Midline theta dissociates agentic extraversion and anhedonic depression

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A B S T R A C T
The agency facet of extraversion is related to individual differences in reward anticipation and has been linked to the neurotransmitter dopamine. Dopamine has also been associated with components of anhedonia, which is one of the cardinal symptoms of depression and refers to lack of responsiveness to pleasurable stimuli. This raises the question whether low agency is associated with anhedonia symptoms in depression and if agency and anhedonia are characterized by similar neurobiological mechanisms. To address this hypothesis, we tested whether questionnaire measures of agency and anhedonia are correlated within depressed (n = 20) and non-depressed (n = 22) participants. Further, we investigated whether dopamine-related signatures in the EEG recorded during a gambling task (feedback-evoked theta activity, and frontal versus posterior theta activity) similarly relate to agency and anhedonia. Results indicated that anhedonia was significantly elevated in the depression group, and negatively correlated with agency. However, while theta activity evoked by negative vs. positive feedback was sensitive to anhedonia and depression status but unrelated to agency, frontal versus parietal theta activity predicted agency, but was unrelated to anhedonia and depression. Together, this double dissociation suggests that in spite of considerable phenotypical overlap, anhedonia and agency may be linked to partially distinct neurobiological markers.

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1. Introduction
Depression is a debilitating condition with a high prevalence and economic burden for society across cultures (Kessler & Bromet, 2013). In order to better understand its etiology and pathophysiology it has been recommended to study more narrowly defined phenotypes or symptoms of this complex and relatively heterogeneous mental illness. A core symptom of depression that has received increasing interest in this regard is anhedonia – the lack of responsiveness to pleasurable stimuli (Hasler, Drevets, Manji, & Charney, 2004; Meehl, 1975; Pizzagalli, 2014). Although the personality dimensions that are specifically associated with an increased risk for anhedonia have not been systematically explored, early theories suggested that low extraversion relates to depression (e.g., Fig. 1 of Eysenck, 1944), or anhedonia in particular (Clark & Watson, 1991); in line with these early theories negative associations between extraversion and depression are well established (e.g., Jylha & Isometsa, 2006). However, extraversion is a relatively broad and heterogeneous construct capturing individual differences in agency, affiliation and impulsivity (Depue & Collins, 1999) and it is not known which of these facets are linked to anhedonia or depression. Furthermore, little is known about biological mechanisms that may link extraversion facets to anhedonia.

For several reasons, it could be hypothesized that it is particularly the agency facet of extraversion that is related to anhedonic symptoms in depression. The agency facet comprises individual differences in one’s sense of accomplishing goals, assertiveness, social dominance, levels of activity, well-being and positive affect and these differences are presumably related to the motivational salience of positive incentives. Thus, both low agency (Depue & Collins, 1999) and anhedonia (Meehl, 1975; Pizzagalli, 2014) are conceptually related to reduced sensitivity for positive incentives or potential rewards and there is some evidence relating behavioral indices of reward processing to questionnaire measures of agency-related constructs (Gupta & Shukla, 1989) and to anhedonia (Pizzagalli, Jahn, & O’Shea, 2005). Second, consistent with reward processing being influenced by the neurotransmitter dopamine (DA), both agency- and anhedonia-related constructs have been theoretically (Depue & Collins, 1999; Dunlop & Nemeroff, 2007; Gray, 1982; Pizzagalli, 2014; Wise, 2008) and empirically (Lambert, Johansson, Agren, & Friberg, 2000; Reuter & Hennig, 2007; Wise, 2008).
2005; Wacker, Chavanon, & Stemmler, 2006) associated with the DA system. Third, in line with DA having a strong association with neurobiological processing of performance-feedback and rewards (Holroyd & Coles, 2002; Schultz, 1998), anhedonia (Liu et al., 2014) and agency (Lange, Leue, & Beauducel, 2012; Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014) have been linked to altered electrophysiological signatures of feedback processing, which are known to be sensitive to DA levels (Mueller, Burgdorf, Chavanon, Schweiger, Hennig, et al., 2014; Santesso et al., 2009). Finally, a correlation of anhedonia and agency in a small healthy sample of an unpublished study was noted (Wacker, Chavanon, & Stemmler, 2010), suggesting that the two constructs covary at the level of behavioral self-reports in non-depressed participants. In spite of these converging lines of evidence, it has not yet been explicitly tested whether agency relates to symptoms of anhedonia in currently depressed individuals.

