Routledge
Taylor & Francis Group

Laterality: Asymmetries of Body, Brain and Cognition

ISSN: 1357-650X (Print) 1464-0678 (Online) Journal homepage: https://www.tandfonline.com/loi/plat20

Beyond frontal alpha: investigating hemispheric asymmetries over the EEG frequency spectrum as a function of sex and handedness

Sebastian Ocklenburg, Patrick Friedrich, Judith Schmitz, Caroline Schlüter, Erhan Genc, Onur Güntürkün, Jutta Peterburs & Gina Grimshaw

To cite this article: Sebastian Ocklenburg, Patrick Friedrich, Judith Schmitz, Caroline Schlüter, Erhan Genc, Onur Güntürkün, Jutta Peterburs & Gina Grimshaw (2019) Beyond frontal alpha: investigating hemispheric asymmetries over the EEG frequency spectrum as a function of sex and handedness, Laterality: Asymmetries of Body, Brain and Cognition, 24:5, 505-524, DOI: 10.1080/1357650X.2018.1543314

To link to this article: https://doi.org/10.1080/1357650X.2018.1543314

Published online: 02 Nov 2018.

LATERALITY: ASYMMETRIES OF BODY, BRAIN AND COGNITION
2019, VOL. 24, NO. 5, 505–524
https://doi.org/10.1080/1357650X.2018.1543314

Beyond frontal alpha: investigating hemispheric asymmetries over the EEG frequency spectrum as a function of sex and handedness

Sebastian Ocklenburg [a*], Patrick Friedrich [a*], Judith Schmitz[a], Caroline Schlüter[a], Erhan Genc[a], Onur Güntürkün[a], Jutta Peterburs[b] and Gina Grimshaw[c]

[a]Department of Psychology, Institute of Cognitive Neuroscience, Biopsychology, Ruhr-University Bochum, Bochum, Germany; [b]Biological Psychology, Heinrich-Heine University Düsseldorf, Bochum, Germany; [c]Cognitive and Affective Neuroscience Lab, School of Psychology, Victoria University of Wellington, Wellington, New Zealand

ABSTRACT
Frontal alpha EEG asymmetry, an indirect marker of asymmetries in relative frontal brain activity, are widely used in research on lateralization of emotional processing. While most authors focus on frontal electrode pairs (e.g., F3/F4 or F7/F8), several recent studies have indicated that EEG asymmetries can also be observed outside the frontal lobe and in frequency bands other than alpha. Because the focus of most EEG asymmetry research is on the correlations between asymmetry and other traits, much less is known about the distribution of patterns of asymmetry at the population level. To systematically assess these asymmetries in a representative sample, we determined EEG asymmetries across the head in the alpha, beta, delta and theta frequency bands in 235 healthy adults. We found significant asymmetries in all four frequency bands and across several brain areas, indicating that EEG asymmetries are not limited to frontal alpha. Asymmetries were not modulated by sex. They were modulated by direction of hand preference, with stronger right-handedness predicting greater right (relative to left) alpha power, or greater left (relative to right) activity. Taken together, the present results show that EEG asymmetries other than frontal alpha represent markers of asymmetric brain function that should be explored further.

ARTICLE HISTORY Received 18 August 2018; Accepted 26 October 2018

KEYWORDS EEG; frontal alpha asymmetry; oscillations; hemispheric asymmetries; laterality

Introduction

Hemispheric asymmetries are a general principle of functional organization in the human brain, and have been investigated using a number of behavioural, electrophysiological, and neuroimaging techniques and paradigms

CONTACT Sebastian Ocklenburg sebastian.ocklenburg@rub.de
*These authors contributed equally to this work.

(Güntürkün & Ocklenburg, 2017). One method of observing these asymmetries is through electroencephalographic (EEG) recording, which captures the oscillations generated within and between populations of neurons. Different populations oscillate at different frequencies (delta, theta, alpha, and beta) that can be isolated using statistical techniques such as the fast fourier transform (FFT). Although the *inverse problem* means that scalp locations cannot be mapped one-to-one to neural sources, source models suggests that, at a gross level, asymmetries observed on the scalp reflect functional asymmetries in underlying neural systems (Pizzagalli, Sherwood, Henriques, & Davidson, 2005; Smith, Cavanagh, & Allen, 2018).

By far the most commonly studied EEG asymmetry resides in the alpha band (8–13 Hz) over frontal sites (see for example the recent special issue of *Psychophysiology* devoted to this asymmetry; Allen, Keune, Schönenberg, & Nusslock, 2018). Frontal alpha asymmetry can be recorded either in the resting-state or in response to some sort of manipulation and is typically studied by researchers interested in emotional/motivational/affective processes and their relationship to psychopathology. Alpha is commonly taken to reflect the inverse of cognitive activity (Bazanova & Vernon, 2014; Coan & Allen, 2003), as alpha suppression is associated with attentional and cognitive engagement (Mazaheri et al., 2014). A number of studies show that resting frontal alpha asymmetry has good internal reliability and is moderately stable over time (Hagemann, Naumann, Thayer, & Bartussek, 2002; Tomarken, Davidson, Wheeler, & Kinney, 1992; Vuga et al., 2006) suggesting that it reflects trait asymmetry in frontal brain activity.

The original impetus for frontal asymmetry research comes from a series of studies showing that depression is associated with a relative decrease in resting-state left frontal (compared to right frontal) brain activity. This decrease in brain activity is reflected by a relative increase in left frontal (compared to right frontal) alpha (Schaffer, Davidson, & Saron, 1983). This finding has been confirmed by meta-analysis (Thibodeau, Jorgensen, & Kim, 2006). Subsequent studies have shown that this shift in resting frontal activity is maintained in those with remitted depression (Gotlib, 1998; Henriques & Davidson, 1990; Stewart, Bismark, Towers, Coan, & Allen, 2010) and in people at genetic or familial risk of disorder (Christou et al., 2016; Field, Fox, Pickens, & Nawrocki, 1995; Lusby, Goodman, Bell, & Newport, 2014) – suggesting that resting alpha asymmetry is a marker of *vulnerability* to depression, and not a marker of the depressed state itself. These findings have prompted a number of explanatory frameworks that might account for such a relationship. Some have tied these asymmetries to emotional/motivational states, with left hemisphere activity related to positive/approach-related emotions, and the right hemisphere with negative/withdrawal-related emotions (Davidson, 1998; Harmon-Jones, 2003). Yet others have focused on the role of frontal asymmetry in executive or regulatory functions that affect emotional processing (Gable, Neal, & Threadgill, 2018; Grimshaw & Carmel, 2014) or on trait asymmetry as a marker of capability to regulate emotional responses under challenge (Coan, Allen, & McKnight, 2006).

Beyond the large literature that has specifically addressed resting asymmetries in frontal alpha, resting-state asymmetries have also been studied in other brain regions, for example in temporo-parietal areas (Bruder et al., 2005; Bruder, Tenke, Warner, & Weissman, 2007; Grimshaw, Foster, & Corballis, 2014; Metzger et al., 2004; Stewart, Towers, Coan, & Allen, 2011), and in other frequency bands (Hale et al., 2010; Hale et al., 2014; Hofman & Schutter, 2012; Kremer, Lutz, McIntosh, Dévieux, & Ironson, 2016; Simon-Dack, Holtgraves, Marsh, & Fogle, 2013; van Bochove et al., 2016). Presumably asymmetries in different frequency bands in different locations reflect asymmetries in different brain networks, although, for the most part, the link between EEG asymmetries and functional brain asymmetries has not been established.

