Brief report

Frontal alpha-asymmetry in adults with attention deficit hyperactivity disorder: Replication and specification

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ABSTRACT

Recent findings suggest that adults suffering from attention deficit hyperactivity disorder (ADHD) display an atypical pattern of hemispheric asymmetry, assessed through the alpha band in resting-state electroencephalogram. In the context of the approach–withdrawal model of hemispheric asymmetry, this pattern has been identified as a correlate of approach-related behavior, particularly in anterior brain regions. The current study sought to replicate previous findings on alpha asymmetry in ADHD, and to specify them based on the assumption that ADHD represents a disorder of excessive approach tendencies.

A group of ADHD patients (n = 19) was compared to a group of healthy controls (n = 19) on measures of alpha asymmetry and aggression, an approach-related trait. Observed region-specific group differences in alpha asymmetry approximated assumptions of the approach–withdrawal model. In addition ADHD subjects displayed elevated levels of a subcomponent of aggression. These results provide support for a conceptualization of ADHD as a disorder of excessive approach tendencies.

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1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a psychiatric condition characterized by concentration deficits, hyperactivity and impulsivity (American Psychiatric Association, 2000). While traditionally regarded as a disorder of childhood, ADHD has also been found to persist into adulthood (Faraone, 2000; Spencer et al., 1994). Various neurophysiological and anatomical anomalies have been reported in ADHD children and adults, including abnormal brain laterality. These findings resulted in a right-hemisphere deficit perspective according to which the disruption of particularly right-hemispheric processes related to attention and arousal regulation may yield a symptomatology characteristic of ADHD (Fassbender and Schweitzer, 2006; Schneider et al., 2006; Stefanatos and Wasserstein, 2001). Alternatively, it has been suggested that ADHD is not related to strictly right-hemispheric deficits, but to compromised hemispheric interactions, undermining the networked processing of right-hemispheric functions (Hale et al., 2009a).

Recently, research which may be relevant for the approach–withdrawal model of hemispheric asymmetry (Davidson, 2004) has provided support for abnormal laterality in adult ADHD. The approach–withdrawal model posits the predictive utility of tonic relative left-hemispheric anterior cortical activity for global response tendencies of approach, in contrast to right-hemispheric anterior cortical activity for responses of withdrawal. Hale et al. (2009b) report that adults suffering from ADHD display a distinct pattern of alpha asymmetry, indicative of stronger relative left-hemispheric cortical activity, compared to controls. In the latter study ADHD subjects showed relatively stronger right-hemispheric alpha power (rightward alpha asymmetry), which was observed in the low and high alpha band in resting-state electroencephalogram (EEG). Since alpha power is assumed to be an inverse indicator of underlying cortical activity (Allen et al., 2004), one may assume that adults suffering from ADHD are characterized by the neurophysiological conspicuity of elevated relative left-hemispheric cortical trait activity. Similar results have been reported for ADHD children, where boys displayed an elevation of relative left-hemispheric anterior cortical activity, while girls exhibited the opposite pattern (Baving et al., 1999). Given these findings, a complementary perspective on ADHD, especially in case of males, might be that this psychiatric condition can be classified as a disorder of overdriven approach tendencies. The latter notion is also supported by a recent study, in which self-reported behavioral approach tendencies predicted hyperactive-impulsive ADHD symptoms in male adults (Mitchell, 2010).

