Neuroticism and Extraversion Moderate Neural Responses and Effective Connectivity During Appetitive Conditioning

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Abstract: Classical appetitive conditioning constitutes a basic learning process through which environmental stimuli can be associated with reward. Previous studies showed that individual differences in neuroticism and extraversion influence emotional processing and have been shown to modulate neural activity in subcortical and prefrontal areas in response to emotional stimuli. However, the role of individual differences in appetitive conditioning has so far not been investigated in detail. The aim of this study was to assess the association between neuroticism and extraversion with neural activity and connectivity during appetitive conditioning. The conditioned stimulus (CS) was either a picture of a dish or a cup. One stimulus (CS+) was paired with a monetary reward and the other stimulus (CS−) was associated with its absence while hemodynamic activity was measured by means of functional magnetic resonance imaging. A significant negative correlation of neuroticism scores with amygdala activity was observed during appetitive conditioning. Further, extraversion was positively associated with responses in the hippocampus and the thalamus. In addition, effective connectivity between the amygdala as a seed region and the anterior cingulate cortex, the insula, and the thalamus was negatively correlated with neuroticism scores and positively correlated with extraversion scores. The results may indicate a neural correlate for the deficits in appetitive learning in subjects with high neuroticism scores and point to a facilitating effect of extraversion on reward-related learning. *Hum Brain Mapp* 37:2992–3002, 2016. © 2016 Wiley Periodicals, Inc.

Key words: reward; classical conditioning; connectivity

INTRODUCTION

The ability to form associations between a cue (conditioned stimulus; CS) and a reward (unconditioned stimulus; UCS) is an important part of approaching behavior. In appetitive conditioning paradigms, one formerly neutral stimulus (CS+) is associated with a reward stimulus, while a second neutral stimulus (CS−) predicts the absence of the reward. After a few pairings, the CS+ may elicit conditioned reactions (CRs) like changes in preference ratings, peripheral-physiological responses (e.g., SCRs), and brain activity [Andreatta and Pauli, 2015; Kirsch et al., 2003; Klucken et al., 2015b; Martin-Soelch et al., 2007]. Appetitive conditioning is hypothesized to underlie motivated approach-like behavior and is considered to constitute a central mechanism in the development, maintenance, and treatment of psychiatric disorders like addiction and eating disorders [Klucken et al., 2016; Martin-Soelch et al., 2007]. Thus, it is important to identify individual differences that are associated with appetitive conditioning.

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Extensive research has linked appetitive conditioning to the mesocorticolimbic dopamine (DA) system [Berridge and Kringelbach, 2015; Berridge and Robinson, 1998; Haber and Knutson, 2010; Martin-Soelch et al., 2007; Schultz et al., 1997]. The nucleus accumbens (NAcc), the anterior cingulate cortex (ACC), and the (medial) orbitofrontal cortex (OFC) constitute central structures of this network. Further structures such as the amygdala, the hippocampus, the insula, and the thalamus exert a regulating influence on the reward network, especially during reward learning and anticipation [Haber and Knutson, 2010; Martin-Soelch et al., 2007]. NAcc activations have been repeatedly associated with the valence transfer of the reward to the CS+ [O'Doherty et al., 2004; Schultz, 1997]. In addition, current studies extended the role of the NAcc by showing an involvement in the development of CS/UCS contingency awareness, which is also modulated by the ACC [Klucken et al., 2009a; Mechias et al., 2010]. The amygdala, which receives sensory input from the thalamus, is considered to be crucial for the CS/UCS association and the modulation of CRs [Martin-Soelch et al., 2007], while OFC and insula activations have been linked to a more detailed and conscious evaluation of CS valence and interoceptive processing [Craig, 2009; O'Doherty, 2007]. Finally, hippocampal activations during appetitive conditioning might be important for the consolidation of the newly learned associations.

Extraversion and neuroticism are among the best studied traits due to their well-documented association with health, well-being, and the development of psychiatric disorders [Klein et al., 2011; Munafò et al., 2007]. Extraversion entails different aspects of long-term positive affectivity and satisfaction and has been hypothesized to increase the sensitivity for reward signals, the attentional bias for appetitive stimuli, and to facilitate stimulus-reward association processes [Depue and Collins, 1999; Depue and Fu, 2013; Munafò et al., 2007].