Beyond the well-researched associations with depression and other affective variables, asymmetries have also been investigated in relation to personality traits, schizophrenia, autism, and attention deficit disorder (for a review, see Allen et al., 2018). Given this large body of research, which indicates that asymmetries in EEG power have important functional consequences across multiple domains, it is somewhat surprising that there is almost no data (and certainly no consensus) on the distribution of these trait resting asymmetries in the population. This neglect of population-level asymmetries stands in stark contrast to all other areas of laterality research (e.g., in handedness, language asymmetry, spatial asymmetry etc.) where such population-level asymmetries are often a focus of research (Ocklenburg & Güntürkün, 2017). Theoretical advances in understanding the functional significance of EEG asymmetry may therefore be facilitated by a better description of the asymmetries themselves.

To that end, we measured resting-state EEG asymmetries in a large sample of neurologically healthy young adults, across brain regions, and in alpha, beta, delta and theta bands. Our primary goal was to identify the mean and distribution of asymmetry scores in each region/band, and to explore the relationships amongst them. In addition, we determined whether asymmetries were moderated by handedness or sex. Both direction and consistency of handedness are known to moderate other hemispheric asymmetries (Ocklenburg, Beste, & Güntürkün, 2013; Peters & Servos, 1989; Propper, Wolfarth, Carlei, Brunye, & Christman, 2018). These handedness effects likely explain why most EEG asymmetry studies exclude left-handers – meaning that we know very little about them. Some studies, however, have examined the relationship between EEG asymmetry and degree or consistency of hand preference within right-handers. In two studies ($N = 60$ and $N = 128$, respectively), Papousek and Schulter (1999) examined resting alpha asymmetry across regions, finding a negative correlation to degree of handedness at medial frontal (F3/F4) and central (C3/C4) sites, reflecting greater relative left hemisphere alpha power (or greater relative right hemisphere activity) in those with weaker right-handedness. A similar effect was reported by Propper and colleagues (Propper, Pierce, Geisler, Christman, & Bellorado, 2012) who compared frontal alpha asymmetry in consistent and inconsistent right-handers ($N = 17$), and found greater left hemisphere alpha (or greater right hemisphere activity) in inconsistent right-handers. These findings hint at a relationship between EEG asymmetry and handedness, but require further exploration in a sizeable sample of left-handers.

The second possible moderator we considered was sex, another variable that has been shown to influence hemispheric asymmetries in other domains (Hirnstein, Hugdahl, & Hausmann, 2018). Although a number of studies report that the relationship between frontal asymmetry and depression or other variables is different in men and women (Miller et al., 2002; Stewart et al., 2010), no studies specifically examine (or at least report) sex differences in resting asymmetry itself. Another line of research has focused on sex differences in task-related asymmetry (Galin, Ornstein, Herron, & Johnstone, 1982; Glass, Butler, & Carter, 1984) – however, these may well reflect sex differences in strategies used during task performance, and are again not informative about sex differences in resting-state EEG asymmetries that are our concern. Our study will therefore address this gap in the literature.

Materials and methods

Sample

Overall, 235 adults (125 women and 110 men; mostly university students) were tested. All participants reported no history or current treatment or diagnosis of psychiatric or neurological disorder. The average age was 23.60 years (standard deviation, SD = 3.66, range: 18 to 34 years). Participants' handedness was assessed using the Edinburgh inventory (Oldfield, 1971). Lateralization quotient (LQ) was determined following the formula $LQ = [(R-L)/(R + L)]*100$, with R reflecting the sum right-hand responses and L reflecting the sum of left hand responses.

There were 171 right-handers (average LQ: 87.29; SD = 18.14) and 64 left-handers (average LQ: −78.02; SD = 22.05). Left-handedness was deliberately oversampled in comparison to the general population, where it typically shows a distribution of 90% right-handers to 10% left-handers (Ocklenburg & Güntürkün, 2017). This was done in order to allow for a statistical analysis of a possible covariation effect with sufficient statistical power. Participants were treated in accordance with the declaration of Helsinki and gave written informed consent prior to participating in the study. The study was approved by the institutional ethics committee of the Faculty of Psychology at Ruhr-University Bochum, Germany.

EEG recording

EEG was recorded from 64 channels using an actiCAP electrode system with Ag-AgCL electrodes and a standard BrainAmp amplifier and the corresponding recording software BrainVision Recorder (Brainproducts, Gilching, Germany) at a sampling rate of 1000 Hz. Electrodes were arranged according to the International 10–20 system (FCz, FP1, FP2, F7, F3, F4, F8, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, T8, TP9, CP5, CP1, CP2, CP6, TP10, P7, P3, Pz, P4, P8, PO9, O1, Oz, O2, PO10, AF7, AF3, AF4, AF8, F5, F1, F2, F6, FT9, FT7, FC3, FC4, FT8, FT10, C5, C1, C2, C6, TP7, CP3, CPz, CP4, TP8, P5, P1, P2, P6, PO7, PO3, POz, PO4, PO8). Electrode FCz was used as primary reference during recording, but signals later underwent current source density (CSD) transformation (Peters & Servos, 1989). The CSD transformation replaces the potential at each electrode with the current source density, thus eliminating the reference potential. This was done in order to avoid contamination of asymmetries in specific electrode pairs by reference site and to minimize smearing of EEG power between electrode sites; the CSD transformation has been strongly recommended for EEG asymmetry analysis (Smith, Zambrano-Vazquez, & Allen, 2016). Impedances were kept below 10 kΩ.

EEG asymmetry measures were determined using recommended procedures (Allen, Coan, & Nazarian, 2004; Hagemann, 2004). Recording took place for 5 min with eyes closed, but for later analysis, the first and the last 30 s were deleted from the data. Thus, the overall duration of the EEG recording used for analysis was 4 min (4 blocks with a length of 1 min each). EEG data were processed off-line using BrainVision Analyzer 2 (BrainProducts, Gilching, Germany). Raw data were filtered with 1 Hz low cut-off and 30 Hz high cut-off (12 dB/oct). Data were then segmented into non-overlapping epochs of 1024 ms. Each epoch was then baseline-corrected to a mean voltage of zero to ensure comparability between segments and adjust for drift. Artefact rejection was conducted with a two-step procedure. First, the filtered data were visually inspected and gross technical artefacts were rejected. Segmented data were then subjected to automatic artefact rejection with an allowed minimum amplitude of −100 µV and a maximum amplitude of 100 µV. The overall number of trials rejected by this procedure was below 5% of the overall data. Fast Fourier Transformation was performed to obtain frequency band power, using a Hamming window of 10%. In order to retain as much data as possible we did not eliminate segments containing blinks, as these do not affect calculations of asymmetry. Also, blinks were a very rare occurrence, given participants had their eyes closed.

