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Dopamine-D2-Receptor Blockade Reverses the Association Between Trait Approach Motivation and Frontal Asymmetry in an Approach-Motivation Context

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Abstract

Individual differences in the behavioral approach system (BAS)—referred to as trait approach motivation or trait BAS)—have been linked to both frontal electroencephalogram (EEG) alpha asymmetry between left and right hemispheres (frontal alpha asymmetry) and brain dopamine. However, evidence directly linking frontal alpha asymmetry and dopamine is scarce. In the present study, female experimenters recorded EEG data in 181 male participants after double-blind administration of either a placebo or a dopamine D2 blocker. As expected, trait BAS was associated with greater left- than right-frontal cortical activity (i.e., greater right- than left-frontal EEG alpha) in the placebo group, but a reversed association emerged in the dopamine-blocker group. Furthermore, frontal alpha asymmetry was associated with a genetic variant known to modulate prefrontal dopamine levels (the catechol-O-methyltransferase Val158Met polymorphism). Finally, each of these effects was significant only in the subgroup of male participants interacting with female experimenters rated as most attractive; this finding suggests that associations between frontal alpha asymmetry and both dopamine and trait BAS are detectable only in approach-motivation contexts.

Keywords

personality, frontal EEG alpha asymmetry, dopamine, COMT Val158Met, approach motivation, sexual attraction, experimenter effect, neurotransmitters, electrophysiology, frontal lobe, genetics

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Several models describe a broad motivational system underlying the modulation of incentive salience, reward sensitivity, and behavioral approach (e.g., Depue & Collins, 1999; Pickering & Gray, 1999). Basic neuroscience studies in humans and animals have firmly established a central role for mesocorticolimbic dopamine signaling in the functioning of this behavioral approach system (BAS; for a review, see Depue & Collins, 1999). In parallel, and largely on the basis of findings from electroencephalogram (EEG) studies in humans, Davidson (1998) postulated a conceptually similar approach system that is activated by the perception of goals, initiates goal-directed behavior toward those goals, and is associated with approach-related motivational and emotional states (i.e, desire, wanting, enthusiasm, pregoal-attainment positive affect, but also anger; see Harmon-Jones, 2004). Neuroanatomically, this approach system is thought to encompass not only regions of the left prefrontal cortex, but also the dopaminergic circuitry central to the BAS. Despite considerable conceptual overlap, it is still a matter of debate whether and how Davidson's description of a left-prefrontal approach system can be integrated with BAS models that do not make any assumptions on asymmetric (i.e., left-lateralized) cortical-activation patterns but focus on dopaminergic neurotransmission in largely subcortical brain structures.

Initial indirect evidence linking the approach system and the BAS came from work applying the two theoretical frameworks to the personality domain. Specifically, Depue and Collins (1999) suggested that individuals with higher trait levels of mesocorticolimbic dopamine signaling (or BAS activity) are more responsive to all kinds of positive incentives, which results in higher reward responsiveness, assertiveness,

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drive, and ambition, or briefly, trait approach motivation or trait BAS. Broadly supporting this conceptualization, research has begun to link measures of trait BAS to various indicators of brain dopamine (e.g., Depue, Luciana, Arbisi, Collins, & Leon, 1994; Reuter, Schmitz, Corr, & Hennig, 2006; Wacker, Chavanon, & Stemmler, 2006; Wacker & Stemmler, 2006). Moreover, self-report measures of trait BAS have been repeatedly found to correlate with left-lateralized frontal cortical activity during rest, as measured by frontal EEG alpha asymmetry between left and right hemispheres (frontal alpha asymmetry; e.g., Amodio, Master, Yee, & Taylor, 2008; Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997), which in turn has been associated with dopamine metabolite levels (Field, Diego, Hernandez-Reif, Schanberg, & Kuhn, 2002).

Despite these encouraging findings, more direct evidence for an overlap between the dopaminergic BAS and the left-frontal approach system is still lacking, and it is currently unknown whether pharmacologically induced changes or genetically driven differences in dopaminergic neurotransmission are associated with frontal alpha asymmetry (for unsuccessful previous attempts to demonstrate such associations, see Schmidt, Fox, Perez-Edgar, & Hamer, 2009; Wacker et al., 2006). Furthermore, the association between questionnaire measures of trait BAS and resting frontal alpha asymmetry is far less consistent than generally appreciated (for a recent meta-analysis, see Wacker, Chavanon, & Stemmler, 2010); this lack of consistency leads to the proposal that the situational context moderates the magnitude or even the direction of the observed correlations and that associations between personality traits and frontal alpha asymmetry are to be expected especially or even exclusively in situational contexts relevant to the traits of interest (Coan, Allen, & McKnight, 2006; Crost, Pauls, & Wacker, 2008; Kline, Blackhart, & Joiner, 2002; Stemmler & Wacker, 2010; Wacker, 2001; Wacker, Chavanon, Leue, & Stemmler, 2008; Wacker et al., 2006). For example, because trait BAS is thought to be based on individual differences in approach motivation and incentive processing, trait-BAS scores should predict the degree of left-lateralized frontal asymmetry specifically in a positive-incentive motivational context.