While earlier models assumed that extraversion was related to differences in a reticulothalamic-cortical arousal system [Matthews and Gilliland, 1999], a more recent account theorizes that extraversion is directly related to dopaminergic transmission within the reward system [Depue and Collins, 1999; Depue and Fu, 2013]. Consistent with this idea, fMRI studies have observed positive correlations of activation of central areas of the reward system, such as the NAcc, the OFC, the cingulate cortex, and the amygdala with extraversion in response to reward stimuli [Canli et al., 2001, 2002; Canli, 2004; Cohen et al., 2005; Kehoe et al., 2012; Mobbs et al., 2005]. Moreover, dopaminergic receptor availability in the striatum has been observed to be positively correlated with extraversion [Baik et al., 2012]. Only few studies investigated the association between appetitive conditioning and extraversion with contrary results [Corr, 2004; Depue and Fu, 2013; Matthews and Gilliland, 1999]. Hooker et al. [2008] reported a negative correlation of

BOLD responses in the amygdala with extraversion scores using an observational reward conditioning paradigm. However, to date no study has examined the influence of extraversion on brain activity in a classical appetitive conditioning paradigm.

In contrast to extraversion, neuroticism comprises different aspects of negative affectivity and dissatisfaction and is linked to increased experience of negative affect, hypervigilance to negative stimuli, and an attentional bias toward negative stimuli [Canli, 2008; Goldstein and Klein, 2014]. The effects of neuroticism have been linked to amygdala activity, which has been shown to be engaged as a function of neuroticism in response to emotionally negative stimuli [Canli, 2008; Ormel et al., 2013]. In addition, a negative correlation between neuroticism and activity of the reward system during the processing of appetitive stimuli has been reported [Mobbs et al., 2005], which implicates that neuroticism also affects the processing of appetitive stimuli. Importantly, amygdala responses as well as functional connectivity of the amygdala have been reported to be associated with neuroticism during classical conditioning [Hooker et al., 2008; Tzschoppe et al., 2014], which implies that neuroticism also affects learning processes.

The aim of this study was to test the association between extraversion, neuroticism, and neural responses during an appetitive conditioning paradigm. Neutral pictures served as CS and monetary reward served as appetitive reinforcement. Based on the aforementioned results, we expected extraversion to be positively related to BOLD responses in areas of the reward system. Further, we hypothesized that neuroticism would be inversely related to amygdala activity. In addition to the analysis of parameters of activation, we also investigated whether task-dependent neural coupling of regions of the reward network was affected by extraversion and neuroticism, respectively.

METHODS AND MATERIALS

Subjects

20 healthy (10 females; $M_{\text{age}} = 23.6$; $SD_{\text{age}} = 3.1$; range: 19–33 years) subjects were recruited from campus advertisements. All subjects were students at Justus Liebig University Giessen, right-handed, and had normal or corrected-to-normal vision. Current or past mental and chronic health problems, consumption of psychotropic medication, and psychotherapeutic treatment were defined as exclusion criteria. Participants were informed about the procedure in general and gave written informed consent. All experimental procedures were in accordance with the Declaration of Helsinki and were approved by the local ethics committee of the institute for Psychology and Sports Science at the Justus Liebig University Giessen.

Stimuli

Two pictures of household items (a dish and a cup) served as CS. Pictures were taken from the International Affective Pictures System (Lang et al., 2008; picture numbers: 7006, 7009). All stimuli were comparable with regard to complexity as far as possible in order to prevent confounding effects. Stimuli were projected onto a screen at the end of the scanner (visual field = 18°) using an LCD projector (EPSON EMP-7250) and were viewed through a mirror mounted on the head coil.

Procedure

Subjects were informed that they would be exposed to pictures of everyday items as well as a monetary reward. Since contingency awareness may significantly impact CRs [Hamm and Weike, 2005; Lovibond and Shanks, 2002], subjects were instructed to look at the stimuli and to pay attention to possible relationships between the monetary reward (UCS) and the stimuli (CS) during the experiment to ensure that all participants acquired contingency awareness [Klucken et al., 2012, 2016; Phelps et al., 2004; Schiller et al., 2008]. In accordance, all subjects acquired contingency awareness during the experiment which was measured by a short structured interview. Further, subjects were instructed that they would receive 10€ for participation plus the money they gained during the experiment.