Power densities (power per unit bandwidth) for the four different frequency bands (Alpha (8–13 Hz), Beta (13–30 Hz), Theta (4–8 Hz) and Delta (1–4 Hz)) were then averaged across the whole recording session. We used densities (instead of raw power) to control for differences in bandwidth. Twelve electrode pairs (see Figure 1) were used to extract power for the different frequency bands (FP1/FP2, F3/F4, F7/F8, T7/T8, C3/C4, P3/P4, P7/P8, O1/O2, FC3/FC4, FT7/FT8, TP7/TP8, CP3/CP4). EEG asymmetry indices were determined using the formula (ln[right electrode] – ln[left electrode]) (Reznik & Allen, 2018). Thus, positive scores reflect higher right-sided power, and negative scores reflect higher left-sided power. Although alpha power is thought to reflect an inverse of cortical activity, the same is not true of the other frequency bands. Therefore, we report all asymmetries in terms of power, and not activity. This means that alpha (particularly) is not reported according to the conventional transformation from power to activity.

Results

General power differences between the frequency bands

In order to get a general impression of power differences between the four investigated EEG frequency bands independently of asymmetry, we first calculated the power density averaged across all 24 investigated electrode

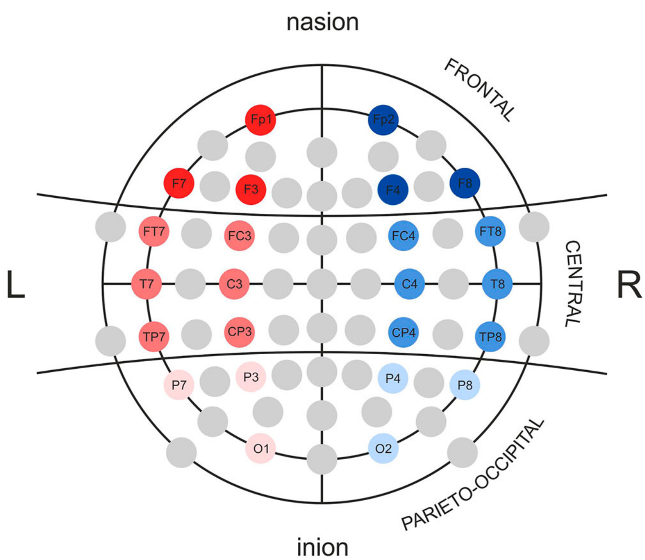

Figure 1. The twelve electrode pairs that were used to extract power for the different frequency bands and their classification into frontal, central and parieto-occipital regions (L: left; R: right).

sites for each frequency band (see Figure 2) and analyzed the data using a repeated measures analysis of variance (ANOVA) with the within-subjects factor frequency band (alpha, beta, delta, theta).

The main effect frequency band reached significance ($F_{(3,\ 234)} = 148.38$; $p < 0.001$; partial $\eta^2 = 0.39$), indicating significant power differences between the frequency bands. Bonferroni corrected post-hoc tests showed that power differed between all frequency bands (all $p < 0.0001$). Results showed that the highest power was detected in the delta frequency band (437.24; SE = 31.08), followed by the alpha (127.69; SE = 7.49), and theta (78.44; SE = 3.86) band. Notably, beta power (18.34; SE = 0.82) was relatively low, possibly because participants had their eyes closed.

EEG asymmetries at the electrode level

Because absolute power density differs across frequency bands, we use asymmetry indices in the remaining analyses. These are based on log transformed power densities (see Methods), and therefore largely control for differences in absolute power between frequencies. This allows one to interpret the interaction over electrodes as a change in topography without any further transformations (i.e., McCarthy & Wood, 1985).

In order to determine whether EEG asymmetries in different frequency bands were moderated by electrode location, we analyzed the asymmetry index by using a 12×4 repeated measures ANOVA with the within-subjects

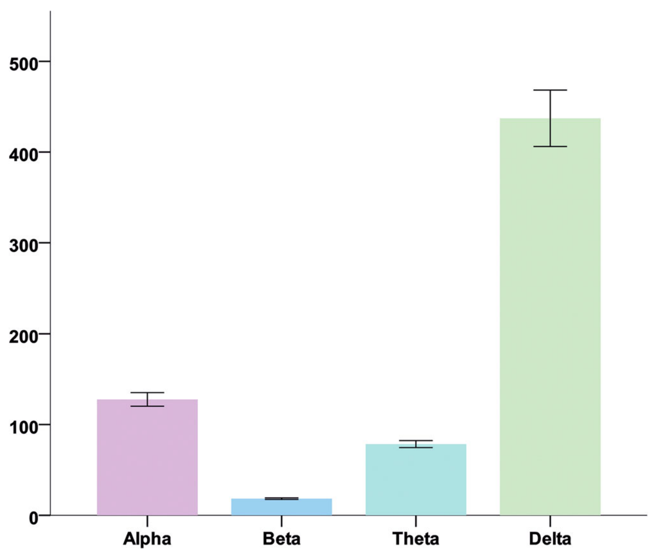

Figure 2. Average power ($\mu V/m^2$) in the alpha, beta, delta, theta, and gamma frequency bands. Error bars show standard errors.

factors electrode pair (FP1/FP2, F3/F4, F7/F8, T7/T8, C3/C4, P3/P4, P7/P8, O1/O2, FC3/FC4, FT7/FT8, TP7/TP8, CP3/CP4) and frequency band (alpha, beta, delta, theta). We observed a significant main effect of frequency band ($F_{(3,233)} = 3.69$; $p < 0.05$; partial $\eta^2 = 0.02$), a significant main effect of electrode pair ($F_{(11,233)} = 12.81$; $p < 0.001$; partial $\eta^2 = 0.05$), and a frequency band by electrode pair interaction ($F_{(33,233)} = 7.84$; $p < 0.001$; partial $\eta^2 = 0.03$). The interaction indicates that the distribution of asymmetries across the head differs across frequency bands.

In order to disentangle this interaction and determine which frequency bands showed significant asymmetries at which electrode pairs, we calculated one-sample t-tests against zero for the asymmetry scores for all frequency bands and electrode pairs. This allowed us to focus on our primary goal of describing the level of asymmetries in each location and in each frequency band in our sample. Since we conducted 4 (band) × 12 (electrode pair) comparisons this way, the p-value needed to reach significance was Bonferroni-corrected to $\alpha < (0.05/48) = 0.00105$. The distributions of individual data points for all electrode pairs and frequency bands are shown in Figure 3.

Significant hemispheric asymmetries were observed in each band except delta. The highest number of significant hemispheric asymmetries was observed in the alpha band. Here, the asymmetry index reached significance for electrode pairs C3/C4 (rightward; 0.23; $p < 0.001$), P7/P8 (rightward; 0.33; $p < 0.001$) and FC3/FC4 (rightward; 0.15; $p < 0.001$). A strong nonsignificant trend was also observed for electrode pair F7/F8 (leftward; −0.09; $p < 0.01$). Further non-significant trends were observed for electrode pairs FT7/FT8 (rightward; $p < 0.05$), P3/P4 (rightward; $p < 0.05$) and O1/O2 (rightward; $p < 0.05$). Surprisingly, the comparison failed to reach significance for electrode pair F3/F4 (−0.01; $p = 0.66$) – the electrode pair for which alpha band asymmetry has most often been correlated with traits or behaviour. For the beta band, the asymmetry index reached significance only for electrode pair C3/C4 (rightward; 0.23; $p < 0.001$), but nonsignificant trends were observed for electrode pairs F7/F8 (leftward; −0.10; $p = 0.003$), FC3/FC4 (rightward; 0.12; $p = 0.003$) and TP7/TP8 (leftward; −0.15; $p = 0.002$). For the theta band, electrode pair C3/C4 reached significance (rightward; 0.19; $p < 0.001$) and nonsignificant trends were observed for F7/F8 (leftward; −0.10; $p < 0.01$), T7/T8 (rightward; $p < 0.05$) and TP7/TP8 (rightward; $p < 0.05$). For the delta band, no significant asymmetries were observed, but electrode pair F7/F8 showed a nonsignificant trend (leftward; −0.12; $p = 0.003$).