Although resting EEG is typically recorded in a neutral situation, many features of the experimental session (e.g., gender and other characteristics of the experimenter) that are typically not reported may nevertheless exert a strong moderating influence by adding a specific emotional or motivational flavor (see also Kline, Donohue, LaRowe, & Joiner, 2002). As briefly reported in Wacker et al. (2008), we previously found that the difference score between trait BAS and trait sensitivity of the behavioral inhibition system (BIS; cf. Sutton & Davidson, 1997) correlated with left-frontal resting asymmetry as expected only when male participants were tested by female experimenters. We reasoned that if this moderating experimenter effect were due to female experimenters constituting a positive-incentive motivational context for male participants, highly attractive female experimenters should constitute an even more effective situational context. Furthermore, because males report lower commitment to their current relationship when presented with a female target of high attractiveness only when the female target is also low in dominance (Kenrick, Neuberg, Zierk, & Krones, 1994), female experimenters perceived as more attractive than dominant should constitute a strong positive incentive context for male participants independent of their current relationship status and thus provide an ideal situational context for detecting associations between frontal alpha asymmetry and individual differences in the dopaminergic BAS.

The Present Study

Here, we aimed to test, for the first time, whether the association between frontal alpha asymmetry and both trait BAS and pharmacologically induced changes or genetically driven differences in dopaminergic neurotransmission are moderated by subtle variations of the situational context in which resting EEG is recorded. For the pharmacological manipulation of dopamine, we employed a selective dopamine-D2-receptor blocker (sulpiride 200 mg); for the assessment of genetic differences, we focused on a common genetic variant of the catechol-O-methyltransferase (COMT) gene, the COMT Val-158Met polymorphism. The enzyme COMT plays an important role in dopamine degradation in the prefrontal cortex, where other routes of dopamine elimination (e.g., the dopamine transporter) are less abundant (e.g., Matsumoto et al., 2003; Tunbridge, Bannerman, Sharp, & Harrison, 2004). In individuals homozygous for the COMT Val allele (Val/Val carriers), the enzyme is more active and dopamine is thus more rapidly degraded than in individuals homozygous for the Met allele (Met/Met carriers), with heterozygous individuals (Val/Met carriers) lying in between (Lachman et al., 1996). In addition, previous research has demonstrated higher trait-BAS scores in Val/Val carriers compared with both Val/Met and Met/Met carriers (Wacker, Mueller, Hennig, & Stemmler, 2012). Finally, subtle variations of the situational context of the resting EEG session were indexed by the attractiveness (vs. dominance) of the female experimenters.

We hypothesized that (a) in our male participants, left-frontal cortical activity would be associated with both trait BAS and the Val allele of the COMT Val158Met polymorphism only in the presence of female experimenters who were more attractive than dominant and that (b) administration of the selective dopamine-D2-receptor blocker would modulate these associations.

Method

Participants

Of the 203 young male volunteers who completed the initial resting EEG session of the study, 7 (3.4% of the sample) were tested by experimenters who could not be classified because of insufficient rating data (see the Results section), 14 (6.8% of

the sample) did not have a sufficient amount of artifact-free EEG data (see the Supplemental Material available online), and 1 could not be genotyped for COMT Val158Met because of insufficient quality of the DNA sample. The average age of the remaining 181 participants included in the analysis was 23.9 years (range = 20–35, *SD* = 3.0), and 97% were university students. All participants were right-handed, had no history of psychiatric disorders (as assessed with a standardized clinical interview based on criteria in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*; American Psychological Association, 1994), described themselves as nonsmokers, and reported that they did not use either prescription or illegal drugs during the 3 months preceding the study.

The present study was part of a larger study involving additional measurements and paradigms (for details, additional selection criteria, and further results obtained in the larger study, see Mueller, Makeig, Stemmler, Hennig, & Wacker, 2011; Wacker et al., 2012). All volunteers gave written informed consent before participating and received €70 (~$100) for approximately 7 hr involvement in the project. The study protocol was approved by the Ethics Committee of the German Society for Psychology.

Procedure

After obtaining written informed consent, we administered a standardized clinical interview. If no exclusion criteria applied, each participant received a standardized breakfast and ingested either a sulpiride pill (200 mg) or placebo capsule (double-blind administration). Thereafter, participants completed several intelligence tests and personality questionnaires (see Wacker et al., 2012), following which they were seated in the experimental chamber, where EEG electrodes, additional electrodes, and a transducer for measurement of various somatovisceral signals (data are not reported here) were attached by 1 of 12 female experimenters. Experimenters were instructed to treat participants in a friendly but neutral, business-like way and closely follow a standardized checklist in preparing participants and giving instructions. Approximately 3 hr after administration of the pill, the experimenter left the room, a prerecorded female voice told participants to relax with their eyes closed, and resting EEG recordings were started automatically. Subsequently, participants completed a number of additional tasks, which are not reported here (for data from one of these tasks, see Mueller et al., 2011). They also answered a forced-choice question asking them to guess whether they had received sulpiride and to state how sure they were of their answer.

