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The functional role of individual-alpha based frontal asymmetry in stress responding

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ABSTRACT

Asymmetry in frontal electrical activity has been suggested to index tendencies in affective responding and thus may be associated with hormonal stress responses. To assess the functional role of frontal asymmetry (FA) in stress, we measured FA at rest and following exposure to acute stress induced with the Maastricht Acute Stress Task (MAST; $N = 70$) in the standard 8–13 Hz band as well as based on individual alpha frequency (IAF) band. IAF-based resting FA_{F4-F3} was associated with the stress-induced neuroendocrine response, such that left individual frontal activity predicted smaller total cortisol increases in response to the MAST. Like previous studies, we found resting left-sided FA_{F8-F7} to predict trait behavioural activation measured with the BIS/BAS scales. FA remained unaffected by stress-induced cortisol response. These findings suggest that individual FA might reflect a trait-like characteristic that moderates the stress response. Our results underscore the utility of IAF in studying individual differences in stress responding.

1. Introduction

Research suggests that a functional lateralization in the prefrontal cortex is involved in affective processing (Coan, Allen, & McKnight, 2006; Davidson, 2004; Harmon-Jones, Gable, & Peterson, 2010; Heller, 1993). A reliable correlate of frontal activity is frontal asymmetry (FA) measured with electroencephalography (EEG). FA refers to the average difference in alpha-band activity (typically 8–13 Hz) between the left and right frontal areas across several minutes. FA measured while participants are at rest has been regarded as an index of individuals' trait-like style of affective processing, whereas FA measured during or after emotional challenge has been linked to state-dependent individual differences in affective processing (Coan & Allen, 2003b; Coan & Allen, 2004; Coan et al., 2006; Goodman, Rietschel, Lo, Costanzo, & Hatfield, 2013; Perez-Edgar, Kujawa, Nelson, Cole, & Zapp, 2013). For instance, more left-sided resting FA (i.e., higher activity in the left hemisphere) has been linked to superior emotional flexibility (Papousek, Reiser, Weber, Freudenthaler, & Schulter, 2012), more effective emotion regulation (Jackson et al., 2003) as well as to more positive and decreased negative affect (Tomarken, Davidson, Wheeler, & Doss, 1992). Furthermore, an association between right-sided FA and higher basal cortisol levels has been found in animal studies at baseline (Kalin, Larson, Shelton, & Davidson, 1998) and after maternal separation (Rilling et al., 2001) as well as in human studies in six-month-old infants at baseline and during a withdrawal task (Buss et al., 2003) and in students during a stressful exam period (Hewig et al., 2008).

While these findings suggest that resting FA may be predictive of stress hormonal responses, other lines of research indicate that the stress response itself might involve lateralized processes in the brain. That is, animal and human studies suggest that the right hemisphere initiates neuroendocrine and behavioural fight-or-flight responses, while the left hemisphere regulates them (Baeken et al., 2014; Davidson, 2000; Lueken et al., 2009; Sullivan & Gratton, 2002; Sullivan, 2004; Wittling & Pfluger, 1990). Right-sided FA at rest and in response to stress could thus be expected to predict stronger hormonal stress responses. However, to date, only three experimental studies have examined the relationship between FA, stress, and stress hormonal responses, and have yielded mixed results. Tops et al. (2005) found that the administration of cortisol shifted the relative FA to the right. In a follow-up study, however, these authors found that cortisol administration in a formal and arousing testing condition shifted FA to the left (Tops, van Peer, Wester, Wijers, & Korf, 2006). Alternatively, Lewis, Weekes, and Wang (2007) found that high in comparison to low examination stress increased relative right-sided FA activity.

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Previous research has shown that alpha frequency varies in peak and bandwidth from individual to individual (Bazanova & Vernon, 2014; Doppelmayr, Klimesch, Pachinger, & Ripper, 1998; Gasser, Bacher, & Steinberg, 1985; Tomarken, Davidson, Wheeler, & Kinney, 1992). Moreover, individual differences in alpha peak frequency have been related to several cognitive functions including perception, attention, memory (Klimesch, Schimke & Pfurtscheller 1993; for review see Klimesch, 1999). Thus, the use of fixed frequency bands in previous studies may have obscured information about specific individual differences in neurophysiology of the brain. Using individual alpha frequency bands could potentially improve the signal-to-noise ratio and thus improve reliability of FA measurements.

In the current study, we used the Maastricht Acute Stress Task (MAST: Smeets et al., 2012) to induce neuroendocrine stress responses and investigated the functional role of asymmetric frontal alpha oscillations. Based on previous studies, it was hypothesized that more right-sided FA at rest and in response to stress, would be related to higher cortisol increases in response to the MAST. Furthermore, it was expected that FA at rest would be associated with level of trait motivation. The second aim of the study was to examine whether FA based on an individualized alpha frequency band can provide a more sensitive measure of individual differences in lateralized stress responding.