Apart from studies which have focused on alpha asymmetry and psychopathology, the relation of alpha asymmetry and motivational direction has also been explored in the general pop-
ulation. Constructs which have received considerable attention in this context are anger and aggression. Both have been classified as approach-related (Carver and Harmon-Jones, 2009; Harmon-Jones, 2007; Harmon-Jones et al., 2010) and frontal alpha asymmetry has been consistently found to predict anger and aggressive tendencies in healthy subjects (Harmon-Jones, 2004; Harmon-Jones and Sigelman, 2001; Hewig et al., 2004). However, to our knowledge, no study has yet been conducted to assess approach-related behavioral traits and frontal alpha asymmetry in adults with ADHD, as well as the relation of these variables. With regard to trait aggression, in the current study such an attempt was made to foster the integration of the described notions, and to provide further evidence for the assumption that ADHD may be categorized as a disorder of excessive approach tendencies. In particular, we intended to provide a replication of findings reported by Hale et al. (2009b), and compared resting-state EEG measures of alpha asymmetry in adult ADHD patients to those of healthy controls. It should be noted that the initial work by Hale et al. (2009b) involved some methodological limitations. Firstly, the data analysis involved uncorrected multiple comparisons of asymmetry measures derived from nine homologous electrode pairs in two frequency bands and three conditions, potentially yielding an inflation of Type I error. Secondly, since only indices of relative hemispheric activity were considered, no conclusions could be drawn as to whether the observed asymmetry pattern involved left hyperactivity or right hypoactivity. Finally, since interactions of hemisphere and location (anterior vs. posterior) by group (ADHD vs. control) were not assessed, no conclusions were possible as to whether the effects were specific to anterior regions. The latter pattern would be expected according to the approach–withdrawal model and this point requires verification.

In an attempt to address these issues, in the current study, we intended to focus on a single resting condition and the whole alpha band (8–13 Hz). We included a comparison of hemisphere-specific absolute alpha power, and examined whether alpha power varied as a function of hemisphere and location across groups. We also assessed trait aggression as a behavioral operationalization of approach tendencies and expected elevated aggression in ADHD patients. Finally, we assumed higher aggression scores to be significantly associated with stronger relative left-hemispheric anterior activity in both groups.

2. Methods

2.1. Participants

The sample consisted of 38 participants (19 ADHD and 19 controls). Sample characteristics are reported in Table 1. Patients were recruited through the University’s psychotherapeutic outpatient clinic. The diagnostic procedure, carried out by a highly trained clinical psychologist, comprised the German version of the Structured Clinical Interview for DSM-IV (American Psychiatric Association, 2000; Wittchen et al., 1997), and the Homburger ADHD-Scales for Adults (Rösler et al., 2008a). The latter comprise transcriptions of the Wender-Reimherr Interview (Rösler et al., 2008b), a structured clinical interview tapping psychopathologic characteristics which have been identified as particularly relevant in the context of adult ADHD, the Wender Utah Rating Scale for Adults (Retz-Junginger et al., 2002), a scale for the retrospective diagnosis of symptoms during childhood, the ADHD diagnostic checklist, a rating scale for the diagnostician with diagnostic criteria of DSM-IV and ICD-10 (World Health Organization, 1992), as well as a self-report measure of ADHD symptoms. In addition, patients completed the Wortschatztest (Stephan, 1995), a test of verbal IQ, and the Amsterdam Short-Term Memory Test (ASTM; Schmand and Lindeboom, 2005), designed to evaluate putative aggrandizement of symptoms in relation to concentration deficits. Participation in the study required individuals to be between 18 and 65 years of age. Members of the ADHD group had to fulfill the diagnosis of ADHD based on DSM-IV criteria and had to display no signs of symptom aggravation according to ASTM. Exclusion occurred in case of current anxiety disorder, a psychiatric history of schizophrenia, schizoaffective disorder, epilepsy or any other neurological disorder, and an IQ score lower than 80. In addition, controls were required to not fulfill diagnostic criteria of ADHD, and to have no psychiatric or neurological history.

2.2. Self-report measures

Administered self-report measures involved German versions of the Buss-Perry Aggression Questionnaire (BPAQ; Rösler et al., 2008c), the Beck Depression Inventory (BDI-II; Hangartner et al., 2007), and the German version of the Positive and Negative Affect Schedule (PANAS; Kroehe et al., 1996). The BPAQ yields a global score for aggression, as well as scores for four underlying factors, i.e. physical aggression, verbal aggression, anger and hostility. The BDI-II yields a single score of depression referring to depressive symptoms experienced in the past two weeks. The PANAS comprises the two factors of momentary experienced positive and negative affect.