Approximately 1 year after completion of the study, all participants were contacted again and asked to rate the attractiveness and dominance of the female experimenter who had conducted the study 1 year before. Participants were paid €5 (~$6.50) for completing and returning the questionnaire. All experimenters gave written informed consent to be rated by participants before the questionnaires were mailed. We considered it important for experimenters to be completely unaware that their appearance could have an effect on participants' EEG and therefore did not ask experimenters to sign informed consent concerning participants' ratings in advance, which would have enabled us to obtain ratings directly after each experimental session. To ensure that all experimenters could freely decide whether they agreed to be rated by participants, we postponed obtaining experimenters' informed consent until all experimenters were no longer employed in the study and were also no longer students of the authors of this article.

Experimenter attractiveness and dominance

Using a brief questionnaire, we first provided participants with a short description of the study they had participated in. They were also informed that their ratings would be kept confidential and would not be shared with the experimenters. Then they were asked to separately rate how attractive and dominant their experimenter had appeared to them on 6-point scales ranging from 0, *not at all*, to 5, *very*.

Sulpiride

Sulpiride is a substituted benzamide that acts as a selective D2-receptor antagonist. Sulpiride is generally well-tolerated, shows high affinity to both pre- and postsynaptic D2 receptors (Missale, Nash, Robinson, Jaber, & Caron, 1998), and does not appear to significantly block other types of receptors (e.g., histaminergic, cholinergic, serotonergic, adrenergic, and gamma-aminobutyric acid receptors). It is slowly absorbed from the gastrointestinal tract, with peak serum levels occurring 1 to 6 hr after oral ingestion; the average elimination half life is in the range of 3 to 10 hr (Mauri, Bravin, Bitetto, Rudelli, & Invernizzi, 1996).

Genotyping

DNA was extracted from buccal cells, purified, and genotyped for COMT Val158Met following the procedures of Reuter and Hennig (2005). The resulting genotype distribution for Val/Val (n = 34), Val/Met (n = 91), and Met/Met (n = 56) carriers was in accordance with the principle of Hardy-Weinberg equilibrium, $\chi^2(1, N = 181) = 0.08$, $p = .78$.

Personality assessment

As in previous research (Wacker et al., 2012), we administered a variety of personality scales. Because most of the research on resting frontal alpha asymmetry and the BAS has employed Carver and White's (1994) BIS/BAS scales (see Wacker et al., 2010), we focused the presentation of our findings on a German translation of these scales. Note, however, that all F and t tests for group differences in trait-BAS effects presented in

the Results section remained significant ($p < .05$) when the analyses were conducted using factor scores (or even residualized factor scores) from the agency factor described in Wacker et al. (2012). In the present sample, Cronbach's alpha was .78 for BAS scores and .75 for BIS scores.

EEG recording and analysis

Full details of EEG recording and analysis are reported in the Supplemental Material. Briefly, five EEG recordings of 95 s each were obtained, and EEG asymmetry indices were computed separately for each of the five recordings and the broad alpha band (8–12 Hz) as well as several other frequency bands by subtracting alpha power at the left from alpha power at the right homologous electrode (e.g., ln-transformed alpha power at F4 minus ln-transformed alpha power at F3). Asymmetry indices were then averaged across the five recordings. As in prior research (see Wacker et al., 2010), we focused our analyses on the alpha frequency band and the midfrontal region (F4, F3).

Results

Blindness to pharmacological treatment

The percentage of participants in each group who guessed that they had taken the drug did not differ significantly (sulpiride group: 26.0%, placebo group: 22.4%), $\chi^2(1, N = 181) = 0.33$ $p = .56$. Of the 25 participants who correctly guessed that they had received sulpiride, none reported being more than 80% sure of their guess, and the average of self-reported certainty for these 25 participants was 58.6% ($SD = 11.05\%$).

Experimenter attractiveness and dominance

For 2 of the 12 experimenters, less than two ratings were obtained; consequently, their data were excluded from further analyses. Of the 87 participants who provided ratings for the 10 remaining experimenters, 10 participants indicated that they had no recollection of the experimenter in this study, which left 77 ratings for further analysis. The 10 experimenters scored, on average, 3.03 ($SD = 1.11$) in attractiveness and 2.98 ($SD = 0.89$) in dominance. For two reasons, all further analyses were conducted with attractiveness-dominance difference scores. First, as noted in the introduction, high attractiveness and low dominance in an unknown female have been shown to jointly determine her impression on males (Kenrick et al., 1994). Second, the use of a difference score reduces the impact of individual differences in general response biases (e.g., the tendency to generally provide high vs. low ratings), which are likely to play a considerable role in retrospective ratings such as the present one.