EEG asymmetries for regions of interest

Since technical differences between EEG systems built by different manufacturers could introduce mechanical artifacts at specific electrodes that limit the comparability of our study with previous works, we also used a broader

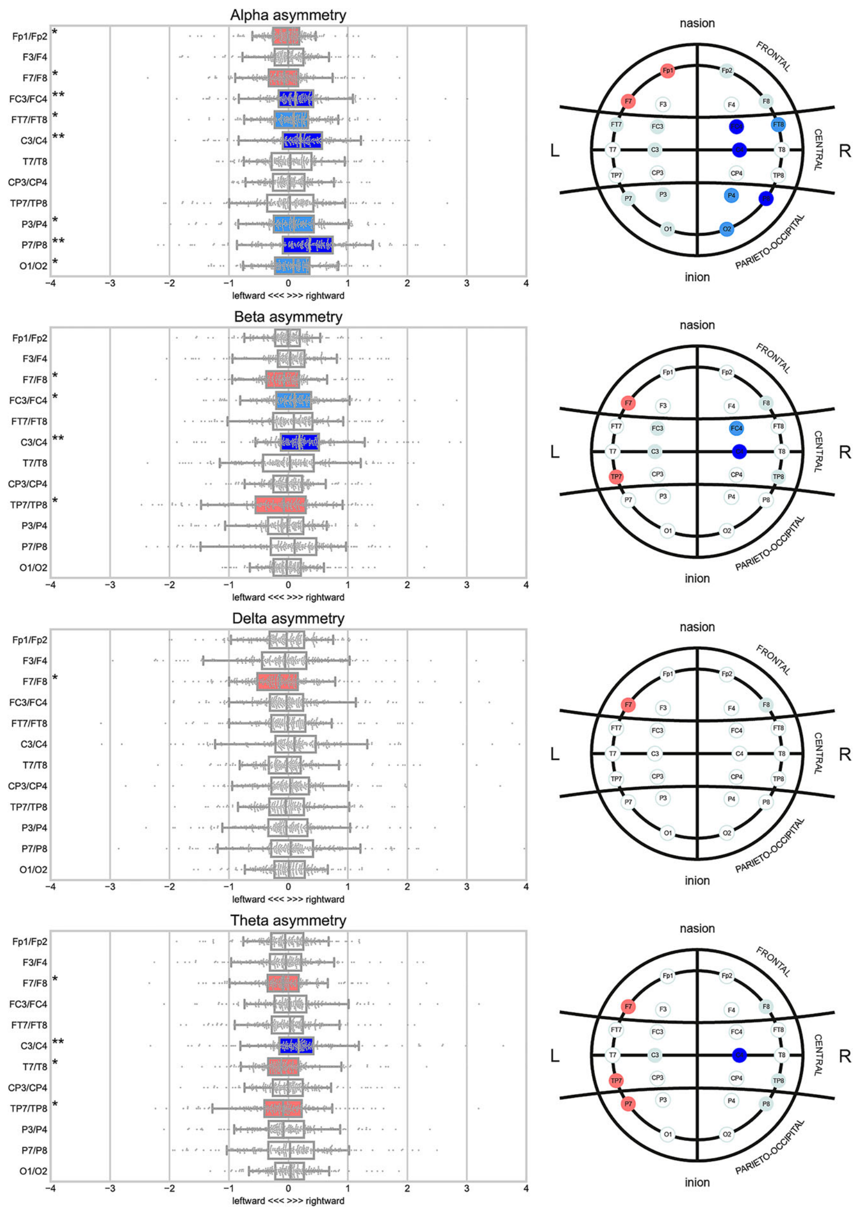

Figure 3. Distributions and topographical representations of individual asymmetry scores for all frequency bands and electrode pairs. Boxplots show the upper and lower quartile. Whiskers are showing the 5 to 95 percent percentile of the data. Colour coding indicates significance of t-tests and direction of effects. Deep red/blue indicates a leftward/rightward asymmetry that is significant after Bonferroni correction. Light red/blue indicates leftward/rightward asymmetry that is significant on the nominal significance level of $p < 0.05$. [To view this figure in color, please see the online version of this journal.]

classification scheme in which we investigated the average EEG asymmetry indices in frontal (FP1/FP2, F3/F4, F7/F8), central (T7/T8, C3/C4, FC3/FC4, FT7/FT8, TP7/TP8, CP3/CP4) and parieto-occipital (P3/P4, P7/P8, O1/O2) electrode regions (see Figure 1).

In order to determine which frequency bands showed significant asymmetries in which region of interest, we again calculated one-sample t-tests against zero for all frequency bands and regions of interest. Since we conducted 4×3 comparisons this way, the p-value needed in order to reach significance was Bonferroni-corrected to $\alpha < (0.05/12) = 0.004$.

Three asymmetry indices reached significance after correction for multiple comparisons: Alpha central (rightward; 0.08; SE = 0.02; $p < 0.001$), alpha parieto-occipital (rightward; 0.16; SE = 0.03, $p < 0.001$) and delta frontal (leftward; −0.09; SE = 0.03; $p < 0.001$). In addition, the asymmetry indices for alpha frontal (leftward; −0.05; $p = 0.036$) and theta frontal (leftward; −0.07; $p = 0.01$) reached nominal significance but did not survive the Bonferroni correction.

In order to determine whether there were asymmetries in the frequency bands independent of electrode pairs or regions (that is, across whole hemispheres), we also calculated the average asymmetry index collapsed across all 12 electrode pairs for each frequency band. Only the alpha band showed a significant rightward asymmetry (0.07; $t_{(234)} = -3.47$; $p < 0.001$), the other frequency bands failed to reach significance (all p's >0.60).

Correlations between asymmetry indices of different frequency bands

The average asymmetry indices collapsed across all 12 electrode pairs were highly and positively correlated between all frequency bands. Alpha correlated with beta ($r = 0.77$, $p < 0.001$), delta ($r = 0.50$, $p < 0.001$), and theta ($r = 0.74$; $p < 0.001$). Additionally, beta correlated with delta ($r = 0.57$, $p < 0.001$) and theta ($r = 0.75$, $p < 0.001$), and also delta with theta ($r = 0.88$, $p < 0.001$).