The differential delay conditioning design was adopted from previous studies in our lab [Schweckendiek et al., 2013]. During the experiment, one neutral stimulus (CS+) was presented 16 times (8 s duration) and was followed on 12 trials (75% reinforcement) by a picture (1.5 s duration) that announced a monetary reward of 1 € (UCS). The other stimulus (CS-) was also presented 16 times with the same duration (8 s). After the CS- and the non-reinforced CS+ (4 trials), a picture (non-UCS) was presented, which announced that subjects did not get a monetary reward in this trial, with the same stimulus duration as the UCS (1.5 s).

Stimulus allocation as CS+ and CS- was counterbalanced between participants. The first presentation of a CS+ was always followed by a reward. The inter trial interval (ITI) was equally distributed between 10 and 12.5 s and was calculated to contain stimulus-onset-asynchronies (ranging from 0 to 2.5 s) in order to optimize signal acquisition for the whole brain. A fixation cross was presented for the duration of the ITI. All CS were presented in a pseudo-randomized order with the restrictions: (1) no more than two consecutive presentations of the same CS, (2) an equal quantity of each CS within the first and the second half of the experiment. Throughout the experiment an MRI-compatible video camera was used to ensure that subjects watched the stimuli. Before and after the conditioning, subjective valence and arousal ratings of the CS were collected.

Self-report data

Extraversion and neuroticism were assessed by use of the NEO-FFI (Neo Five-Factor Inventory; Costa and McCrae, 1992; German version: Borkenau and Ostendorf, 1993). There were no significant differences in neuroticism ($t_{18} = 0.724$; $P = 0.478$) and extraversion ($t_{18} = 0.504$; $P = 0.620$) between males and females and extraversion and neuroticism correlated moderate only ($P < 0.01$; $r^2 = 0.42$). Before and after conditioning, subjects rated valence and arousal for each CS on a nine-point Likert scale using self-assessment manikins [Bradley and Lang, 1994]. Statistical analyses of the ratings were performed by means of a 2×2 ANOVA with the within-subject factors "stimulus" (CS+ vs. CS-) and "time" (before vs. after conditioning) as implemented in SPSS 22 (IBM Corporation, Armonk, NY) separately for the two rating dimensions (valence, arousal). In addition, we correlated changes of valence and arousal ratings [i.e., (CS+ post-CS+ pre) - (CS- post-CS- pre)] with extraversion and neuroticism scores. All statistical analyses were computed with no degree of freedom corrections.

fMRI

Functional and anatomical scans were obtained using a 1.5 T whole-body tomography (Siemens Symphony) with a standard head coil. Structural image acquisition consisted of 160 T1-weighted sagittal images (MPRage, 1 mm slice thickness). A gradient echo field map sequence was acquired before the functional image acquisition to obtain information for unwarping B0 distortions. For functional imaging, a total of 320 volumes were recorded using a T2*-weighted gradient echo-planar imaging sequence (EPI) with 25 slices covering the whole brain (voxel size: 3 mm $\times$ 3 mm $\times$ 4 mm; gap = 1 mm; descending slice order; TA = 100 ms; TE = 55 ms; TR = 2.5 s; flip angle = 90°; field of view = 192 mm $\times$ 192 mm; matrix size = 64 $\times$ 64). The orientation of the axial slices was tilted 30° to the AC-PC line to keep susceptibility artifacts in ventromedial parts of the frontal cortex to a minimum. Functional data were analyzed for outliers [Schweckendiek et al., 2013]. These outliers were later modeled within the general linear model (GLM) as a covariate of no interest. Prior to all analyses, unwarping and realignment to the first volume (b-spline interpolation), slice time correction, and normalization to the standard space of the Montreal Neurological Institute brain (MNI-brain) were performed. Smoothing was executed with an isotropic three dimensional Gaussian kernel with a full-width-at-half-maximum (FWHM) of 9 mm. Experimental conditions were modeled using stick functions convolved with the hemodynamic response function: CS+, CS-, reward, and no-reward. To account for collinearity between the regressors, the absolute values of cosine of angles between the CS+ and the reward were calculated (all values were below <0.20). Further, the six movement parameters obtained by the realignment