Moreover, it is unclear, whether agency and anhedonia only relate to each other at the level of questionnaire measures or if they also show similarities at the neurobiological level. Based on the common link to DA and reward processing, it could thus be hypothesized that agency and anhedonia show similar modulations of neural activity evoked by reward-related feedback. A recently discovered neural correlate of reward-related feedback processing is feedback-evoked frontomedial theta (4–8 Hz) activity as measured with EEG. Of relevance, it has been shown that feedback-evoked theta (1) is lower for positive “reward” feedback vs. negative “loss” feedback (Cohen, Elger, & Ranganath, 2007) and (2) is associated with individual differences in agency and DA (Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014). To our knowledge, whether feedback-evoked theta also relates to anhedonia or depression has not yet been tested.

In addition to feedback-evoked theta, the FzPz index, a feedback-independent measure of frontal versus parietal theta topography is a potentially relevant marker as it has been consistently associated with agency and shown to be modulated by DA (Chavanon, Wacker, & Stemmler, 2011; Wacker et al., 2006, 2010). Whether the FzPz index relates to anhedonia has not yet been tested, although there is some evidence for altered theta activity in healthy individuals with high vs. low anhedonia (Wacker, Dillon, & Pizzagalli, 2009).

Taken together, anhedonia and low agency share a number of features but their correlation has not yet been tested in a clinical sample. Further, it is unknown if agency and anhedonia are characterized by the same electrophysiological correlates. The aim of the current study was to address these issues by performing secondary analyses of a dataset recently described (Mueller, Panitz, Nestoriuc, Stemmler, & Wacker, 2014).

2. Methods

2.1. Sample

Data from N = 21 participants with depression and N = 23 control participants were analyzed for the present study. These participants constitute a subsample of a larger study that also included N = 22 participants with panic disorder and investigated brain–heart coupling in panic disorder rather than theta oscillations (Mueller, Panitz, et al., 2014). Due to missing questionnaire data, 1 participant from each group had to be removed, yielding a final sample of N = 42 participants. Sample characteristics are provided in Table 1.

2.2. Participants

Participants were invited to a first session where they signed informed consent and a brief standardized clinical interview was conducted (Margraf, 1994). If participants met DSM-IV criteria for a major depressive episode (MD group) or no criteria for any DSM-IV diagnosis (control group) they were sent home with a series of questionnaires to complete (see below) and re-invited to the EEG session within seven days after the interview. The experimenter of the EEG session was blind to the participants’ diagnoses. After an initial 10-min resting phase, participants completed the gambling task including a 15-trial practice block. After the gambling task participants were debriefed and compensated with 35 € (about $46). The study was approved by the Ethics Committee of the Psychology Department of Marburg University.

2.3. Paradigm

The paradigm was a 360-trial gambling task which is described in more detail elsewhere (Mueller et al., 2010; Sato et al., 2005). At the beginning of each trial the amount of money to win or lose was displayed (0, 10, or 50 cent). Subsequently, participants were presented a card showing a number (from 2 to 7) and were asked to guess by button press if a second card drawn by the computer would have a lower or higher value. 3000 ms after the button press, participants received positive (green circle), negative (red cross), or uninformative (blue question mark) feedback to inform them if they had won or lost the amount. Unbeknownst to the participants, presentation of feedback was quasi-randomized with balanced frequencies for the different feedback types. Participants were told in advance that they could win a total between 10 and 15 €, however, every participant received 15 € at the end of the session.