Sex differences in EEG asymmetries

In order to test whether EEG asymmetries were moderated by sex in our sample (125 women and 110 men), we re-calculated the above-mentioned ANOVA on asymmetry indices for the different electrode sites and frequency band with sex (male, female) as an additional between-subjects factor. Once again we observed a significant main effect of frequency band ($F_{(3,233)} = 8.25$; $p < 0.001$; partial $\eta^2 = 0.03$), a significant main effect of electrode pair ($F_{(11,233)} = 9.06$; $p < 0.001$; partial $\eta^2 = 0.04$), and a frequency band by electrode pair interaction ($F_{(33,233)} = 7.70$; $p < 0.001$; partial $\eta^2 = 0.03$). These effects reflect differences in asymmetry indices as a function of location and frequency band described above. However, neither the main effect of sex (p = 0.82), nor the two two-way interactions (both p-values > 0.36) reached significance.

EEG asymmetries and handedness direction

Since handedness has been suggested to be a major modulator of hemispheric asymmetries in the brain (Güntürkün & Ocklenburg, 2017; Willems, van der Haegen, Fisher, & Francks, 2014), we analyzed asymmetry indices for the different frequency bands by using a $12 \times 4 \times 2$ repeated measures ANOVA with the within-subjects factors electrode pair (FP1/FP2, F3/F4, F7/F8, T7/T8, C3/C4, P3/P4, P7/P8, O1/O2, FC3/FC4, FT7/FT8, TP7/TP8, CP3/CP4) and frequency band (alpha, beta, delta, theta), and the between-subjects factor handedness direction (left-handed, right-handed).

Again, the above-described main effects for frequency band and electrode pair, as well as the interaction of frequency band by electrode pair reached significance. In addition, the interaction between frequency band and handedness reached significance ($F_{(3,233)} = 4.30$; $p < 0.05$; partial $\eta^2 = 0.02$). To investigate this effect, we performed Bonferroni corrected post-hoc tests to compare left and right handers in each frequency band. However, the comparison between left- and right-handers did not reach significance for any one of the four frequency bands (all p's > 0.11). Rather, as can be seen in

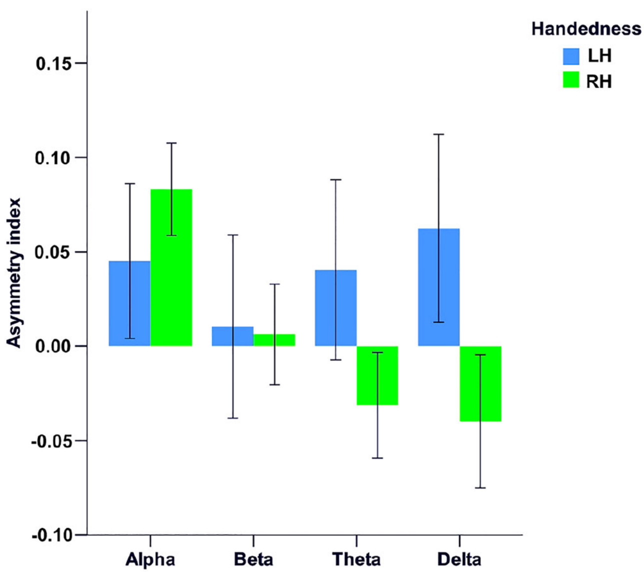

Figure 4. Average EEG asymmetries in the different frequency bands in relation to handedness.

Figure 4, left-handers show rightward asymmetries in all four frequency bands, while right-handers show a strong rightward asymmetry in the alpha band, while the asymmetry index is close to zero in the beta band. In the theta and delta band, right-handers, in contrast to left-handers, show leftward asymmetry. As indicated by the error bars in the figure, there seems to be a substantial degree of interindividual differences, which might explain why all post-hoc tests failed to reach significance.

Given the strong interest in frontal alpha asymmetry in the literature, we also conducted planned comparisons of left- and right-handers at each frontal electrode pair using independent samples t-tests. None of the comparisons reached significance and only for FP1/FP2 a nonsignificant trend was observed ($p = 0.07$), indicating a more negative (leftward) asymmetry index in left-handers (−0.13) than right-handers (−0.02).

EEG asymmetries and handedness LQ

In order to further explore the relation of handedness and EEG asymmetries, we calculated a linear regression model with the average EEG asymmetry indices in the alpha, beta, delta and theta band as predictors and handedness LQ as the dependent variable. Overall, the model reached significance ($R = 0.21$; $R^2 = 0.05$; corrected $R^2 = 0.03$; $F_{(4,234)} = 2.68$; $p < 0.05$), indicating that EEG asymmetries predict handedness LQ. The beta-weight for the alpha band ($\beta = 0.29$; $p < 0.05$) reached significance, while all other beta-weights failed to reach significance (all p's > 0.09). This indicates that participants with a higher LQ, e.g., stronger right-handedness, also show greater right relative to left alpha power. Given the common interpretation of alpha in terms of activity, this signifies that stronger right-handedness is association with greater relative left frontal activity (see Figure 5).

EEG asymmetries and handedness consistency

Because EEG alpha asymmetries have been studied in relation to consistency of hand preference (Propper et al., 2012), we recalculated the $12 \times 4 \times 2$ ANOVA handedness analysis, but instead of using handedness direction (left, right) as group factor we grouped participants into consistently handed ($n = 159$; LQ between −100 and −80 or between 80 and 100) or inconsistently handed ($n = 76$; LQ between −80 and 80). A cut-off of 80 on the Edinburgh Handedness Inventory has been commonly used to distinguish between consistent and inconsistent handers (Propper et al., 2018). Again, the same main effects for frequency band and electrode pair, as well as their interaction reached significance. However, the main effect of consistency and all interactions with this factor failed to reach significance (all p's > 0.20).

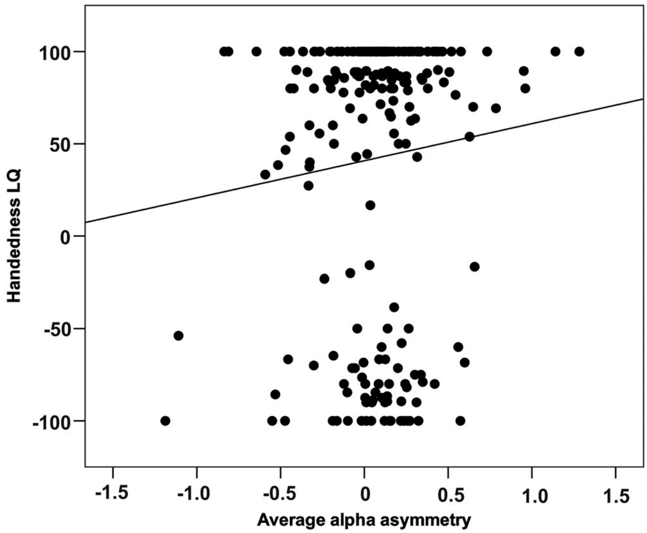

Figure 5. Individual handedness LQ in relation to average EEG alpha asymmetry. The line indicates the central tendency.

EEG asymmetries and handedness strength

In order to further explore the relation of handedness consistency and EEG asymmetry indices, we calculated a linear regression model with the average EEG asymmetry indices in the alpha, beta, delta and theta band as predictors and absolute handedness LQ as an interval-scaled measure of handedness strength independent of direction as the dependent variable. Overall, the model reached significance ($R = 0.20$; $R^2 = 0.04$; corrected $R^2 = 0.02$; $F_{(4,234)} = 2.42$; $p < 0.05$), indicating that EEG asymmetries predict absolute handedness LQ. The beta-weight for the beta band approached significance ($\beta = 0.20$; $p = 0.08$), while all other beta-weights failed to reach significance (all p's > 0.42). Notably, alpha asymmetry was not related to consistency in handedness.

