. A&B) F3, C&D) F7, E&F) P3, G&H) P7, I&J) F4, K&L) F8, M&N) P4 and O&P) F8 show recording conducted with EEG system 1 (Brain Products) on the left and heatmaps of recordings conducted with EEG system 2 (BioSemi) on the right. Positive correlations are shown in red, negative correlations are shown in blue. The

darker the color, the higher the correlation. The number in each square shows the rounded correlation coefficients. Nominal p-value of all recordings was *** p<.001

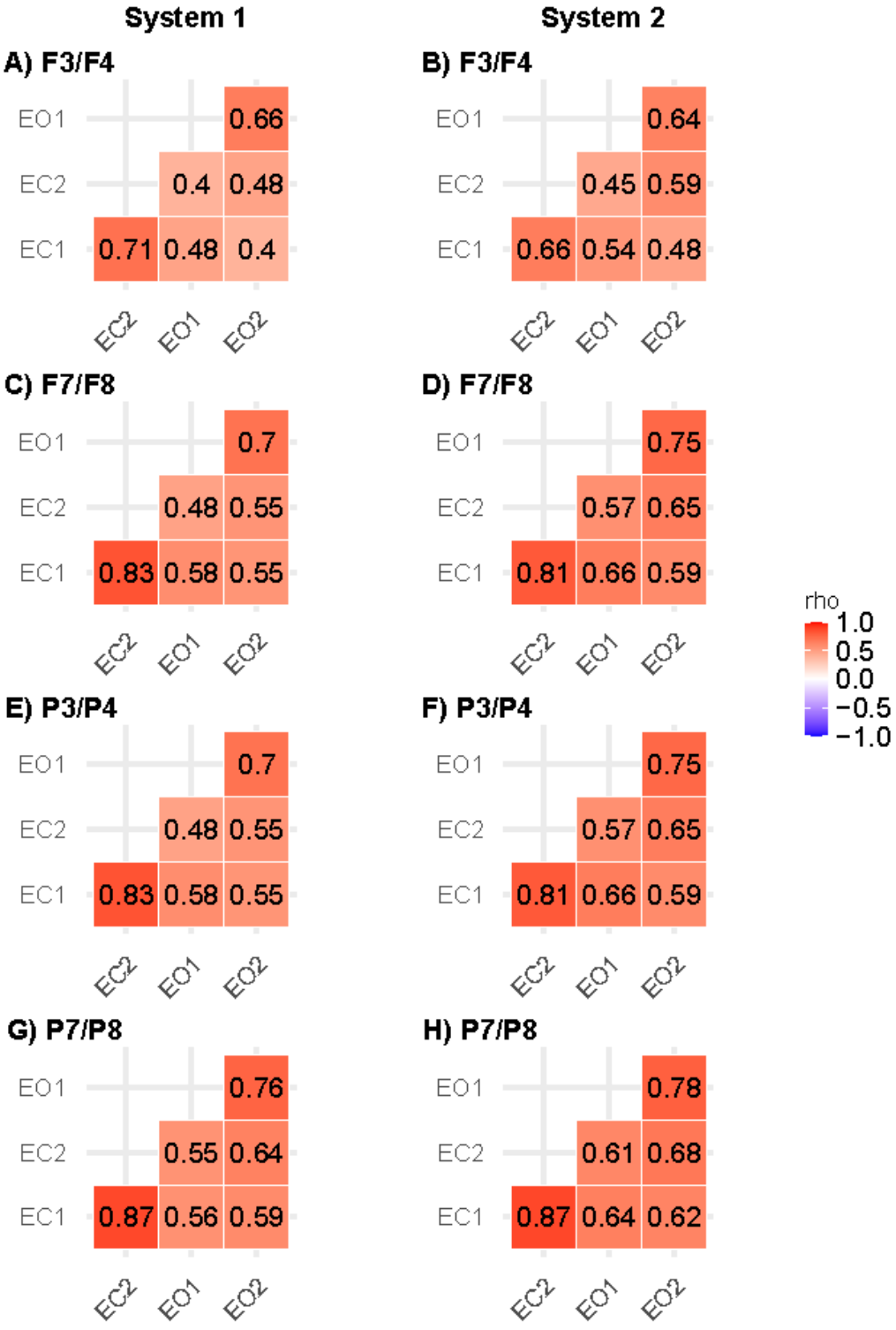

Figure 4

Spearman's rank correlation heatmap of EEG alpha asymmetry per electrode pair. The eight panels show heatmaps of correlation coefficient ρ between the eight different measurements for the four electrode pairs. A&B) F3/F4, C&D) F7/F8, E&F) P3/P4, and G&H) P7/P8 show recordings conducted with EEG

system 1 (Brain Products) on the left and recordings conducted with EEG system 2 (BioSemi) on the right. Positive correlations are shown in red, negative correlations are shown in blue. The darker the color, the higher the correlation. The number in each square shows the rounded correlation coefficients. Nominal p-value of all recordings was *** p<.001

Figure 5

Spearman's rank correlation heatmap of EEG asymmetry per system and electrode pair, and handedness measures. The calculation was conducted with the mean of all recordings of an electrode pair on the two systems. Positive correlations are shown in red, negative correlations are shown in blue. The darker the color, the higher the correlation. The number in each square shows the rounded correlation coefficients. The asterisks indicate the coefficient's nominal p-value (* p<.05, ** p<.01, *** p<.001)