2.4. Questionnaire measures

Anhedonia was measured using a German adaptation of the 10-item anhedonic depression subscale from the 30-item version...
(Wardenaar et al., 2010) of the Mood and Anxiety Symptoms Questionnaire (MASQ) (Watson et al., 1995). In the present sample the internal consistency of the 10-item anhedonic depression scale was high (Cronbach's alpha = .92). In addition to anhedonia, depression severity was measured using the Beck Depression inventory II (Beck, Steer, Ball, & Ranieri, 1996) which showed a high internal consistency of the 13 items was satisfactory for the BAS scale (Cronbach’s alpha = .83).

2.5. EEG-recording and preprocessing

EEG was recorded at 512 Hz using a 64-channel Active Two system (BioSemi, Amsterdam, Netherlands) as reported in more detail elsewhere (Mueller, Makeig, Stemmler, Hennig, & Wacker, 2011). EEG was re-referenced to the average reference, down-sampled to 128 Hz, highpass filtered (1 Hz) and manually screened for artifacts using EEGLAB (Delorme & Makeig, 2004). Independent Component Analysis was used to remove eye-blinks prior to segmentation.

2.6. Data reduction

EEG-segments from 0 to 2 s relative to feedback onset were computed and power spectral density was estimated using the EEGLAB function spectopo.m (Delorme & Makeig, 2004), which uses Welch’s method as implemented in MATLAB (i.e., pwelch.m; Mathworks). By default, this function divides each segment into eight sections with 50% overlap and each section is Hamming-windowed prior to computation of periodograms. The periodograms of the eight sections are then averaged to achieve a periodogram for each segment. After confirming that groups did not systematically vary in the number of segments available for analyses (p > .05), the theta (4–8 Hz) power (in dB) was averaged across segments for each condition, which resulted in 3 (Feedback: Positive vs. Negative vs. Uninformative) x 3 (Reward Magnitude: 0 vs. 10 vs. 50 cent) values per participant per electrode. Theta power at channels Fz and Cz was used for analysis of feedback-evoked theta (Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014).

Correlations for N = 42. Anhedonia: questionnaire score of the MASQ Anhedonic Depression scale. Agency: questionnaire score of the BIS/BAS scales BAS score. FMT: Feedback modulated theta, frontomedial theta power to uninformative minus positive feedback. FzPz index: Theta power at channel Fz minus Pz. p-Values for correlations involving feedback-evoked theta are two-sided, all other p-values are one-sided. Internal consistencies are displayed in the diagonal. Internal consistency of theta was computed based on inter-channel correlations. Correlations above the diagonal are corrected for unreliability of both measures (significance level taken from uncorrected correlations). Correlations below the diagonal are not corrected.

whereas the FzPz index was calculated as the difference of theta power at channels Fz and Pz (Wacker et al., 2010).

2.7. Statistical analyses

Effects of depression group were analyzed with ANOVAs involving the between-subjects factor Group (Control vs. MD) and the within-subject factors Feedback (Positive vs. Negative vs. Uninformative) and Magnitude (0 vs. 10 vs. 50 cent). Analyses of feedback-evoked theta further included the factor Electrode (Cz vs. FCz). For brevity, only interactions involving Group are reported. Informed by the ANOVA results, difference scores (feedback-evoked theta to uninformative minus positive feedback) or aggregate scores (FzPz index across task conditions) were subsequently computed and correlated with the dimensional measures of agency and anhedonia. The critical p-level was set to .05. Two-sided p-values were used for analyses involving feedback-evoked theta. For all other tests, a one-sided significance threshold was chosen based on our a priori hypotheses.

3. Results

3.1. Depression, anhedonia and agentic extraversion

As shown in Table 1, patients with depression had significantly enhanced anhedonia scores. Moreover, anhedonia and agency were negatively correlated with each other (r(42) = −.39, p < .01; Table 1) and these correlations could also be observed within the depression scores.
group ($r(20) = -0.49, p < .05$). Notably, among the depressed group, the correlations between anhedonia and agency remained significant when overall symptom severity (as measured with the Beck Depression Inventory) was partialled out ($r(17) = -0.67, p < .002$). Together, these results indicate that agency and anhedonia capture common variance associated with a more specific aspect of depression that is independent of overall symptom severity.