2.3. Procedures, electrophysiological recording and analysis

The current study was conducted with the written consent of each participant, and approval of the ethical committee of the involved institution. Prior to EEG assessments, participants completed the BDI-II and the BPAQ. Subsequently, EEG was recorded during a resting condition, which comprised eight one-minute resting trials, four with eyes open (O) and four with eyes closed (C), in counterbalanced order (CODOCOCOC). After the first four trials, subjects completed the PANAS. EEG was recorded from 18 sites (F1, F2, Fz, F3, F4, F7, F8, Cz, C3, C4, T7, TR, P3, P4, P7, P8, M1 and M2), with a 32-channel system with active Ag/AgCl electrodes (ActiCap; Brain Products, Gilching, Germany). All sites were referenced to the nose during recording and re-referenced off-line to an average mastoid reference (M1/M2) for analysis. Four electrodes placed around the eyes were used to monitor blinks and eye movements. Impedances were kept below 7 kΩ for the EEG and below 10 kΩ for the ocular electrodes. EEG was amplified with a BrainAmp Standard (Brain Products, Gilching, Germany; bandpass = 0.05 and 40 Hz, 50 Hz notch filter in) with 16-bit A/D conversion, a resolution of 0.1 μV, and a sampling rate of 200 Hz.

Portions of data with blinks were semi-automatically excluded with a rejection criterion of ±15 μV. Each 1-min segment was divided into epochs of 1.28 s (50% overlap). Artifact-free epochs were extracted through a Hamming window which tapered data at the distal 10% of each epoch, and subjected to a fast Fourier transform yielding measures of spectral power density (μV²/Hz) in 0.5 Hz bins. The resulting spectra were averaged across the artifact-free epochs of a 1-min trial and power density in the alpha band (8–13 Hz) was computed by averaging power density values across all bins in this frequency range. In line with previous suggestions (Allen et al., 2004), we used a natural log transformation to normalize the values of a given trial and computed weighted means for eyes-open and eyes-closed baselines for each participant, according to the number of artifact-free segments within each baseline. The average of the eyes-open and eyes-closed baselines was computed to generate a composite measure of EEG power density. In their study, Hale et al. (2009b) analyzed these conditions separately, however for research specifically related to the approach–withdrawal model, the current analysis is most common (Allen et al., 2004). Asymmetry scores were computed for three pairs of symmetrical sites, medial frontal (F3/F4), central (C3/C4), and medial parietal (P3/P4), by subtracting power density in the left from power density in the right hemisphere site: In(R) alpha power density – In(L) alpha power density. Since alpha power is assumed to be an inverse indicator of underlying cortical activity, higher values on the derived indices reflect a relative left-hemispheric cortical activity (Allen et al., 2004). Effects were rejected from the analysis if there were less than 30 artifact-free segments in total, across the eyes-open or eyes-closed trials. All participants showed sufficient quality of EEG data based on this criterion, and there were no group differences in the average number of artifact-free segments for eyes-closed or eyes-open trials (all ps > .05).

2.4. Statistical analyses

We conducted a repeated-measures analysis of variance (ANOVA) with the within-subjects factor Region having three levels (frontal: F3, F4; central: C3, C4; parietal: P3, P4), and Hemisphere (left vs. right). In addition, we included the between-subjects factor Group. The analysis focused on the three-way interaction of the indicated factors. Follow-up analyses were conducted with repeated-measures ANOVAs for each region with the factors Hemisphere and Group, and subsequent Bonferroni-corrected simple comparisons of the relevant asymmetry measures. In case of self-reported aggression, general linear univariate models were used, testing differences in global aggression and the four underlying factors, respectively. In this case, Bonferroni-correction was applied as well.