2. Methods

2.1. Participants

The present experiment was part of a larger study that investigated frontal alpha asymmetry and resilience. Right-handed healthy male ($n = 30$) and female ($n = 40$) undergraduates (mean age: 20.83 SD 2.67; range: 18–31 years) were recruited via advertisements at Maastricht University. Participants were screened for eligibility using the following exclusion criteria: history of psychiatric, neurologic, cardiovascular or neuroendocrine diseases, heavy smoking (i.e., more than 15 cigarettes/day), medication use known to affect the autonomic nervous system (ANS) or hypothalamic–pituitary–adrenal (HPA) axis, drug use, or body mass index outside the normal range. Moreover, for women, the use of oral contraceptives served as an inclusion criterion to reduce variability in cortisol responses related to hormonal alterations throughout the menstrual cycle phase (e.g., Kudielka, Hellhammer, & Wust, 2009). Test protocols were approved by the standing ethics committee of the Faculty of Psychology and Neuroscience, Maastricht University. All participants signed a written informed consent and were given a small reward (course credits or money) in return for their participation.

2.2. Procedure

An overview of the experimental session is displayed in Fig. 1. All testing took place between 12:30 and 18:00 h to avoid morning fluctuations in the circadian rhythm of cortisol and time-of-day effects on frontal asymmetry (Velo, Stewart, Hasler, Towers, & Allen, 2012). Beforehand, participants were asked via email to refrain from eating, exercising extensively or drinking anything but non-sparkling water for 2 h prior to the experimental session. Upon arrival in the laboratory, participants received information on the experimental procedure and gave written consent. Next, a saliva sample was taken and participants were told that this sample would be immediately assayed to check their adherence to the instructions not to eat, drink, etc. This was done to increase truth-telling behaviour. In reality, the sample was discarded without being analyzed. Participants were seated in front of a 22-in. widescreen monitor (Philips, The Netherlands) at approximately 56 cm viewing distance and drank 200 ml of apple juice to standardize glucose levels (Kudielka, Hellhammer, & Kirschbaum, 2007).

2.3. Stress manipulation

The Maastricht Acute Stress Test (MAST: Smeets et al., 2012) consists of a 5 min preparation phase in which the task is explained and a 10 min acute stress phase that includes several exposures to cold pressor stress and various mental arithmetic challenges along with social-evaluative pressure (i.e., negative feedback). Specifically, in 5 trials that varied in duration from 60 to 90 s, participants immersed their hand into ice-cold water (2 °C; plexiglas box with an electrical cooler and a circulation pump from JULABO Labortechnik, Seelbach, Germany). In between the hand immersion trials, participants engaged in mental arithmetic challenges in which they had to count backwards as fast and accurately as possible in steps of 17 starting at 2043 for 45, 60 or 90 s. Whenever they counted too slowly or made a mistake, they received negative feedback (i.e., to count faster or start over again at 2043). To increase unpredictability and uncontrollability, participants were told that the order and duration of the hand immersion and mental arithmetic trials would be randomly chosen by the computer and that they would be videotaped.

2.4. Neuroendocrine stress responses

Cortisol values prior to and in response to the MAST were obtained with synthetic Salivettes (Sarstedt®, Etten-Leur, The Netherlands). Participants provided saliva samples 20 min after arrival in the lab (t_{base}), 5 min before ($t_{pre\text{-}stress}$) the MAST and 5 times afterwards (t_{+0}, t_{+10}, t_{+30}, t_{+40}, $t_{+55\,min}$ with reference to the end of the stressor). Samples were stored at −20 °C until cortisol levels were determined by a commercially available luminescence immune assay kit (IBL, Hamburg, Germany). Mean intra- and inter-assay coefficients of variation are typically less than 5%, and the lower and upper detection limits were 0.015 mg/dl (0.41 nmol/l) and 4.0 mg/dl (110.4 nmol/l), respectively. One female participant did not provide enough saliva to be analyzed. Thus, the final sample consisted of 69 participants.

Cortisol after arrival in the lab (t_{base}) and before the MAST ($t_{pre\text{-}stress}$) did not differ significantly ($F_{(1,64)} = 1.91$, $p = 0.17$). For the correlations, the Area Under the Curve with respect to increase (AUCi) from the pre-stress sample was calculated as a single measure of the total cortisol concentration in response to the MAST for each participant individually (cf. Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003).