The average attractiveness-dominance difference scores for the 10 experimenters differed significantly, $F(9, 67) = 2.19$, $p = .034$, which indicates that the experimenters varied in the impression they left on participants. Next, we averaged the first and second half of the ratings obtained for each experimenter. The intraclass correlation (ICC; Shrout & Fleiss, 1979) between these halves was ICC(2, k) = .81, which indicates considerable agreement across participants concerning experimenters' attractiveness-dominance. We grouped experiments on the basis of their attractiveness-dominance ratings: 4 experimenters were rated as more attractive than dominant, and 6 experimenters were rated as being either equally as dominant as attractive or more dominant than attractive. Ninety participants (44 in the placebo group, 46 in the sulpiride group; 20, 46, and 24 in the COMT Val/Val, Val/Met, and Met/Met groups, respectively) were tested by the experimenters rated as highly attractive; 91 participants (41 in the placebo group, 50 in the sulpiride group; 14, 45, and 32 in the COMT Val/Val, Val/Met, and Met/Met groups, respectively) were tested by experimenters rated as having normal attractiveness. The average attractiveness-dominance scores were 0.59 (range = 0.18–1.14) for the experimenters rated as highly attractive and −0.41 (range = −0.75–0.00) for experimenters rated as having normal attractiveness.

EEG asymmetry

We computed a general linear model predicting midfrontal (F4, F3) alpha asymmetry based on group (placebo, D2 blocker), COMT (Val/Val, Val/Met, Met/Met), experimenter attractiveness (normal, high), and the continuous predictor BAS (centered within Group × Experimenter Attractiveness groups) plus all interaction terms except those involving both BAS and COMT (restrictions of sample size did not permit a full factorial model). We obtained a significant Group × BAS interaction, $F(1, 165) = 8.64$, $p = .0038$, which was due to the expected pattern of a positive association between BAS and frontal alpha asymmetry in the placebo group ($r = .27$, $p = .014$) and a negative association between the two in the sulpiride group ($r = -.22$, $p = .032$; see Fig. 1). There was also a significant Group × Experimenter Attractiveness × BAS interaction, $F(1, 165) = 5.27$, $p = .023$, which indicated that the pattern of BAS correlations just noted was specific to the group of experimenters rated as more attractive than dominant. The correlations between BAS and frontal alpha asymmetry were significant for experimenters rated as highly attractive in the placebo group ($r = .36$, $p = .016$) and in the D2-blocker group ($r = -.39$, $p = .008$), but not for experimenters rated as having normal attractiveness in the placebo group ($r = .11$, $p = .48$) and in the D2-blocker group ($r = .02$, $p = .91$).

Finally, a COMT × Experimenter Attractiveness interaction emerged, $F(2, 165) = 4.12$, $p = .018$; this interaction was the result of a positive association between the COMT Val allele and frontal alpha asymmetry that was likewise specific to experimenters rated as more attractive than dominant (see Fig. 2): The difference between the Val/Val and Met/Met genotypes was significant for participants whose experimenters were rated as highly attractive, $t(165) = 2.32$, $p = .022$, but not for participants whose experimenters were rated as having

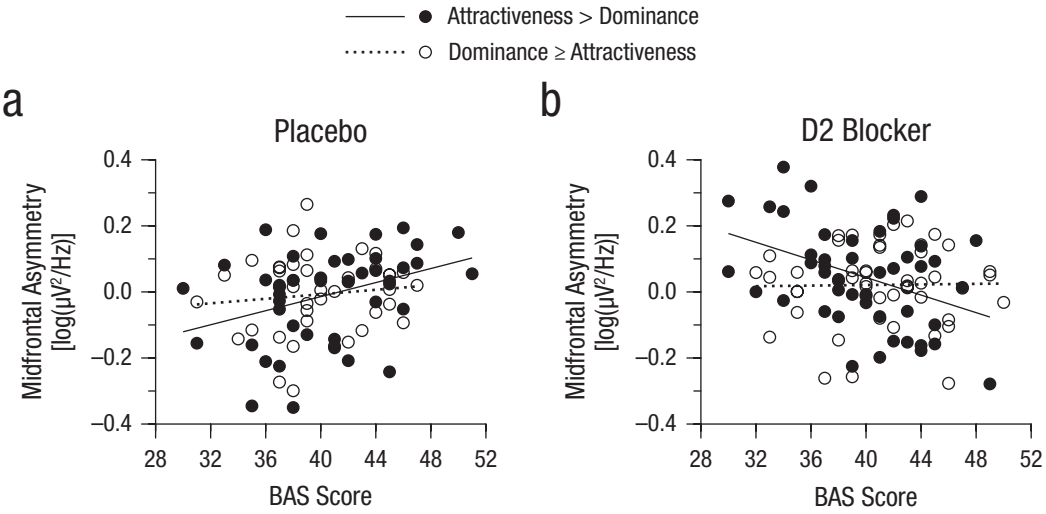

Fig. 1. Scatter plots (with best-fitting regression lines) showing mean midfrontal (F4, F3) asymmetry as a function of behavioral-approach-system (BAS) score (Carver & White, 1994) and participants' rating of their experimenters' attractiveness. Results are shown separately for participants who received (a) a placebo and (b) 200 mg of the dopamine-D2-receptor blocker sulpiride approximately 3 hr before midfrontal asymmetry was recorded. Positive asymmetry scores indicate greater left- than right-frontal cortical activity (greater right- than left-frontal alpha activity). Negative asymmetry scores indicate greater right- than left-frontal cortical activity (greater left- than right-frontal alpha activity).

normal attractiveness, $t(165) = -1.69$, $p = .093$. Apart from a trend for a main effect of group, $F(1, 165) = 3.24$, $p = .074$, which resulted from somewhat more left-frontal cortical activity in the D2-blocker group than in the placebo group, no other effects in the general model approached significance, $p \geq .21$.