3. Results

3.1. Aggression

ADHD subjects (M = 71.63, SD = 15.15) reported insignificantly higher global aggression than controls (M = 64.88, SD = 13.60; F(1,37) = 1.91, p > .05, partial η² = 0.06). This difference was characterized by ADHD subjects displaying significantly greater hostility (M = 19.87, SD = 4.82) than controls (M = 15.65, SD = 3.93; F(1,37) = 8.18, p < .01, partial η² = 0.20). In addition, a marginally
significant difference in anger was observed ($F(1,37) = 2.01, p = .08$, partial $\eta^2 = 0.06$). ADHD subjects ($M = 18.67, SD = 4.50$) reported greater anger than controls ($M = 16.17, SD = 5.97$). There were no significant effects for physical or verbal aggression (all $p$s $>.1$).

### 3.2. EEG asymmetry

There was a significant Region $\times$ Hemisphere ($F(2,72) = 8.89, p < .01$) and a significant Region $\times$ Hemisphere $\times$ Group interaction ($F(2,72) = 4.95, p < .05$). Analyses for the single brain regions revealed that the Hemisphere $\times$ Group interaction was significant for frontal ($F(1,36) = 14.39, p < .01$) and central sites ($F(1,36) = 6.84, p < .05$), whereas it was not significant for parietal ones ($F(1,36) = 1.21, p > .05$). Bonferroni-corrected simple comparisons of the asymmetry metrics revealed that at frontal sites, members of the ADHD group ($M = 0.05, SD = 0.08$) displayed significantly stronger relative left-hemispheric anterior cortical activity than controls ($M = -0.06, SD = 0.10, t(36) = 3.79, p = .001$). The same pattern was observed for the central leads (ADHD: $M = 0.04, SD = 0.13$; Control: $M = -0.08, SD = 0.14, t(36) = 6.84, p < .01$, Fig. 1). In contrast, there were no significant differences in asymmetry activity for parietal sites (ADHD: $M = 0.08, SD = 0.14$; Control: $M = 0.18, SD = 0.38, t(36) = 1.10, p > .05$). A group comparison of absolute alpha power density at frontal and central sites, conducted by means of simple comparisons separately for each hemisphere, did not yield significant results (all $p$s $>.05$).

A post hoc analysis showed that the initial results remained unchanged when medication status and state affect were entered as covariates, and when non-right-handed participants were excluded. Since gender-specific effects on alpha asymmetry have been reported in ADHD children (Baving et al., 1999), in the post hoc analysis, we also included Sex as an additional between-subjects factor. This revealed no significant effect (all $p$s $>.05$).

### 3.3. Relation among measures

We used correlation analyses to assess the relation between relevant measures of aggression and frontal alpha asymmetry within the ADHD and the control group. With regard to aggression, the scales of hostility and anger were considered. Relevant asymmetry measures included alpha asymmetry obtained for frontal and central leads. This analysis did not reveal any significant results. Similarly, an exploratory analysis showed that self-reported depression scores and asymmetry values were not significantly correlated in the ADHD group (all $p$s $>.05$). When the same tests were run for both groups combined in a post hoc analysis, a marginally significant positive association of anger and asymmetry scores for the frontal electrodes was observed ($r = .27, p = .06$).

### 4. Discussion

The purpose of the current study was to test the assumption that ADHD may be classified as a disorder characterized by overdriven approach tendencies. In particular, the intention was to replicate and specify findings of elevated relative left-hemispheric cortical activity in adult ADHD patients relative to controls, as initially reported by Hale et al. (2009b). Additionally, trait aggression, tapping approach tendencies, was supposed to be examined in this patient population, as well as its relation to functional brain asymmetry.