2.5. Approach behaviour

Behavioural Inhibition and Activation System Scales (BIS/BAS scales; Carver & White, 1994). The BIS/BAS Scales were used to assess a person's disposition towards the two motivational systems i.e., approach and withdrawal. The questionnaire consists of 22 items assessing behavioural inhibition (BIS; 7 items) and behavioural activation (BAS; 13 items). The BAS is further divided into three subscales: fun seeking (BAS-F; 4 items), reward responsiveness (BAS-R; 5 items), and drive (BAS-D; 4 items). Participants answer the extent to which they agree with the statements on a four-point Likert-type scale, ranging from 1 (strong agreement) to 4 (strong disagreement). Higher scores relate to higher BIS/BAS sensitivity.

2.6. EEG data acquisition and analysis

The electroencephalogram (EEG) was recorded from 23 Ag/AgCl electrodes (F7, F3, Fz, F4, F8, FC3, FC4, T7, T8, C3, Cz, C4, CP3, CPz, CP4, P7, P3, Pz, P4, P8, O1, Oz, O2) positioned in an elastic cap according to the international 10–20 system using a BrainAmp amplifier and Brain Recorder software (BrainProducts, Germany). Signals were sampled continuously at 100 Hz, referenced online to the left mastoid (A1) and band-pass filtered (0.01–30 Hz). An electrode at AFz served as signal ground. Two electrodes at the outer canthi of both eyes recorded horizontal eye movements and two electrodes above and below the left eye recorded vertical eye movements. Scalp-electrode impedance was kept below 5 kΩ to ensure high-quality EEG recordings and homologous scalp electrodes were within 1 kΩ of each other. Participants were shown the raw recording signals to demonstrate common artefacts that occur due to body and eye movements. FA was measured before and after stress induction during two 4 min blocks, whereby participants focused on a black fixation cross on grey background on the computer monitor.

Offline analyses were performed with Vision Analyzer 2.0 (Brain Products, Germany). Consistent with data reduction procedures in previous FA studies (e.g., Meyer et al., 2014; for review see Allen, Coan, & Nazarian, 2004), the data was re-referenced offline to the average of A1 and A2, band-pass filtered from 1 to 30 Hz and corrected for EOG activity using an algorithm similar to Gratton, Coles, and Donchin (1983). To derive resting-state FA scores, 2 s epochs with 75% overlap were extracted. Epochs containing EEG changes exceeding ±75 μV were automatically omitted from averages. On average 955.61 (range = 895–1005; SEM = 2.49) of baseline and 963.67 (range = 913–1020; SEM = 2.10) of post stress epochs were artefact free. Artefact-free epochs were analyzed using fast-Fourier transformation (FFT) with a 100% Hanning window to compute power density values. Average power densities of the two 4 min resting state measurements were calculated and weighted for the number of artefact-free epochs for both the baseline and the post-stress measurement.

The individual alpha peak frequency (IAF) was determined as the dominant frequency rhythm between 5 and 15 Hz at the posterior electrode (Pz) on 3 min of resting eyes closed data (Doppelmayr et al., 1998; Klimesch, 1999). The IAF bandwidth was defined as the IAF ± 0.20 × IAF. The asymmetry scores were based on the IAF band and on the standard alpha band between 8 and13 Hz (FA) and were calculated on log-transformed alpha-power density values, ln(right) − ln(left). Positive alpha asymmetry scores indicate greater left than right frontal activity since alpha band power is inversely related to brain activity (Pfurtscheller, Stancak, & Neuper, 1996).

2.7. Data analysis

Cortisol data were log-transformed before analysis as Shapiro–Wilk tests of normality showed typical positive skewness of the data. Effectiveness of the stress induction procedure on neuroendocrine measures including differences between men and women were addressed using repeated measures ANOVA with time (6

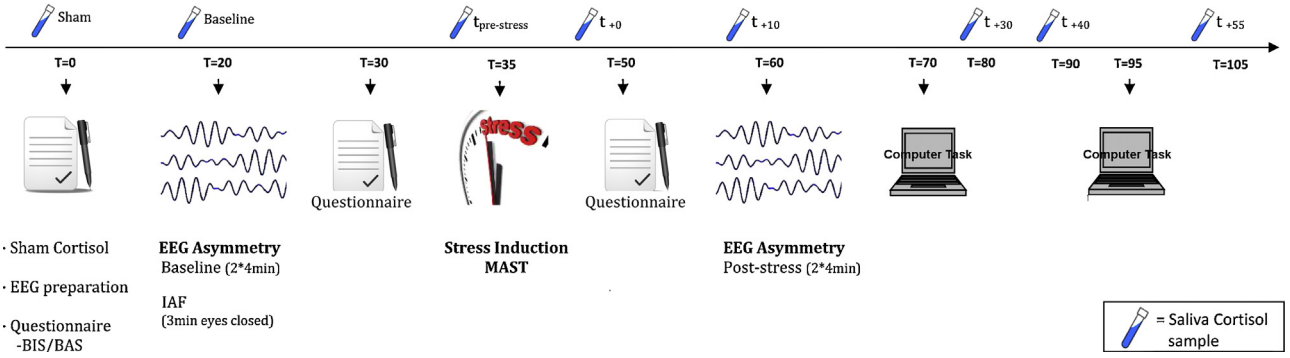

Fig. 1. Overview of the study procedure. t_{+0} refers to the end of the stress procedure. Abbreviations: IAF: Individual Alpha Frequency, MAST: Maastricht Acute Stress Test.