### 3.2. Feedback-evoked theta

#### 3.2.1. Group analysis

The Feedback $\times$ Reward Magnitude $\times$ Electrode $\times$ Group ANOVA on feedback-evoked theta power revealed a significant Group $\times$ Feedback interaction ($F(1,40) = 4.49, p < .02$). As shown in Fig. 1, this effect occurred at centro- and frontomedial electrodes and was driven by a theta power modulation to positive vs. negative or uninformative feedback that was present in the control group (negative vs. positive: $F(1,21) = 6.72, p < .02$; uninformative vs. positive: $F(1,21) = 24.10, p < .002$) but absent in depressed participants (negative vs. positive: $F(1,18) = .72, p > .4$; uninformative vs. positive: $F(1,18) = .17, p > .6$). Unlike controls, depressed individuals did not show reduced theta power to positive vs. negative or uninformative feedback (Fig. 1).

In addition, there was a significant Group $\times$ Magnitude $\times$ Feedback interaction ($F(1,40) = 2.66, p < .05$). Separate ANOVAs for both groups showed that there was a marginally significant Feedback $\times$ Magnitude interaction ($F(1,21) = 2.65, p = .051$) in the controls but not in the MD group ($F(1,18) = .67, p > .5$).

#### 3.2.2. Correlation analysis

Consistent with the ANOVA analyses, the difference score (uninformative versus positive feedback) was significantly lower in depressed vs. healthy participants ($r(42) = 2.91, p < .007$). As shown in Table 2, this score further correlated with anhedonia ($r(42) = -0.31, p < .05$) but not with agency ($r(42) = 0.12, p > .2$).

### 3.3. Frontal vs. parietal theta

#### 3.3.1. Group analysis

As expected, the Group $\times$ Feedback $\times$ Magnitude ANOVA on the FzPz index showed no significant main effects or interactions, (all $p$'s $> .05$) indicating that the FzPz index is task independent and unrelated to depression group.

#### 3.3.2. Correlation analyses

Because the ANOVA on the FzPz index revealed no significant main effects or interactions, the FzPz index was aggregated across conditions (Cronbach’s alpha = .97). As with the ANOVA, the FzPz index did not differ between the control and MD group ($t(40) = .87, p > .3$) and was not significantly correlated with anhedonia. In contrast, the FzPz index correlated with agency ($r(42) = -0.27, p < .05$, one-sided). As in prior studies (Wacker et al., 2010), this correlation was negative, indicating that low agency was linked to relatively increased frontal theta activity. As shown in Fig. 2, the correlation was specific to the theta frequency. Moreover, controlling for handedness did not affect the correlation between agency and the FzPz index ($r(39) = -0.31, p < .05$).

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2 The Group $\times$ Valence interaction remained significant, when $n = 9$ depressed participants who were concurrently taking psychoactive medication where excluded from analyses ($F(1,31) = 3.87, p < .05$). The Group $\times$ Valence interaction remained significant, when $n = 7$ left-handed individuals were excluded from analyses ($F(1,33) = 3.36, p < .05$). Control analyses conducted on feedback-evoked delta ($1–4$ Hz) or alpha ($8–12$ Hz) power confirmed that the reported Group $\times$ Valence interaction was specific for the theta band (Group $\times$ Valence interaction, delta: $F(1,40) = .30, p > .7$; alpha: $F(1,40) = .06, p > .9$).

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### 4. Discussion

The goal of the present study was to test the relationship of anhedonia and agentic extraversion at the levels of self-report measures and electrophysiology in a sample of depressed and healthy individuals. Although questionnaire measures of anhedonia and agency showed a substantial negative correlation, the two constructs diverged with regard to EEG markers: (1) Depression and anhedonia – but not agency – predicted blunted frontal midline theta modulation to positive vs. negative or uninformative feedback and (2) agency – but not depression or anhedonia – was significantly correlated with the FzPz index.