With regard to the first purpose, we were successful in replicating previous findings and to further specify them in terms of brain physiological correlates of approach behavior. Adults suffering from ADHD showed a pattern of stronger relative left-hemispheric cortical activity for frontal and central sites, compared to healthy participants. Differences were observed for a composite measure of alpha asymmetry for the whole alpha band, derived from an eyes-closed and an eyes-open condition, as suggested in previous work (Allen et al., 2004). The results are original in this respect, since these conditions had only been analyzed separately before, involving the low and high alpha band across three conditions, with uncorrected, separate analyses for nine homologous electrode pairs (Hale et al., 2009b). The analyses applied in the latter study therefore involved multiple uncorrected comparisons and significant findings might have arisen by chance. In contrast, in the current study...
study, conservative correction procedures were applied and it was shown that the effects were specific to anterior and central sites, but were absent for posterior ones. This novel finding is in line with previous observations made in male ADHD children (Baving et al., 1999), and suggests that abnormal functional brain asymmetry in anterior regions may represent an ontogenetically stable trait in individuals suffering from ADHD. In addition, it approximates assumptions of the approach–withdrawal model, according to which differences in relative asymmetric activity in anterior locations, but not in posterior ones, would be expected (Davidson, 2004).

Interestingly, a group comparison conducted separately for each hemisphere did not yield any significant differences. The observed contrast of the absence of such hemisphere-specific effects on the one hand, and the presence of differences in relative asymmetric activity on the other (Fig. 1) represents a novel finding as well. Contrary to other psychiatric conditions, such as depression, for which left frontal hypofrontality has been observed (Henriques and Davidson, 1991), ADHD appears to be characterized by differences in relative interhemispheric activity. This finding might be interpreted as putative evidence against the suggested right-hemisphere deficit perspective on ADHD (Fassbender and Schweitzer, 2006), according to which right hypofrontality, i.e. elevated right-hemispheric alpha power in ADHD subjects compared to controls, would be expected. Our results therefore complement the suggestion that ADHD is not strictly associated with right-hemispheric deficits (Hale et al., 2009a). While the current results do not allow for a more specific interpretation, they allow to putatively suggest, that an alternative model focusing on compromised hemispheric interactions may be more appropriate (Hale et al., 2009a). Future research should examine this notion in more detail.

The pattern of asymmetric activity which was observed in the current study has repeatedly been shown to be associated with behavioral approach tendencies, such as aggressive behavior, on a trait level (Carver and Harmon-Jones, 2009; Harmon-Jones, 2007; Harmon-Jones et al., 2010). Congruent with these findings, ADHD subjects also displayed elevated trait hostility, a subcomponent of aggression as conceptualized by Buss and Perry (1992). However, these findings are limited by the fact, that contrary to our hypotheses, frontal alpha asymmetry did not predict trait hostility in the ADHD or the control group. Only in a post hoc analysis which was conducted for both groups combined, a minor, marginally significant association of anger and stronger relative left-hemispheric asymmetry was observed. This may only be seen as very limited support for the approach–withdrawal model as a whole. The fact that alpha asymmetry as a physiological index of approach behavior and elevated levels of trait hostility. As indicated, this conclusion is limited by the fact that self-reported aggression was not associated with alpha asymmetry in either of the involved groups.

The current work has several other limitations, in particular the use of a relatively small sample size. Further, future studies should incorporate additional comparison groups, besides healthy controls, which have been more thoroughly assessed in the context of the approach–withdrawal model. One such group could consist of individuals suffering from major depression. The inclusion of this group may be of particular interest since for ADHD patients of the current study, major depression was not an exclusion criterion, and elevated depressive symptoms were observed relative to controls (Table 1). Depression is commonly regarded as a withdrawal-related disorder, and may be associated with increased relative right-hemispheric cortical activity (Davidson, 1998), albeit gender-specific effects on this association have been reported (Stewart et al., 2010). In the current sample, one could have expected that increased depressive symptomatology would imply buffered neurophysiological correlates of approach. Nevertheless, members of the ADHD group still displayed a pattern of alpha asymmetry opposite to the one which might be expected for depressed individuals. Even though self-reported depression and alpha asymmetry were not associated in the ADHD group of the present study, in future studies it would probably be feasible to compare different subgroups of ADHD patients, i.e. those with comorbid major depression, and those without.

Conflicts of interest

The authors state that there are no actual or potential conflicts of interest.

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