levels: $t_{\text{pre-stress}}$, t_{+0}, t_{+10}, t_{+30}, t_{+40}, $t_{+55\,\text{min}}$) as within subject variable and gender as between subject variable. Effects of the stress on FA as well as differences between men and women were addressed using repeated measures ANOVA with manipulation (baseline, post-stress) and location (F4–F3, F8–F7) as within subject variables and gender as between subject variable. To explore possible relationships between participants' physiological stress response (i.e., AUCi) and brain asymmetry, bivariate Pearson correlations were conducted. We used a hypothesis driven approach (i.e., including asymmetry scores at frontal electrodes only) to limit the inflation of Type I error rates in these analyses and corrected for multiple testing (i.e., F4–F3 and F8–F7) by using a significance level of $p \leq 0.025$. When sphericity assumptions for ANOVAs were violated, Greenhouse–Geisser corrected p-values, along with the respective epsilon and uncorrected degrees of freedom are reported.

3. Results

3.1. Stress manipulation: neuroendocrine responses

Mean cortisol concentrations prior to and following the MAST are shown in Fig. 2. Repeated measures ANOVAs revealed a significant time × gender interaction ($F_{(5,310)} = 5.09$, $p = 0.004$, Epsilon = 0.48). Follow-up analyses per gender reveal a main effect of time (6 levels: $t_{\text{pre-stress}}$, t_{+0}, t_{+10}, t_{+30}, t_{+40}, $t_{+55\,\text{min}}$; Males: $F_{(5,130)} = 22.84$, $p < 0.001$, Epsilon = 0.44; Females: $F_{(5,180)} = 8.14$, $p < 0.001$, Epsilon = 0.44). Bonferroni corrected simple effects per saliva time point revealed a significant increase between $t_{\text{pre-stress}}$ and t_{+10} (males: $p < 0.001$; females: $p = 0.01$) and a significant decrease between t_{+30} and t_{+40} (males: $p < 0.001$; females: $p < 0.001$) to a return to baseline at the end of the experiment ($t_{\text{pre-stress}}$ vs t_{+55} males: $p > 0.99$; females: $p > 0.99$).

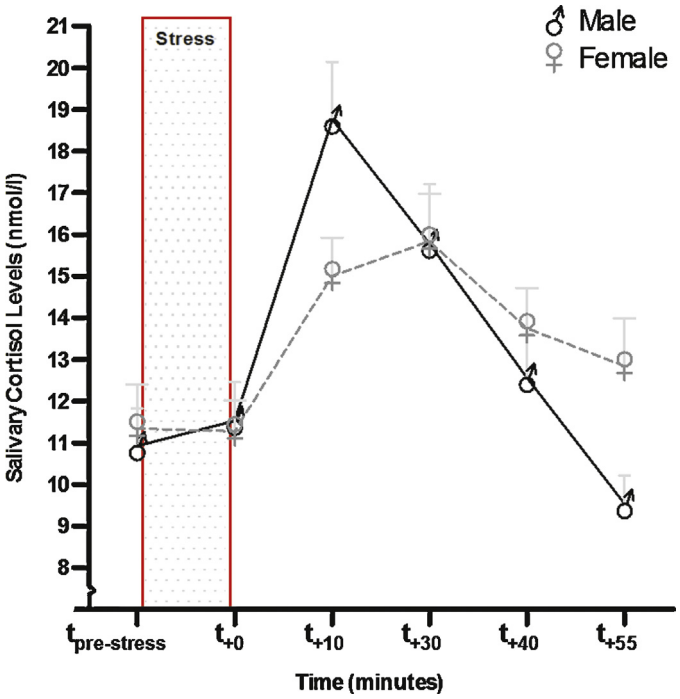

Fig. 2. Salivary cortisol responses to the Maastricht Acute Stress Test (MAST). Graphs show mean ± SE.

3.2. Frontal asymmetry: standard vs individual alpha

The mean of the IAF was 9.98 Hz (SEM 0.11; minimum = 7.4 maximum = 11.3) and was not statistically different from the centre (10 Hz) of the standard alpha band ($F_{(1,50)} = 0.05$, $p = 0.82$). Bivariate Pearson correlations were conducted between the first and second block of the baseline FA_{F4-F3} for the standard and IAF band separately to evaluate whether IAF-based FA yielded higher (test–retest) reliability scores than the standard 8–13 Hz alpha band. The standard alpha (8–13 Hz) based baseline FA_{F4-F3} correlation between the two four minute blocks was $r_{67} = 0.70$ and the IAF-based FA correlation was $r_{67} = 0.85$. These correlations were significantly different (baseline: $Z = -2.22$, $p = 0.026$, two-tailed) indicating a better test-retest stability for IAF-based FA_{F4-F3}.