In addition, to test the regional specificity of the significant BAS and COMT effects emerging for participants tested by experimenters rated as more attractive than dominant, we computed analogous statistical models for the asymmetry scores from all regions for this subgroup. As shown in Figure 3, both findings were specific to frontal sites with maximal effects for the midfrontal (F4, F3) and frontopolar (Fp2, Fp1) sites, respectively. Furthermore, additional analyses (again only for the experimenter group rated as more attractive than dominant) showed that the Group × BAS interaction at midfrontal sites, albeit highly significant for the alpha band, $F(1, 82) = 13.59$, $p = .0004$, was not significant for any of the other frequency bands (delta, theta, beta 1, and beta 2), $F(1, 82) \leq 2.16$, $p \geq .15$. In contrast, the COMT main effect at frontopolar sites was strongest in the alpha band but marginally significant for all other frequency bands—delta: $F(2, 82) = 3.54$, $p = .03$; theta: $F(2, 82) = 3.98$, $p = .02$; alpha: $F(2, 82) = 5.74$, $p = .005$; beta 1: $F(2, 82) = 4.90$, $p = .01$; and beta 2 $F(2, 82) = 2.87$, $p = .06$.

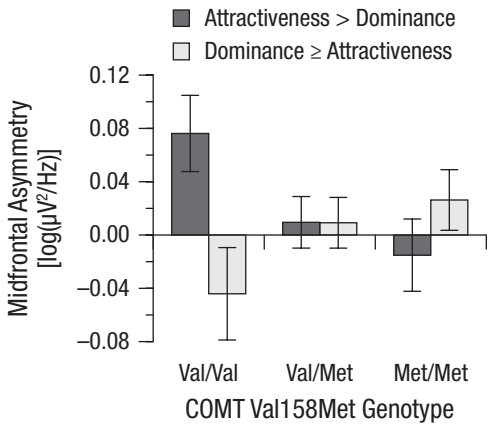

Fig. 2. Mean midfrontal (F4, F3) asymmetry as a function of genotype and participants' ratings of their experimenters' attractiveness. Participants were genotyped according to which catechol-O-methyltransferase (COMT) gene they carried. Positive scores indicate greater left- than right-frontal cortical activity (greater right- than left-frontal alpha activity). Negative asymmetry scores indicate greater right- than left-frontal cortical activity (greater left- than right-frontal alpha activity). Error bars show standard errors of the mean.

Discussion

Two of the observations in the present study provide the strongest evidence to date for a link between dopaminergic neurotransmission and frontal alpha asymmetry, which was predicted based on the conceptual similarity between the dopaminergic BAS (e.g., Depue & Collins, 1999; Pickering & Gray, 1999) and the left-frontal approach system (Davidson, 1998). First, we found that a negative association between trait BAS and greater left- than right-frontal cortical activity (greater right- than left-frontal alpha activity) emerged

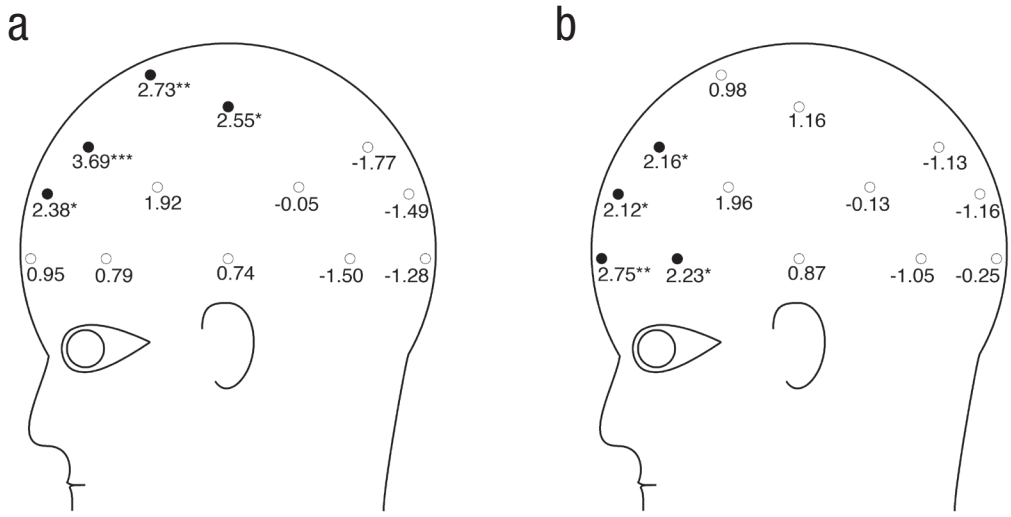

Fig. 3. Scalp topography of asymmetry effects: *t* values for the comparison of behavioral-approach-system (BAS) regression weights across groups within the subgroup of participants who rated their experimenters as more attractive than dominant. The diagram in (a) shows results for the comparison of subjects who received the placebo and those who received the D2 blocker, and the diagram in (b) shows results for the comparison of participants with the catechol-O-methyltransferase (COMT) Val/Val genotype and participants with the COMT Met/Met genotype. Positive *t* values indicate a more positive association between BAS and left-frontal cortical activity (right-frontal alpha activity) under placebo and stronger left-frontal cortical activity (right-frontal alpha activity) for the Val/Val genotype, respectively. Asterisks indicate significant differences between groups (*$p < .05$, **$p < .01$, ***$p < .001$). The asymmetry measures displayed (from top to bottom and left to right) are FC2, FC1; F4, F3; C4, C3; P4, P3; AF4, AF3; FC6, FC5; CP6, CP5; PO4, PO3; Fp2, Fp1; F8, F7; T8, T7; P8, P7; and O2, O1.