procedure were introduced as covariates in the model. A high pass filter (time constant = 128 s) was implemented. The subject level models were estimated after pre-whitening. The individual contrasts (CS+/CS−; reward–no-reward) were analyzed in second level random effects analyses using one-sample *t*-tests. In order to link BOLD responses to the personality traits, we correlated (voxel-wise simple regression) extraversion and neuroticism scores with the contrast CS+/CS− implemented in the multiple regression analysis in SPM8. In addition, although males and females did not show significant differences in the traits, we also conducted an analysis with the additional factor sex to control for potential effects. This analysis showed comparable results. In addition, no significant differences occurred when comparing CS+ trials in which the UCS was administered, and CS+ trials in which no UCS was administered.

In order to assess task-dependent coupling of the amygdala and the NAcc with regions of the reward network, we conducted psycho-physiological-interaction analyses (PPI) exploring the effective connectivity between a seed region and other brain areas in interaction with an experimental task [Friston et al., 1997; Gitelman et al., 2003; O'Reilly et al., 2012]. The first eigenvariate was extracted from our target regions as implemented in SPM8. Next, the interaction term was created by multiplying the extracted signal with the contrast of interest (CS+–CS−) for each participant. Then, the created interaction vector was entered into first level analyses alongside the extracted first eigenvariate, the task regressors (CS+, CS−, reward, and no-reward), the movement parameters, and the outlying volumes. Subsequently, the interaction term was tested on the group level using one-sample *t*-tests to assess coupling and decoupling. Finally, correlational analyses (simple regression) were run to investigate the association of coupling with extraversion and neuroticism, respectively.

For all models, the significance threshold was set to $\alpha = 0.05$ corrected for multiple testing using family-wise-error (FWE) correction as implemented in SPM8. Within all models, we performed explorative whole-brain analyses ($P_{\text{FWE}} < 0.05$ corrected for the whole-brain) and tested our a priori ROI using the small volume correction feature of SPM ($P_{\text{FWE}} < 0.05$ corrected for search volume) with no correction of the degree of freedom. The ROI analyses were performed for the following structures: NAcc, ACC, OFC, amygdala, insula, hippocampus, and the thalamus. All masks were created with the probabilistic Harvard–Oxford Cortical and Subcortical Structural Atlases (included in FSLView version 3.1). Anatomical labeling of the exploratory whole-brain analyses was also carried out using the Harvard–Oxford Cortical and Subcortical Atlases. In order to account for the functional heterogeneity of the ACC, additional ROI-analyses were conducted focusing on different parts of the ACC due to recent findings that associate different (emotional) functions to spe-

cific ACC subdivision [Etkin et al., 2011; McCormick et al., 2006]. Therefore, the ACC mask was divided into a more ventral part and a more dorsal part at the MNI coordinate $y = 32$. Results of the different ACC parts are presented if differences were found between them.

RESULTS

Subjective Ratings

Evaluative conditioning effects were detected in both rating dimensions: Regarding the valence ratings, ANOVA revealed a significant time $\times$ CS-type interaction ($F_{(1,19)} = 5.31$; $P = 0.033$). As expected, the CS+ was rated as significantly more pleasant compared with the CS− after conditioning ($t_{19} = 2.17$; $P = 0.042$), but not before ($t_{19} = -0.35$; $P = 0.733$) (Fig. 1B). In addition, a significant time $\times$ CS-type interaction was observed in the analysis of arousal ratings ($F_{(1,19)} = 11.85$; $P = 0.003$), with higher arousal ratings to the CS+ as compared with the CS− after conditioning ($t_{19} = 3.50$; $P = 0.002$), but not before ($t_{19} = 0.0$; $P > 0.9$). Correlation analyses of subjective valence and arousal ratings with neuroticism and extraversion did not yield significant results, but a marginal trend ($P = 0.067$; $r = 0.416$).

fMRI

Conditioned responses (CS+–CS−)

We first tested for effects of appetitive conditioning by analyzing the contrast CS+–CS−. The explorative whole-brain analysis revealed significant activity in the inferior frontal gyrus (pars opercularis) ($x = -51$, $y = 14$, $z = 10$; $t = 7.40$; $P_{\text{FWE}} = 0.018$), as well as in the superior frontal gyrus ($x = 6$, $y = 17$, $z = 62$; $t = 7.08$; $P_{\text{FWE}} = 0.034$).