3.3. Frontal asymmetry and stress induction

For the mean power density values based on standard alpha band (8–13 Hz), repeated measures ANOVA with manipulation (baseline, post-stress) and location (F4–F3, F8–F7) as within subject variables and gender as between subject variable revealed no significant interactions and only a main effect of location ($F_{(1,67)} = 25.84$, $p < 0.001$). Likewise, for the IAF-based FA, no significant interactions and only a main effect of location ($F_{(1,67)} = 25.69$, $p < 0.001$) was found, indicating that stress did not directly affect frontal asymmetry[1] (see Fig. 3).

3.4. Frontal asymmetry, neuroendocrine response and behavioural activation

Bivariate Pearson correlations between participants' physiological stress response and brain asymmetry were computed. Table 1 displays the correlations between total cortisol concentration (AUCi) and the standard alpha band (8–13 Hz) and IAF for baseline, post-stress and stress-reactivity (i.e., $\text{Asym}_{\text{baseline}} - \text{Asym}_{\text{post-stress}}$) asymmetry measures. For IAF-based baseline F4–F3 asymmetry, a negative correlation ($r_{67} = -0.27$; $p = 0.025$) was found, showing

[1] Hemisphere specific stress effects were assessed using a MANOVA with manipulation (baseline, post-stress) and hemisphere (left, right) as within subject variables and gender as between subject variable. No manipulation × hemisphere interaction was found ($F_{(1,67)} = 2.58$, $p = 0.12$).