following administration of a dopamine-D2-receptor blocker, which contrasted with the positive association between these two variables in the placebo group. Second, we observed that the COMT Val158Met polymorphism, a genetic variant known to modulate prefrontal dopamine levels, was likewise associated with frontal alpha asymmetry. This novel support for the surprisingly underresearched neurophysiological construct validity of frontal alpha asymmetry is informative for a large and still rapidly growing body of research linking this physiological measure to an extensive network of diverse psychological constructs across more than 150 studies (Allen & Kline, 2004).

Although the present data do not speak to the precise nature of the dopamine-linked asymmetries underlying the observed effects, Tomer, Goldstein, Wang, Wong, and Volkow's (2008) observation of more left-lateralized striatal dopamine D2-receptor availability in individuals high in achievement striving (a BAS spectrum trait; see Wacker et al., 2010), together with reports of positive associations between striatal dopamine D2-receptor availability and prefrontal cortical activity (e.g., Volkow et al., 2008), suggests a role for D2-receptor asymmetries on the striatal level. Such asymmetries could also explain the opposite effects of the D2-receptor blocker sulpiride in individuals high in trait BAS observed here: At low doses, sulpiride preferentially blocks presynaptic D2 autoreceptors, which leads to an increase in dopamine signaling, whereas at high doses, postsynaptic blockade and reduced dopamine signaling prevail (Serra et al., 1990). The single dose of 200 mg of sulpiride used here likely produced both pre- and postsynaptic effects (although presynaptic effects are thought to prevail; see Mueller et al., 2011). If striatal D2-receptor availability moderates the balance of sulpiride's pre- and postsynaptic effects and trait BAS is associated with striatal dopamine D2-receptor availability asymmetry, one would expect asymmetries in sulpiride's effect on dopamine signaling to depend on trait BAS.

The link between the COMT Val158Met polymorphism, a genetic marker for variation in prefrontal dopamine levels, and frontal alpha asymmetry is reported here for the first time. As expected, the Val allele previously associated with measures from trait-BAS spectrum in the present sample and several others (see Wacker et al., 2012) was associated with greater left- than right-frontal cortical activity (greater right- than left-frontal alpha activity). This association was independent of the trait-BAS effect and not moderated by the dopamine D2 blocker. In addition, compared with the trait-BAS effect, the COMT-asymmetry effect extended from midfrontal to frontopolar/lateral frontal rather than to central regions and was less specific to the alpha frequency band. These differences suggest a separable underlying mechanism for the COMT-asymmetry link, possibly one without striatal involvement, consistent with the particularly important role of COMT for dopamine elimination in the prefrontal cortex (e.g., Matsumoto et al., 2003; Tunbridge et al., 2004). The present

findings suggest that previously reported associations between COMT Val158Met and prefrontal activity in cognitive and emotional tasks (Mier, Kirsch, & Meyer-Lindenberg, 2010) may also extend to measures of asymmetric prefrontal activity.

Furthermore, we predicted and found a moderating effect of experimenter attractiveness on all frontal-alpha-asymmetry effects. Specifically, strong and significant associations between frontal alpha asymmetry and both trait BAS and COMT Val158Met were only observed for the subgroup of participants tested by experimenters rated as more attractive than dominant, that is, in a situational context in which approach motivation and behavioral activation was presumably highly salient. These results bolster our conceptualization of "resting" frontal alpha asymmetry as an indicator (or mediator) of emotional and motivational states rather than a stable trait variable that moderates individual's reactions to emotional challenges (see also Coan et al., 2006).

It should be noted that the variation in the approach/incentive context used here was extremely subtle. As in previous EEG studies, some of which did and many of which did not uncover the expected association between trait BAS and left-frontal asymmetry (Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997; Wacker et al., 2010), all experimenters were instructed to interact with participants in the same friendly, neutral way, and none were aware of their subsequent classification in terms of attractiveness versus dominance at the time of the recording session. Nonetheless these participant-rated features of the experimenter had a substantial impact, which suggests that resting frontal alpha asymmetry is likely to show consistent associations only when the situational context is explicitly considered and relevant to individual differences in the psychological measures of interest (cf. Stemmler & Wacker, 2010).