ROI analyses showed significant activity in the entire ACC ($x = -3$, $y = 26$, $z = 31$; $t = 6.12$; $P_{\text{FWE}} = 0.003$) with activated clusters in the ventral and the dorsal part, the frontal medial cortex ($x = -6$, $y = 35$, $z = -17$; $t = 4.11$; $P_{\text{FWE}} = 0.045$), the left OFC ($x = -12$, $y = 32$, $z = -20$; $t = 5.04$; $P_{\text{FWE}} = 0.014$), the right insular cortex ($x = 30$, $y = 23$, $z = -2$; $t = 4.24$; $P_{\text{FWE}} = 0.049$), as well as in the left NAcc ($x = -12$, $y = 11$, $z = -5$; $t = 3.51$; $P_{\text{FWE}} = 0.022$) for the contrast CS+–CS− (Fig. 1A).

Correlations of CRs with neuroticism

Using ROI analysis, a significant negative correlation of CRs and neuroticism was detected in the left amygdala ($x = -21$, $y = -4$, $z = -17$; $t = 4.09$; $P_{\text{FWE}} = 0.019$; $r = 0.69$; Fig. 2). No significant positive correlation was observed ($P_{\text{FWE}} > 0.665$). Finally, we further tested if the correlations between females and males significantly differed. The analysis showed no significant differences between these two correlations ($z = 0.28$; $P = 0.80$).

Figure 1.

Results from the analyses of the conditioned stimuli. **(A)** Results of a ROI analysis of the contrast CS+/CS-. Image threshold was set to $t > 3$ for illustrational reasons. **(B)** Changes in mean valence and arousal

ratings before and after conditioning. Error bars represent standard errors of the mean. * $P < 0.05$; ** $P < 0.01$. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 2.

Negative correlation of neuroticism scores with neural activity in the contrast CS+/CS- in the left amygdala (**right**). Image threshold was set to $t > 3$ for illustrational reasons. Scatter plot of the contrast estimates at the peak voxel in the left amygdala and neuroticism scores (**left**). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 3.

Positive correlations of extraversion scores with neural activity in the contrast CS+/CS− in the left thalamus, the hippocampus, and the right thalamus (**above**). Image threshold was set to $t > 3$ for illustrational reasons. Scatter plots of the contrast estimates at the respective peak voxels and extraversion scores (**below**). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Correlations of CRs with extraversion

Regarding the correlational analyses of CRs and extraversion (Fig. 3), ROI analyses revealed significant positive correlations in the left hippocampus ($x = -24$, $y = -19$, $z = -17$; $t = 4.88$; $P_{FWE} = 0.011$; $r = 0.75$), the left thalamus ($x = -15$, $y = -31$, $z = 7$; $t = 4.58$; $P_{FWE} = 0.027$; $r = 0.73$), and the right thalamus ($x = 9$, $y = -7$, $z = 1$; $t = 4.29$; $P_{FWE} = 0.042$; $r = 0.71$). No significant negative correlations were observed in all ROI (max $t = 3.13$ all $P_{FWE} > 0.217$).

PPI analyses

To further explore whether neuroticism had an influence not only on reactivity but also on connectivity of the left amygdala, we extracted the significant voxels from the correlational analysis in the left amygdala and explored whether

effective connectivity of this cluster was predicted by neuroticism scores. Neuroticism scores correlated significantly negatively with coupling between the left amygdala and the ventral and dorsal ACC (whole brain analysis; $x = 9$, $y = 2$, $z = 40$; $t = 7.79$; $P_{FWE} = 0.012$; $r = 0.88$), the left insula (ROI analysis; $x = -36$, $y = 14$, $z = 1$; $t = 5.56$; $P_{FWE} = 0.006$; $r = 0.79$), the right insula (ROI analysis; $x = 30$, $y = 23$, $z = 7$; $t = 5.94$; $P_{FWE} = 0.003$; $r = 0.82$), the left thalamus (ROI analysis; $x = -18$, $y = -25$, $z = -2$; $t = 4.89$; $P_{FWE} = 0.017$; $r = 0.76$), and the right thalamus (ROI analysis; $x = 18$, $y = -19$, $z = 10$; $t = 4.47$; $P_{FWE} = 0.022$; $r = 0.74$). There were no significant positive correlations with neuroticism ($P_{FWE} > 0.274$). However, a trend with amygdala/hippocampus connectivity and neuroticism was found ($x = -21$, $y = -10$, $z = -26$; $t = 4.01$; $P_{FWE} = 0.053$).