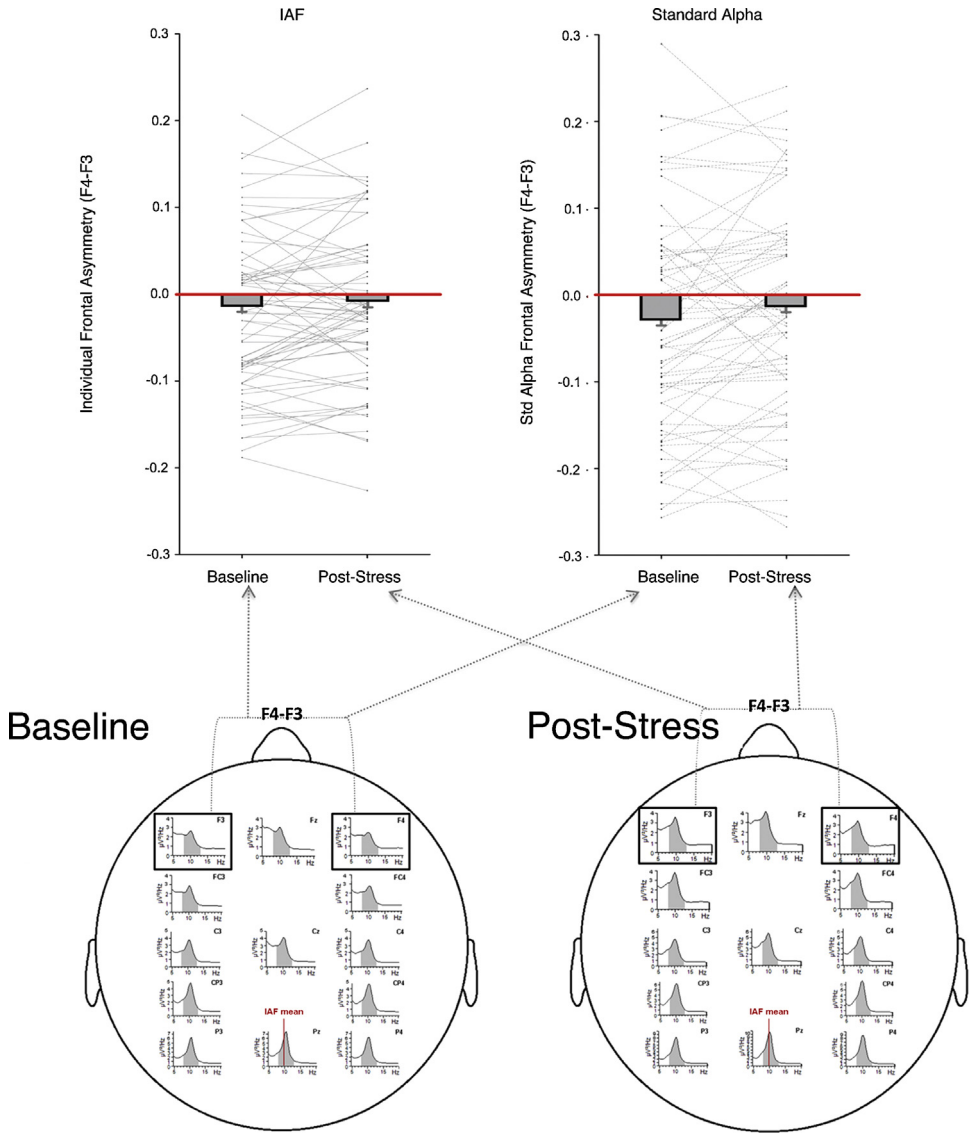

Fig. 3. Effect of stress induction on alpha oscillations. Upper panel: effect of stress induction on frontal alpha asymmetry across the whole sample (mean plus std. error) as well as per individual (lines) for individual (left) and standard (right) alpha band. Lower panel: topographical display of average power density at rest before and after the stress induction. The grey area marks 8–13 Hz, in which power densities were averaged to derive alpha asymmetry scores in the standard alpha band. The redline at Pz marks the mean IAF. Note the difference in *Y*-axis scaling between frontal and parietal electrodes.

that more left-sided frontal activity at baseline was associated with a smaller cortisol response to the stressor (see Fig. 4). Meanwhile, the association with $FA_{F4–F3}$ post-stress based on IAF was at trend level ($r_{67} = -0.24$; $p = 0.05$). However, the associations with $FA_{F4–F3}$ baseline and post-stress based on standard alpha remained non-significant (baseline: $r_{67} = -0.21$; $p = 0.08$; post-stress: $r_{67} = -0.20$; $p = 0.10$). Moreover, the IAF associations for baseline and post-stress FA were specific for the mid-frontal electrodes (F4–F3) since all other correlations were non-significant (all $ps > 0.78$). Stress-reactivity FA did not correlate significantly with the cortisol response, for both standard alpha and IAF (all $ps > 0.68$, see Table 1).[2]

Measures of behavioural activation and inhibition (BIS/BAS) were correlated with brain asymmetry. For both baseline

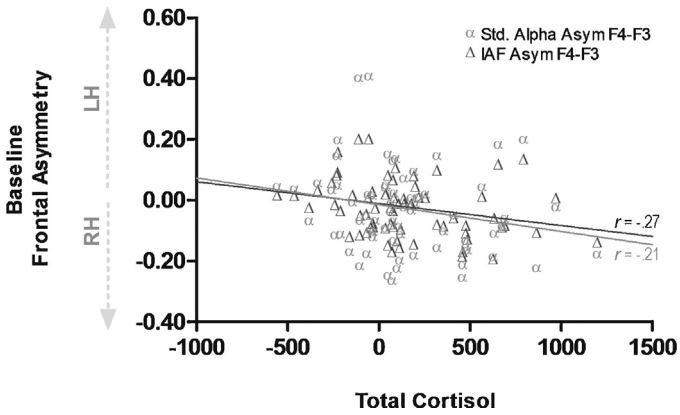

Fig. 4. Association between baseline asymmetry at F4–F3 and total cortisol response. More right-sided asymmetry resulted in a higher cortisol increase. Note that the correlation was only significant for IAF.

[2] Bivariate Pearson correlations between the cortisol response immediately before the frontal asymmetry measurement (i.e., t_{+10}) and brain asymmetry were nearly identical (IAF: $r_{69} = -0.25$; $p = 0.04$; std. alpha $r_{69} = -0.22$; $p = 0.08$).

Table 1
Summary of the EEG results. Upper part: mean ± SEM of the frontal asymmetry before and after stress induction for F4–F3 and F8–F7 separately based on 8–13 Hz or IAF. Lower part: associations between the cortisol response and brain asymmetry based on 8–13 Hz or IAF.

	Standard Alpha 8–13 Hz		Individual Alpha	
	Mean	SEM	Mean	SEM
Baseline				
$Asym_{F4-F3}$	−0.024	0.018	−0.022	0.011
$Asym_{F8-F7}$	−0.186	0.037	−0.118	0.024
Post-stress				
$Asym_{F4-F3}$	−0.010	0.017	−0.012	0.011
$Asym_{F8-F7}$	−0.159	0.034	−0.112	0.023
	Total Cortisol (AUCi)		Total Cortisol (AUCi)	
	r	*p*	*r*	*p*
Baseline				
$Asym_{F4-F3}$	−0.21	0.08	−0.27	0.025
$Asym_{F8-F7}$	0.006	0.96	−0.03	0.78
Post-stress				
$Asym_{F4-F3}$	−0.20	0.10	−0.24	0.05
$Asym_{F8-F7}$	0.03	0.79	−0.03	0.84
Stress-reactivity				
$Asym_{F4-F3}$	0.03	0.80	0.03	0.82
$Asym_{F8-F7}$	0.05	0.68	0.02	0.85