Four limitations of the present study should be mentioned. First, because we investigated only male participants, it is unclear whether the current findings will generalize to female samples. Second, although sulpiride acts quite specifically on D2-type dopamine receptors, the trait-BAS-dependent effects observed here could, in principle, also arise from indirect non-dopaminergic effects (e.g., rather than moderating the sensitivity to changes in dopamine, trait BAS could also moderate the sensitivity of the serotonergic system to changes in dopamine). This ambiguity can be resolved only by uncovering the precise molecular mechanisms by which sulpiride acts on frontal alpha asymmetry.

Third, although frontal asymmetry based on the average reference montage bears the advantage of converging at least to some degree with the two most widely used reference montages (linked earlobes and Cz), it should be noted that activity under this montage cannot be unambiguously ascribed to frontal sources (Hagemann, Naumann, & Thayer, 2001). This issue can be fully resolved only by future studies combining EEG and neuroimaging methodology. Finally, in order to closely conform to the typical "resting" frontal-alpha-asymmetry paradigm, we decided not to directly vary experimenter attractiveness (e.g., via makeup and clothing) and only obtained retrospective ratings months after completion of the study. It is therefore possible that unknown third variables confounded with participants' ratings of experimenter attractiveness underlie the observed effects. However, even if such third variables existed *and* were not related to approach motivation, the main conclusions drawn from the present findings would remain unaffected: Frontal alpha asymmetry is linked to both trait BAS and dopamine, and participants' perceptions of the situational context in which the EEG is recorded strongly moderate frontal-alpha-asymmetry associations.

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Declaration of Conflicting Interests

D. A. P. has received consulting fees from AstraZeneca, Shire, and Ono Pharma USA, as well as honoraria from AstraZeneca for projects unrelated to this study. J. W., E. M. M., J. H., and G. S. declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Supplemental Material

Additional supporting information may be found at http://pss.sagepub.com/content/by/supplemental-data

References

Allen, J. J. B., & Kline, J. P. (2004). Frontal EEG asymmetry, emotion, and psychopathology: The first, and the next 25 years. *Biological Psychology*, *67*, 1–5.

American Psychological Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Amodio, D. M., Master, S. L., Yee, C. M., & Taylor, S. E. (2008). Neurocognitive components of the behavioral inhibition and activation systems: Implications for theories of self-regulation. *Psychophysiology*, *45*, 11–19.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology*, *67*, 319–333.

Coan, J. A., Allen, J. J. B., & McKnight, P. E. (2006). A capability model of individual differences in frontal EEG asymmetry. *Biological Psychology*, *72*, 198–207.

Crost, N. W., Pauls, C. A., & Wacker, J. (2008). Defensiveness and anxiety predict frontal EEG asymmetry only in specific situational contexts. *Biological Psychology*, *78*, 43–52.

Davidson, R. J. (1998). Affective style and affective disorders: Perspectives from affective neuroscience. *Cognition & Emotion*, *12*, 307–330.

Depue, R. A., & Collins, P. F. (1999). Neurobiology of the structure of personality: Dopamine, facilitation of incentive motivation, and extraversion. *Behavioral and Brain Sciences*, *22*, 491–569.

Depue, R. A., Luciana, M., Arbisi, P., Collins, P., & Leon, A. (1994). Dopamine and the structure of personality: Relation of agonist-induced dopamine activity to positive emotionality. *Journal of Personality and Social Psychology*, *67*, 485–498.

Field, T., Diego, M., Hernandez-Reif, M., Schanberg, S., & Kuhn, C. (2002). Relative right versus left frontal EEG in neonates. *Developmental Psychobiology*, *41*, 147–155.

Hagemann, D., Naumann, E., & Thayer, J. F. (2001). The quest for the EEG reference revisited: A glance from brain asymmetry research. *Psychophysiology*, *38*, 847–857.

Harmon-Jones, E. (2004). Contributions from research on anger and cognitive dissonance to understanding the motivational functions of asymmetrical frontal brain activity. *Biological Psychology*, *67*, 51–76.

Harmon-Jones, E., & Allen, J. J. B. (1997). Behavioral activation sensitivity and resting frontal EEG asymmetry: Covariation of putative indicators related to risk for mood disorders. *Journal of Abnormal Psychology*, *106*, 159–163.

Kenrick, D. T., Neuberg, S. L., Zierk, K. L., & Krones, J. M. (1994). Evolution and social cognition: Contrast effects as a function of sex, dominance, and physical attractiveness. *Personality and Social Psychology Bulletin*, *20*, 210–217.

Kline, J. P., Blackhart, G. C., & Joiner, T. E. (2002). Sex, lie scales, and electrode caps: An interpersonal context for defensiveness and anterior electroencephalographic asymmetry. *Personality and Individual Differences*, *33*, 459–478.

Kline, J. P., Donohue, K. F., LaRowe, S. D., & Joiner, T. E. (2002). Affective responses to EEG preparation and their link to resting anterior EEG asymmetry. *Personality and Individual Differences*, *32*, 167–174.

Lachman, H. M., Papolos, D. F., Saito, T., Yu, Y. M., Szumlanski, C. L., & Weinshilboum, R. M. (1996). Human catechol-O-methyltransferase pharmacogenetics: Description of a functional polymorphism and its potential application to neuropsychiatric disorders. *Pharmacogenetics*, *6*, 243–250.