Discussion

While the large majority of researchers interested in EEG asymmetries have focused on frontal alpha asymmetries, recent studies indicate that EEG asymmetries can also be observed in parts of the brain other than the frontal lobe and in frequency bands other than alpha (Simon-Dack et al., 2013). Here, we systematically investigated hemispheric asymmetries in alpha, beta, delta, and theta frequency bands in a large sample of 235 participants (171 right-handers and 64 left-handers) during resting-state.

In general, the highest power was detected in the delta frequency band, followed by alpha, theta and beta. This should be kept in mind when interpreting the EEG asymmetry results, as low power such as in the beta band might make the calculated asymmetry score more prone to distortions by outlier values for one hemisphere.

Overall, our results confirm that EEG asymmetries can be observed outside the alpha band in the frontal lobe. When single electrode sites were analyzed, significant asymmetries were observed in the alpha, beta and theta band, while for the delta band a non-significant trend was observed for electrode pair F7/F8. The highest number of significant hemispheric asymmetries was observed in the alpha band. As expected, we found EEG asymmetries in the alpha band for fronto-central electrode site (C3/C4, FC3/FC4 and a trend for F7/F8) and parietal electrode pairs (P7/P8). These are in line with the descriptive statistics of several previous studies for frontal (Bismark et al., 2010; Gollan et al., 2014; Lopez-Duran, Nusslock, George, & Kovacs, 2012), and parietal electrode pairs (Bruder et al., 2005; Bruder et al., 2007; Grimshaw et al., 2014; Metzger et al., 2004). Note, however, because the focus of these studies was on the correlates of asymmetries, e.g., depression, they did not explicitly report statistical tests for the existence of asymmetries per se, only comparisons of asymmetries between different groups.

For the beta and theta band, we found significant asymmetries at one fronto-central electrode site (C3/C4). For the delta band, a trend for one fronto-central electrode site was observed (F7/F8). Thus, our data show that fronto-central EEG asymmetries can be observed in all four investigated EEG frequency bands, keeping in mind that for the delta band only a trend was observed. Moreover, they indicate that for the alpha band, the parietal area of the brain also shows EEG asymmetries.

Interestingly, the statistical test failed to reach significance for electrode pair F3/F4, the site at which alpha asymmetries are most commonly reported to be related to trait or affective variables. Since this could be explained by the specific positions of the electrodes in our 64 electrode setup, we also analyzed the data using a region of interest approach in which all electrode sites for one brain region were grouped. For the alpha band, central and parieto-occipital regions reached significance with a rightward asymmetry, while frontal regions showed a non-significant trend towards leftward asymmetry. Moreover, a significant leftward asymmetry was also observed for frontal regions in the delta band. Thus, in line with the literature, these results show that most asymmetries can be observed in the alpha band (van der Vinne, Vollebregt, van Putten, & Arns, 2017), a notion that was also confirmed by the whole-brain analysis.

As for the direction of asymmetries, we found that for the alpha band, electrode sites C3/C4, P7/P8 and FC3/FC4 showed a positive asymmetry index, indicating greater right than left alpha power. The significant effects for electrode pair C3/C4 in the beta and theta bands also showed positive asymmetry scores, indicating greater right than left power. However, for the frontal electrode pair F7/F8 a negative asymmetry index was observed. This is in line with a recent meta-analysis on frontal EEG alpha asymmetries in depressed patients and controls (van der Vinne et al., 2017). van der Vinne et al. (2017) meta-analyzed 16 studies with a total of 1883 depressed patients and 2161 controls. Looking at frontal alpha asymmetry operationalized as F4-F3, they found that independent of which form of reference was used, both patients and controls showed a negative asymmetry index, indicating higher alpha power at the leftward electrode F3. Thus, their findings, like ours, indicate higher relative brain activity (at least as can be inferred by alpha power) in the right hemisphere in the resting-state.

Interestingly, EEG asymmetries in each frequency band were significantly correlated with asymmetries in the three other frequency bands, clearly showing that EEG asymmetries in different frequency bands are not independent of each other but that there seems to be some sort of underlying asymmetry "g" factor. This is particularly interesting because alpha and beta frequency bands are thought to reflect somewhat diametrically opposite cognitive functions, e.g., the absence vs. the presence of a concentrated cognitive effort. Thus, one would intuitively think there should be a negative correlation between alpha and beta asymmetries, which, however, was not the case.

Our findings indicated that handedness is a factor that should be at least considered when analyzing EEG asymmetry data, while sex does not seem to have a strong association with EEG asymmetries. Several previous authors reported more or less subtle associations of sex modulating the relation of EEG alpha symmetries with other variables (Glass et al., 1984; Miller et al., 2002; Stewart et al., 2010). In our study, however, we did not find any main effect or interaction including the factor sex. Given our large sample size this indicates that any associations between sex and EEG resting state asymmetries are very subtle at best. This has important implications for studies investigating task-related sex differences in EEG asymmetries. Our finding suggest that if such studies find significant sex differences they are likely not largely accounted for by initial differences in the resting state patterns. Instead they probably reflect task-dependent sex differences.

For handedness, we observed somewhat stronger effects. We found an interaction effect between direction of handedness (left or right) and frequency band for asymmetry scores. However, as all post-hoc tests failed to reach significance, the relation of handedness as a dichotomous variable and EEG asymmetry is hard to interpret and also rather subtle. In contrast, the link between LQ, a continuous measure of handedness, and EEG asymmetries clearly warrants more research. Here, the regression analysis showed that EEG asymmetries predict the LQ. This effect was driven in particular by the alpha band, with stronger right-handedness being associated with greater right relative to left alpha power. This shows that using the LQ as a handedness measure might be more worthwhile in EEG asymmetry studies than either handedness direction or handedness consistency.

For handedness consistency, there was a similar data pattern, with no significant results when handedness consistency was used as a dichotomous grouping factor. However, the regression analysis with handedness strength as a continuous variable again revealed a significant model, this time with beta asymmetries driving the effect.

These findings might appear to contradict the findings reported by Propper et al. (2012) who reported a strong link between inconsistent right-handedness and decreased alpha power over the right hemisphere, indicating increased activation of the right hemisphere activation. Note, however, that Propper et al. (2012) only included right-handers. Thus, our finding mirrors their relationship between LQ and asymmetry, but in a much larger sample.

One methodological point that has to be made about our results is that our sample does not represent the typical sample in the EEG asymmetry literature. On the one hand we deliberately over-sampled left-handers in order to gain sufficient statistical power to do meaningful group comparisons between left- and right-handers. On the other hand, we excluded participants with a history of mental illness, while many previous studies specifically target depressed populations. Researchers should keep these factors in mind when comparing our data with other study cohorts. Nonetheless, our findings provide a baseline for EEG asymmetries in healthy left- and right-handers which might be of interest for researchers planning applied EEG asymmetry research in these populations.