Note: Stress-reactivity is the change in FA (i.e., post-stress – baseline).
p-Values ≤ .025 were considered as statistically significant.

asymmetry measures of $Asym_{F8-F7}$, a positive correlation with BAS drive (IAF: $r_{60} = 0.35$; $p = 0.006$; Standard Alpha: $r_{60} = 0.32$; $p = 0.01$) and a negative correlation with BIS (IAF: $r_{60} = -0.33$; $p = 0.01$; Standard Alpha: $r_{67} = -0.30$; $p = 0.02$) was found, indicating that more left-sided frontal activity at baseline was associated with more behavioural activation (see Fig. 5). The association with FA was specific for the lateral frontal electrodes (F8–F7) since all other correlations were non-significant (all $ps > 0.10$). Bivariate Pearson correlations between BIS/BAS and stress-reactivity FA did not reveal any significant associations for both standard alpha and IAF (all $ps > 0.21$). Bivariate Pearson correlations between BIS/BAS and the participants' physiological stress response did not reveal any significant associations (all $ps > 0.17$).

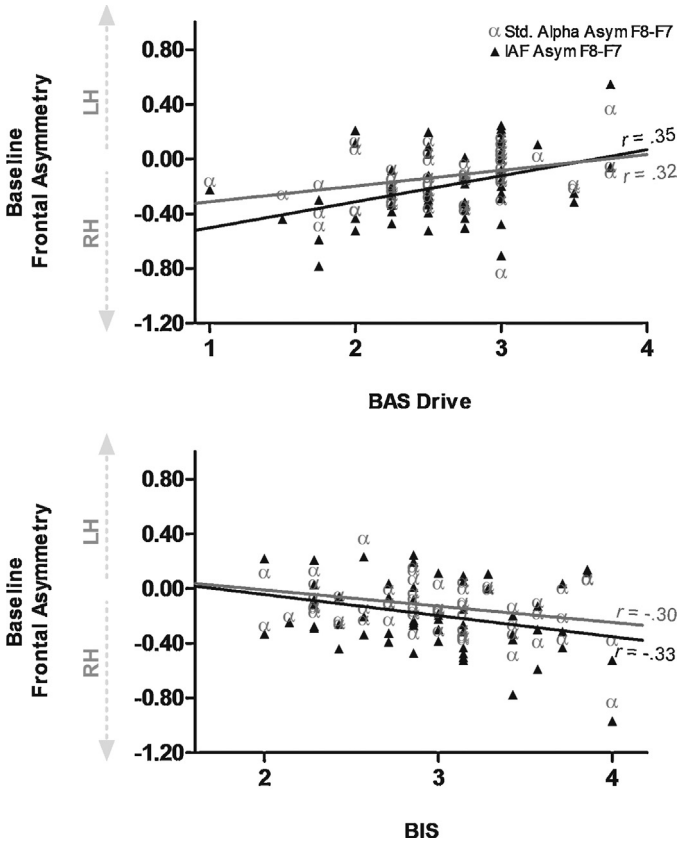

Fig. 5. Association between frontal asymmetry and behavioural activation. Baseline asymmetry at F8–F7 was positively associated with the BAS drive subscale and negatively with BIS.

4. Discussion

The aim of the current study was to investigate the functional role of asymmetric frontal alpha oscillations in stress-induced neuroendocrine responses. Secondly, we explored whether the relationship between FA and individual differences in stress responding are more reliably described if based on IAF instead of the standard 8–13 Hz alpha band. Resting EEG was measured before and after stress induction by means of the MAST (Smeets et al., 2012). The MAST indeed generated robust increases in cortisol levels. The cortisol responses were moderated by gender, which is in line with the typically larger increases found in males compared to females in response to laboratory stressors (Meyer, Smeets, Giesbrecht, Quaedflieg, & Merckelbach, 2013; for review see Kudielka et al., 2009). We found that higher left hemispheric activity at baseline was associated with lower stress-induced cortisol levels (AUCi), an effect that was specific to the sites F4–F3 and was only significant when IAF was used. Besides, we found higher baseline FA_{F8-F7} to correlate with higher BAS and lower BIS scores. Meanwhile, the stress induction did not result in a change in FA, which suggests that individual FA might reflect a trait-like characteristic that relates to cortisol reactivity to a stressor.

The finding that IAF based baseline FA_{F4-F3} was associated with lower stress-induced cortisol levels (AUCi) is in line with our expectations and agrees well with studies suggesting that left frontal activity is involved in the regulation of hormonal stress responses (Baeken et al., 2014; Davidson, 2000; Sullivan & Gratton, 2002). No association was found when FA was based on the standard 8–13 Hz alpha band, which is in agreement with previous studies investigating the relation between cortisol and FA in the standard alpha band (Hewig et al., 2008; Lewis et al., 2007; Tops et al., 2005). The mean of the IAF was not different from the centre of the standard alpha band indicating that the difference in sensitivity and reliability cannot be explained by the use of alpha sub-bands that are, across participants, consistently different from standard alpha. Our results support the idea that the individualized alpha band (IAF) is more reliable than standard alpha in the prediction of individual differences in the processing of stressors.