As in prior work, frontomedial feedback-evoked theta was sensitive to feedback valence and relatively less pronounced for positive relative to negative (or uninformative) feedback in healthy individuals (Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014). To our knowledge, the present study is the first to investigate associations between feedback-evoked theta and depression or anhedonia. In sharp contrast to healthy controls, highly anhedonic or depressed participants were insensitive to different types of feedback as they showed similar theta responses for all three feedback-types. In fact, the pattern of mean theta values (Fig. 1) suggests that depressed and control participants did not differ with regard to negative or uninformative feedback but in contrast to controls, depressed participants failed to show relatively reduced theta power to positive feedback. This abnormality with regard to the processing of positive reward feedback converges with other studies similarly indicating blunted processing of positive feedback or reward in anhedonia (Liu et al., 2014; Pizzagalli et al., 2009). Furthermore, the anhedonia-related abnormalities in feedback processing reported here and elsewhere support accounts that link anhedonia to dopamine (Dunlop & Nemeroff, 2007; Pizzagalli, 2014; Wise, 2008) and dopamine to feedback processing (Holroyd & Coles, 2002; Mueller et al., 2011; Mueller, Burgdorf, Chavanon, Schweiger, Hennig, et al., 2014; Santesso et al., 2009) including feedback-evoked theta (Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014).

Of note, unlike anhedonia, agency was not related to feedback-evoked theta. It was previously reported that agency is related to feedback-evoked theta only when rewards are contingent upon the participants own effort rather than determined by external factors (Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014). Because performance in the current gambling task was also determined externally (i.e., feedback was determined “by chance”) the lack of a correlation between agency and feedback-evoked theta...
can be integrated with prior work. Most importantly, however, the present findings suggest that agency and anhedonia differently relate to frontomedial feedback processing within the same task and sample.

While agency was unrelated to feedback-evoked theta alterations, there was a negative correlation between agency and the feedback-independent FzPz index as in a number of prior studies on resting EEG (Wacker et al., 2010). This correlation is typically most pronounced for the agency facet of extraversion (Chavanon et al., 2011; Knyazev, Bocharov, & Pylkova, 2012) and – as in the present study – always indicates enhanced relative frontal theta power in intro- versus extraverts. Consistent with DA-models of agency (Depue & Collins, 1999), the FzPz index and its relationship to agency are sensitive to DA (Wacker et al., 2006). Further, a source localization study suggests that the rostral anterior cingulate cortex is the primary generator of the FzPz index (Chavanon et al., 2011). Although altered rostral ACC theta and delta activity during rest has been reported in healthy subjects with anhedonic symptoms (Wacker et al., 2009), the correlation between the FzPz index and anhedonia was not significant in the present study of healthy and depressed participants.

Three limitations of the present work should be acknowledged. First, due to restricted power the present analyses do not allow to rule out or confirm that small correlations between anhedonia and FzPz do exist and are, for example, mediated by agency. Second, menstrual cycle was not assessed in this study even though there is some evidence that it may influence EEG activity in the theta range (Solis-Ortiz, Ramos, Arce, Guevara, & Corsi-Cabrera, 1994). Finally, it should be emphasized that relationships between feedback-evoked brain activity and personality appear to be very task-specific (Mueller, Burgdorf, Chavanon, Schweiger, Wacker, et al., 2014). Here, individuals suffering from anhedonia and depression displayed blunted feedback-evoked theta modulations in a gambling task in which good vs. bad performance depends on chance rather than one’s own effort or abilities and in which good performance is associated with monetary rewards. Future extensions of this first EEG study of agency-anhedonia relationships should address these limitations by including tasks, in which feedback can be attributed internally and/or no rewards are associated with positive feedback in larger samples.

While future work is needed to explore the boundary conditions for the present observations, the observed pattern is consistent with the hypotheses that (A) Fz versus Pz theta is a marker for agency and (B) blunted theta sensitivity for feedback-variance reflects a marker for anhedonia and depression. Together with the high correlation between agency and anhedonia, these findings suggest that low agency and anhedonia, despite being strongly linked to each other at the level of self-report may be separable constructs on the neurobiological level. Future longitudinal studies should explore whether low trait agency puts individuals at a heightened risk for episodes of anhedonia, when, for example, stressful events interact with pre-existing abnormalities in the DA system (Pizzagalli, 2014).

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