In addition to the association with neuroticism scores, we also observed significant positive correlations between

extraversion scores and coupling of the left amygdala with the left insula ($x = -33$, $y = 11$, $z = 1$; $t = 4.43$; $P_{\text{FWE}} = 0.038$; $r = 0.72$) and the right insula ($x = 36$, $y = -13$, $z = -2$; $t = 4.38$; $P_{\text{FWE}} = 0.042$; $r = 0.72$). Interestingly, significant positive correlations were found in the dorsal ACC ($x = 12$, $y = -1$, $z = 43$; $t = 4.99$; $P_{\text{FWE}} = 0.019$; $r = 0.76$), but not in the ventral part of the ACC ($P_{\text{FWE}} = 0.261$). In addition, coupling of the left amygdala and the left hippocampus correlated significantly negatively with extraversion scores ($x = -24$, $y = -4$, $z = -29$; $t = 4.78$; $P_{\text{FWE}} = 0.014$; $r = -0.75$).

DISCUSSION

The present study aimed to investigate the association between the traits neuroticism and extraversion with the neural correlates of classical appetitive conditioning. A significant positive correlation between extraversion and neural reactivity was found in the hippocampus and bilaterally in the thalamus, while neuroticism scores were negatively associated with amygdala responses. In addition, neuroticism and extraversion were associated with nearly inverse patterns of functional coupling of the amygdala with the ACC, the insula, and the hippocampus.

Neuroticism and Appetitive Conditioning

The association between neuroticism scores and amygdala responses in the contrast CS+–CS– is in accordance with the well-documented association of amygdala responses with neuroticism during the processing of negatively valenced stimuli [Canli, 2008; Kennis et al., 2013]. Further, our results are in line with reports of neuroticism-dependent modulations of processing of appetitive stimuli, which have been shown in the context of memory, attentional processing, and emotional reactivity to pleasurable stimuli [Canli, 2008; Kehoe et al., 2012; Mobbs et al., 2005]. There is ample evidence that the amygdala plays a key role in classical conditioning of positive and negative affective stimuli. In detail, current models extended the role of the amygdala from the processing of valence to a broader role in information processing like salience detection and the processing of (un-)predictability [Pessoa, 2010; Pessoa and Adolphs, 2011]. However, the role of the amygdala's subnuclei seems to differ in different learning paradigms [Büchel and Dolan, 2000; Haber and Knutson, 2010; Martin-Soelch et al., 2007]. The negative relationship of neuroticism scores and amygdala activity could thus point to an impeded acquisition process for reward stimuli in high neuroticism subjects. A recent study, however, reported an influence of neuroticism on amygdala activity during fear learning only [Hooker et al., 2008]. These discrepancies may be due to differences in the specific neural circuits underlying direct and observational classical conditioning [Burke et al., 2010]. The present results extend the previous findings by showing that the amygdala plays

a central role for the personality trait neuroticism in the processing of appetitive conditioning.