The current results suggest an association of BAS drive with baseline left lateral frontal activity and an association of BIS with baseline right lateral frontal activity (i.e., $Asym_{F8-F7}$). Studies that have investigated the relation between BIS and frontal lateralization have yielded divergent findings, with most reporting weak or no association (Coan & Allen, 2003a; De Pascalis, Cozzuto, Caprara, & Alessandri, 2013; Harmon-Jones & Allen, 1997; Hewig, Hagemann, Seifert, Naumann, & Bartussek, 2006) while Sutton and Davidson (1997) also found a negative correlation. Nevertheless, in line with the current findings, all before mentioned studies hypothesized to find a negative correlation between BIS and FA. BIS is a motivationally complex concept (Amodio, Master, Yee, & Taylor, 2008) that probably is reflected in a less robust relation with right-sided FA. In terms of BAS, relative left sided FA was related to more behavioural drive. This result is consistent with previous studies (Berkman & Lieberman, 2010; De Pascalis, Varriale, & D'Antuono, 2010; Tops & Boksem, 2010) and more

general with studies associating frontal asymmetry with overall behavioural activation (Amodio et al., 2008; Coan & Allen, 2003a; Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997). A noteworthy observation is that most studies found associations between the behavioural activation system and mid-frontal (F4–F3) locations corresponding to the dorsolateral prefrontal cortex (dlPFC; Herwig et al., 2003). Still, associations with lateral FA (F8–F7) have also been demonstrated in previous studies (e.g., Coan & Allen, 2003a; Hewig et al., 2006), suggesting a more ventrolateral PFC source. Numerous neuroimaging studies have demonstrated opposite affective lateralized processing effects within specific areas of the PFC (see for reviews Miller, Crocker, Spielberg, Infantolino, & Heller, 2013; Wager, Phan, Liberzon, & Taylor, 2003), which could explain these divergent location findings and indicates the need to measure EEG at a high spatial density and combine EEG and fMRI (Davidson, 2004).

The finding that FA remained unaffected by stress is at first glance at odds with the study of Lewis et al. (2007) and the prior cortisol administration studies of Tops et al. (2005, 2006). Yet, Lewis et al. (2007) found different results when applying a region or a single electrode analysis and in line with our results, no effect of examination stress was found for the single electrode analysis of F4–F3. One explanation for the disparity with the studies of Tops et al. (2005, 2006) may be that exogenous cortisol administration activates the HPA-axis at a different level than a psychological stressor, which also increases the release of other hormones like catecholamines (Kudielka et al., 2009). Moreover, the timing of the EEG measurements could also account for the differential findings, as Tops et al. (2005, 2006) collapsed multiple asymmetry measurements over 30 min and 2 h, respectively, whereas the current study did not. The current finding that stress induction did not result in a change in FA while at the same time individual $FA_{F4–F3}$ predicted the cortisol response, suggests that individual FA reflects individual differences in a trait-like mechanism that moderates the cortisol stress response.

A few limitations of the current study should be noted. First, this study was performed in healthy subjects. Cortical asymmetry scores are expected to reflect more symmetrical activity in healthy subjects than in clinical populations (Gordon, Palmer, & Cooper, 2010; Quinn, Rennie, Harris, & Kemp, 2014) and therefore statistical results might be dampened. Second, FA was measured before and after the MAST, but not during the MAST. This was done because the MAST consists of mental arithmetic trials, and the induced cognitive effort could confound effects of stress on alpha activity when measured during the MAST. Thus, while we found no change in FA in response to the MAST, FA may still have transiently changed during stress. Finally, the present study is limited in generalizability by the fact that cortisol but no other measures of the stress response, like autonomic or subjective, were assessed.

In sum, the present findings suggest that baseline frontal alpha activity reflects a mechanism that has a moderating role in the fight-or-flight response to acute stress. Specifically, relatively left activation appears to be associated with resilience characterized by behavioural activation and neuroendocrine regulation. Thereby, this study contributes to the relatively sparse and inconsistent literature regarding the role of trait characteristics in moderating responses to state manipulation. Our data show that hemispheric asymmetry measures based on frontal alpha frequencies may serve as a better individual difference variable if they are based on individualized alpha frequencies than if they are based on standard alpha (8–13 Hz). Constructing frontal asymmetry on the individualized alpha band seems a promising avenue to the refinement and extension of our knowledge of the role of asymmetric hemispheric activation as a determinant of individuals' degree of stress resilience or vulnerability.

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