Moreover, the significant positive correlations between the asymmetry indices of different frequency bands are a methodological issue to keep in mind. This might have led to confounding effects in the regression analysis due to multicollinearity of predictors (Farrar & Glauber, 1967). Therefore, the results of this analysis should be interpreted with caution. However, high positive correlations between asymmetries in the different frequency bands constitute an interesting finding on its own that warrants more investigation. It could point to the existence of general EEG asymmetry factor, with participants showing highly positive alpha asymmetry also showing highly positive beta, theta and delta asymmetry. Alternatively, it could reflect structural or technical factors, like effects of the skull or the recording equipment. Beyond this notion, the present work has important implications for future studies. Investigations of the basic neuroscience underlying, for example, clinical applications of EEG asymmetries will need to look beyond frontal alpha.

To conclude, the present findings indicate that EEG asymmetries are neither limited to the alpha band nor are they limited to the frontal lobe. They also suggest that EEG asymmetries other than frontal alpha represent interesting markers of asymmetric brain function that should be explored further. Our findings indicate that asymmetries (at least in the alpha band) are modulated by handedness and thus provide some justification for the practice of excluding left-handers when exploring fundamental relationships between asymmetry and other variables. Nonetheless, investigations that focus on handedness may provide novel insights into these relationships, and so studies that explicitly compare left- and right-handers (with appropriate sample sizes) are called for (Willems et al., 2014).

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This research was supported by Bundesministerium für Bildung und Forschung (BMBF) [grant number 01DR17005] to S.O. and a Royal Society of New Zealand Catalyst Grant to G.G.

ORCID

Sebastian Ocklenburg http://orcid.org/0000-0001-5882-3200
Patrick Friedrich http://orcid.org/0000-0001-5120-5880

References

Allen, J. J. B., Coan, J. A., & Nazarian, M. (2004). Issues and assumptions on the road from raw signals to metrics of frontal EEG asymmetry in emotion. *Biological Psychology*, *67*(1-2), 183–218.

Allen, J. J. B., Keune, P. M., Schönenberg, M., & Nusslock, R. (2018). Frontal EEG alpha asymmetry and emotion: From neural underpinnings and methodological considerations to psychopathology and social cognition. *Psychophysiology*, *55*(1), 1–6.

Bazanova, O. M., & Vernon, D. (2014). Interpreting EEG alpha activity. *Neuroscience and Biobehavioral Reviews*, *44*, 94–110.

Bismark, A. W., Moreno, F. A., Stewart, J. L., Towers, D. N., Coan, J. A., Oas, J., … Allen, J. J. B. (2010). Polymorphisms of the HTR1a allele are linked to frontal brain electrical asymmetry. *Biological Psychology*, *83*(2), 153–158.

Bruder, G. E., Tenke, C. E., Warner, V., Nomura, Y., Grillon, C., Hille, J., … Weissman, M. M. (2005). Electroencephalographic measures of regional hemispheric activity in offspring at risk for depressive disorders. *Biological Psychiatry*, *57*(4), 328–335.

Bruder, G. E., Tenke, C. E., Warner, V., & Weissman, M. M. (2007). Grandchildren at high and low risk for depression differ in EEG measures of regional brain asymmetry. *Biological Psychiatry*, *62*(11), 1317–1323.

Christou, A. I., Endo, S., Wallis, Y., Bair, H., Zeegers, M. P., & McCleery, J. P. (2016). Variation in serotonin transporter linked polymorphic region (5-HTTLPR) short/long genotype modulates resting frontal electroencephalography asymmetries in children. *Development and Psychopathology*, *28*(1), 239–250.

Coan, J. A., & Allen, J. J. B. (2003). Frontal EEG asymmetry and the behavioral activation and inhibition systems. *Psychophysiology*, *40*(1), 106–114.
Coan, J. A., Allen, J. J. B., & McKnight, P. E. (2006). A capability model of individual differences in frontal EEG asymmetry. *Biological Psychology*, *72*(2), 198–207.
Davidson, R. J. (1998). Anterior electrophysiological asymmetries, emotion, and depression: Conceptual and methodological conundrums. *Psychophysiology*, *35*(5), 607–614.
Farrar, D. E., & Glauber, R. R. (1967). Multicollinearity in regression analysis: The problem revisited. *The Review of Economics and Statistics*, *49*(1), 92–107.
Field, T., Fox, N. A., Pickens, J., & Nawrocki, T. (1995). Relative right frontal EEG activation in 3- to 6-month-old infants of "depressed" mothers. *Developmental Psychology*, *31*(3), 358–363.
Gable, P. A., Neal, L. B., & Threadgill, A. H. (2018). Regulatory behavior and frontal activity: Considering the role of revised-BIS in relative right frontal asymmetry. *Psychophysiology*, *55*(1), e12910.
Galin, D., Ornstein, R., Herron, J., & Johnstone, J. (1982). Sex and handedness differences in EEG measures of hemispheric specialization. *Brain and Language*, *16*(1), 19–55.
Glass, A., Butler, S. R., & Carter, J. C. (1984). Hemispheric asymmetry of EEG alpha activation: Effects of gender and familial handedness. *Biological Psychology*, *19*(3-4), 169–187.
Gollan, J. K., Hoxha, D., Chihade, D., Pflieger, M. E., Rosebrock, L., & Cacioppo, J. (2014). Frontal alpha EEG asymmetry before and after behavioral activation treatment for depression. *Biological Psychology*, *99*, 198–208.
Gotlib, I. H. (1998). EEG alpha asymmetry, depression, and cognitive functioning. *Cognition & Emotion*, *12*(3), 449–478.
Grimshaw, G. M., & Carmel, D. (2014). An asymmetric inhibition model of hemispheric differences in emotional processing. *Frontiers in Psychology*, *5*, 489.
Grimshaw, G. M., Foster, J. J., & Corballis, P. M. (2014). Frontal and parietal EEG asymmetries interact to predict attentional bias to threat. *Brain and Cognition*, *90*, 76–86.
Güntürkün, O., & Ocklenburg, S. (2017). Ontogenesis of lateralization. *Neuron*, *94*(2), 249–263.
Hagemann, D. (2004). Individual differences in anterior EEG asymmetry: Methodological problems and solutions. *Biological Psychology*, *67*(1-2), 157–182.
Hagemann, D., Naumann, E., Thayer, J. F., & Bartussek, D. (2002). Does resting electroencephalograph asymmetry reflect a trait? An application of latent state-trait theory. *Journal of Personality and Social Psychology*, *82*(4), 619–641.
Hale, T. S., Kane, A. M., Tung, K. L., Kaminsky, O., McGough, J. J., Hanada, G., & Loo, S. K. (2014). Abnormal parietal brain function in ADHD: Replication and extension of previous EEG beta asymmetry findings. *Frontiers in Psychiatry*, *5*, 87.
Hale, T. S., Smalley, S. L., Walshaw, P. D., Hanada, G., Macion, J., McCracken, J. T., … Loo, S. K. (2010). Atypical EEG beta asymmetry in adults with ADHD. *Neuropsychologia*, *48*(12), 3532–3539.
Harmon-Jones, E. (2003). Early career award. Clarifying the emotive functions of asymmetrical frontal cortical activity. *Psychophysiology*, *40*(6), 838–848.
Henriques, J. B., & Davidson, R. J. (1990). Regional brain electrical asymmetries discriminate between previously depressed and healthy control subjects. *Journal of Abnormal Psychology*, *99*(1), 22–31.