Matsumoto, M., Weickert, C. S., Akil, M., Lipska, B. K., Hyde, T. M., Herman, M. M., . . . Weinberger, D. R. (2003). Catechol O-methyltransferase mRNA expression in human and rat brain: Evidence for a role in cortical neuronal function. *Neuroscience*, *116*, 127–137.

Mauri, M. C., Bravin, S., Bitetto, A., Rudelli, R., & Invernizzi, G. (1996). A risk-benefit assessment of sulpiride in the treatment of schizophrenia. *Drug Safety*, *14*, 288–298.

Mier, D., Kirsch, P., & Meyer-Lindenberg, A. (2010). Neural substrates of pleiotropic action of genetic variation in COMT: A meta-analysis. *Molecular Psychiatry*, *15*, 918–927.

Missale, C., Nash, S. R., Robinson, S. W., Jaber, M., & Caron, M. G. (1998). Dopamine receptors: From structure to function. *Physiological Review*, *78*, 189–225.

Mueller, E. M., Makeig, S., Stemmler, G., Hennig, J., & Wacker, J. (2011). Dopamine effects on human error processing depend on COMT VAL158MET genotype. *Journal of Neuroscience*, *31*, 15818–15825.

Pickering, A. D., & Gray, J. A. (1999). The neuroscience of personality. In L. A. Pervin & O. P. John (Eds.), *Handbook of personality: Theory and research* (2nd ed., pp. 277–299). New York, NY: Guilford Press.

Reuter, M., & Hennig, J. (2005). Association of the functional catechol-O-methyltransferase VAL158MET polymorphism with the personality trait of extraversion. *NeuroReport*, *16*, 1135–1138.

Reuter, M., Schmitz, A., Corr, P., & Hennig, J. (2006). Molecular genetics support Gray's personality theory: The interaction of COMT and DRD2 polymorphisms predicts the behavioural approach system. *The International Journal of Neuropsychopharmacology*, *9*, 155–166.

Schmidt, L. A., Fox, N. A., Perez-Edgar, K., & Hamer, D. H. (2009). Linking gene, brain, and behavior: DRD4, frontal asymmetry, and temperament. *Psychological Science*, *20*, 831–837.

Serra, G., Forgione, A., D'Aquila, P. S., Collu, M., Fratta, W., & Gessa, G. L. (1990). Possible mechanism of antidepressant effect of L-sulpiride. *Clinical Neuropharmacology*, *13*(Suppl. 1), S76–S83.

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: Uses in assessing rater reliability. *Psychological Bulletin*, *86*, 420–428.

Stemmler, G., & Wacker, J. (2010). Personality, emotion, and individual differences in physiological responses. *Biological Psychology*, *84*, 541–551.

Sutton, S. K., & Davidson, R. J. (1997). Prefrontal brain asymmetry: A biological substrate of the behavioral approach and inhibition systems. *Psychological Science*, *8*, 204–210.

Tomer, R., Goldstein, R. Z., Wang, G.-J., Wong, C., & Volkow, N. D. (2008). Incentive motivation is associated with striatal dopamine asymmetry. *Biological Psychology*, *77*, 98–101.

Tunbridge, E. M., Bannerman, D. M., Sharp, T., & Harrison, P. J. (2004). Catechol-O-methyltransferase inhibition improves set-shifting performance and elevates stimulated dopamine release in the rat prefrontal cortex. *Journal of Neuroscience*, *24*, 5331–5335.

Volkow, N. D., Wang, G. J., Telang, F., Fowler, J. S., Thanos, P. K., Logan, J., . . . Pradhan, K. (2008). Low dopamine striatal D2 receptors are associated with prefrontal metabolism in obese subjects: Possible contributing factors. *NeuroImage*, *42*, 1537–1543.

Wacker, J. (2001). *Emotionen, Verhaltenstendenzen und frontales EEG* [Emotion, behavioral tendencies and frontal EEG]. Marburg, Germany: Philipps-Universität Marburg.

Wacker, J., Chavanon, M. L., Leue, A., & Stemmler, G. (2008). Is running away right? The behavioral activation-behavioral inhibition model of anterior asymmetry. *Emotion*, *8*, 232–249.

Wacker, J., Chavanon, M.-L., & Stemmler, G. (2006). Investigating the dopaminergic basis of extraversion in humans: A multilevel approach. *Journal of Personality and Social Psychology*, *91*, 171–187.

Wacker, J., Chavanon, M.-L., & Stemmler, G. (2010). Resting EEG signatures of agentic extraversion: New results and meta-analytic integration. *Journal of Research in Personality*, *44*, 167–179.

Wacker, J., Mueller, E. M., Hennig, J., & Stemmler, G. (2012). How to consistently link extraversion and intelligence to the catechol-O-methyltransferase (COMT) gene: On defining and measuring psychological phenotypes in neurogenetic research. *Journal of Personality and Social Psychology*, *102*, 427–444.

Wacker, J., & Stemmler, G. (2006). Agentic extraversion modulates the cardiovascular effects of the dopamine D2 agonist bromocriptine. *Psychophysiology*, *43*, 372–381.