Hirnstein, M., Hugdahl, K., & Hausmann, M. (2018). Cognitive sex differences and hemispheric asymmetry: A critical review of 40 years of research. *Laterality: Asymmetries of Body, Brain and Cognition*. doi:10.1080/1357650X.2018.1497044

Hofman, D., & Schutter, D. J. L. G. (2012). Asymmetrical frontal resting-state beta oscillations predict trait aggressive tendencies and behavioral inhibition. *Social Cognitive and Affective Neuroscience*, *7*(7), 850–857.

Kremer, H., Lutz, F. P. C., McIntosh, R. C., Dévieux, J. G., & Ironson, G. (2016). Interhemispheric asymmetries and theta activity in the rostral anterior cingulate cortex as EEG signature of HIV-related depression: Gender matters. *Clinical EEG and Neuroscience*, *47*(2), 96–104.

Lopez-Duran, N. L., Nusslock, R., George, C., & Kovacs, M. (2012). Frontal EEG asymmetry moderates the effects of stressful life events on internalizing symptoms in children at familial risk for depression. *Psychophysiology*, *49*(4), 510–521.

Lusby, C. M., Goodman, S. H., Bell, M. A., & Newport, D. J. (2014). Electroencephalogram patterns in infants of depressed mothers. *Developmental Psychobiology*, *56*(3), 459–473.

Mazaheri, A., van Schouwenburg, M. R., Dimitrijevic, A., Denys, D., Cools, R., & Jensen, O. (2014). Region-specific modulations in oscillatory alpha activity serve to facilitate processing in the visual and auditory modalities. *NeuroImage*, *87*, 356–362.

McCarthy, G., & Wood, C. C. (1985). Scalp distributions of event-related potentials: An ambiguity associated with analysis of variance models. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, *62*(3), 203–208.

Metzger, L. J., Paige, S. R., Carson, M. A., Lasko, N. B., Paulus, L. A., Pitman, R. K., & Orr, S. P. (2004). PTSD arousal and depression symptoms associated with increased right-sided parietal EEG asymmetry. *Journal of Abnormal Psychology*, *113*(2), 324–329.

Miller, A., Fox, N. A., Cohn, J. F., Forbes, E. E., Sherrill, J. T., & Kovacs, M. (2002). Regional patterns of brain activity in adults with a history of childhood-onset depression: Gender differences and clinical variability. *The American Journal of Psychiatry*, *159*(6), 934–940.

Ocklenburg, S., Beste, C., & Güntürkün, O. (2013). Handedness: A neurogenetic shift of perspective. *Neuroscience and Biobehavioral Reviews*, *37*(10 Pt 2), 2788–2793.

Ocklenburg, S., & Güntürkün, O. (2017). *The lateralized brain: The neuroscience and evolution of hemispheric asymmetries*. Saint Louis: Elsevier Science.

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, *9*(1), 97–113.

Papousek, I., & Schulter, G. (1999). EEG correlates of behavioural laterality: Right-handedness. *Perceptual and Motor Skills*, *89*(2), 403–411.

Peters, M., & Servos, P. (1989). Performance of subgroups of left-handers and right-handers. *Canadian Journal of Psychology/Revue Canadienne de Psychologie*, *43*(3), 341–358.

Pizzagalli, D. A., Sherwood, R. J., Henriques, J. B., & Davidson, R. J. (2005). Frontal brain asymmetry and reward responsiveness: A source-localization study. *Psychological Science*, *16*(10), 805–813.

Propper, R. E., Pierce, J., Geisler, M. W., Christman, S. D., & Bellorado, N. (2012). Asymmetry in resting alpha activity: Effects of handedness. *Open Journal of Medical Psychology*, *01*(04), 86–90.

Propper, R. E., Wolfarth, A., Carlei, C., Brunye, T. T., & Christman, S. D. (2018). Superior categorical and coordinate spatial task performance in inconsistent-handers relative to consistent-right-handers. *Laterality: Asymmetries of Body, Brain and Cognition*. doi:10.1080/1357650X.2018.1503287

Reznik, S. J., & Allen, J. J. B. (2018). Frontal asymmetry as a mediator and moderator of emotion: An updated review. *Psychophysiology*, *55*(1), e12965.

Schaffer, C. E., Davidson, R. J., & Saron, C. (1983). Frontal and parietal electroencephalogram asymmetry in depressed and nondepressed subjects. *Biological Psychiatry*, *18* (7), 753–762.

Simon-Dack, S. L., Holtgraves, T., Marsh, L. M., & Fogle, K. L. (2013). Resting electroencephalography correlates of pseudoneglect: An individual differences approach. *Neuroreport*, *24*(15), 827–830.

Smith, E. E., Cavanagh, J. F., & Allen, J. J. B. (2018). Intracranial source activity (eLORETA) related to scalp-level asymmetry scores and depression status. *Psychophysiology*, *55* (1), e13019.

Smith, E. E., Zambrano-Vazquez, L., & Allen, J. J. B. (2016). Patterns of alpha asymmetry in those with elevated worry, trait anxiety, and obsessive-compulsive symptoms: A test of the worry and avoidance models of alpha asymmetry. *Neuropsychologia*, *85*, 118–126.

Stewart, J. L., Bismark, A. W., Towers, D. N., Coan, J. A., & Allen, J. J. B. (2010). Resting frontal EEG asymmetry as an endophenotype for depression risk: Sex-specific patterns of frontal brain asymmetry. *Journal of Abnormal Psychology*, *119*(3), 502–512.

Stewart, J. L., Towers, D. N., Coan, J. A., & Allen, J. J. B. (2011). The oft-neglected role of parietal EEG asymmetry and risk for major depressive disorder. *Psychophysiology*, *48* (1), 82–95.

Thibodeau, R., Jorgensen, R. S., & Kim, S. (2006). Depression, anxiety, and resting frontal EEG asymmetry: A meta-analytic review. *Journal of Abnormal Psychology*, *115*(4), 715–729.

Tomarken, A. J., Davidson, R. J., Wheeler, R. E., & Kinney, L. (1992). Psychometric properties of resting anterior EEG asymmetry: Temporal stability and internal consistency. *Psychophysiology*, *29*(5), 576–592.

van Bochove, M. E., Ketel, E., Wischnewski, M., Wegman, J., Aarts, E., Jonge, B. d., … Schutter, D. J. L. G. (2016). Posterior resting state EEG asymmetries are associated with hedonic valuation of food. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, *110*, 40–46.

van der Vinne, N., Vollebregt, M. A., van Putten, M. J. A. M., & Arns, M. (2017). Frontal alpha asymmetry as a diagnostic marker in depression: Fact or fiction? A meta-analysis. *NeuroImage: Clinical*, *16*, 79–87.

Vuga, M., Fox, N. A., Cohn, J. F., George, C. J., Levenstein, R. M., & Kovacs, M. (2006). Long-term stability of frontal electroencephalographic asymmetry in adults with a history of depression and controls. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology*, *59*(2), 107–115.

Willems, R. M., van der Haegen, L., Fisher, S. E., & Francks, C. (2014). On the other hand: Including left-handers in cognitive neuroscience and neurogenetics. *Nature Reviews Neuroscience*, *15*(3), 193–201.