Extraversion and Appetitive Conditioning

The present study further showed that extraversion correlated with hippocampus activity and the thalamus. The positive correlation of hippocampus activity with extraversion is in line with a previous study which used an observational reward learning task [Hooker et al., 2008]. Enhanced hippocampal engagement during conditioning has been observed to improve reward-related long-term memory consolidation [Wittmann et al., 2005] in a process guided by dopaminergic input into the hippocampus [Lisman and Grace, 2005]. It can therefore be speculated that the enhanced hippocampal engagement in individuals with high extraversion scores could be the result of an upregulated dopaminergic input and possibly reflects a facilitation of the reward learning process [Depue and Collins, 1999; Depue and Fu, 2013], which may lead to more stable reward memories. In addition, we observed positive correlations of the bilateral thalamus with extraversion. The thalamus, especially the dorsal medial nuclei, represents important nodes of the reward circuit, which connects prefrontal cortex areas with the ventral striatum [Haber and Knutson, 2010]. Thalamic activity has been reported to be especially related to the anticipation versus the delivery of reward and has been interpreted as reflecting general arousal, due to its equal involvement in the processing of negative affective stimuli [Knutson and Greer, 2008]. Our findings of higher thalamic activity in individuals high in extraversion contradicts earlier assumptions of weaker arousability of extraverts [Matthews and Gilliland, 1999] and are in line with more recent hypotheses of a more active reward system underlying extraversion [Depue and Collins, 1999]. However, we did not find significant associations between extraversion and the NAcc. One explanation for this could be that ceiling effects in NAcc activation may have prevented the detections of potential relationships. A recent meta-analysis was able to show that money provokes stronger activations within the ventral striatum than other rewarding stimuli, which may have led to decreased variance [Sescousse et al., 2013]. Taken together, our results show that extraversion influences the acquisition of conditioned reward responses, which may represent a mechanism causing the more frequent experience of positive affect in individuals with high extraversion.

Although clear conditioning effects were observed in subjective ratings and on the neural level, significant correlations of neuroticism or extraversion were only found with BOLD-responses and effective connectivity, while this was not the case for subjective ratings. This dissociation of subjective ratings and physiological data has been repeatedly observed in appetitive [Klucken et al., 2009b, 2013b] and aversive conditioning [Klucken et al., 2013a,

2015a; Lonsdorf et al., 2009; Michael et al., 2007] studies, which reported correlations of individual differences with startle [Lonsdorf et al., 2009] or BOLD responses [Klucken et al., 2009b]. Taking into consideration that some conditioning phenomena, such as extinction or over-shadowing [Dwyer et al., 2007; Vansteenwegen et al., 2006], have little or no effects on subjective ratings, it may be argued that subjective responses either represent a special form of response level or that they are too insensitive to mirror individual differences. Future studies should explore the mechanisms responsible for the dissociation of physiological and subjective data in more detail and should include further response systems.

Effects of Neuroticism and Extraversion on Amygdala Connectivity

We observed significant negative correlations of neuroticism with coupling of the left amygdala and the ACC, the bilateral insula, and the bilateral thalamus. Negative correlations of amygdala-ACC connectivity with neuroticism and anxiety-related traits have been previously reported during the viewing of negative facial expressions [Cremers et al., 2010] and in the analyses of resting state functional connectivity of the amygdala [Aghajani et al., 2014; Li et al., 2012]. Taken together, these results point to a general effect of neuroticism on amygdala-ACC connectivity, which is potentially independent of the experimental task.

Interestingly, extraversion scores produced a nearly inverse pattern of effective amygdala connectivity, indicating that positive and negative coupling of the amygdala is associated with positive and negative emotionality on the trait-level. In contrast to the negative correlations of amygdala coupling with neuroticism, significant positive correlations were observed between extraversion and amygdala-ACC, amygdala-insula as well as amygdala-thalamus coupling. In addition, post-hoc analyses showed that the observed ACC activations in this study were located considerably more dorsally, or in case of extraversion, were found in the dorsal part only, when dividing the ACC into two distinct regions. This is in line with previous findings, showing that the dorsal subdivision is more involved in the processing of reward [Bush et al., 2000; Etkin et al., 2011; Liu et al., 2011], while the ventral part is more involved in other functions like the expression of emotion per se, which is probably mediated by a (down-) regulation of the limbic system through the ventral ACC via bidirectional connections [Etkin et al., 2011]. However, another previous study [Passamonti et al., 2008] also reported positive correlations between coupling of the amygdala and the ACC with appetitive motivation (i.e., the behavioral activation system; BAS), but activation clusters were located more ventral. In contrast to the present study and others, which showed an involvement of the dorsal ACC in context of reward, Passamonti et al. (2008) investigated predominantly negative stimuli. Future stud-

ies with high-resolution MRI should investigate the subdivisions of the ACC in more detail.

Activity of the insula and the thalamus have both been related to neuroticism as well as extraversion in previous studies using various stimuli and designs [Kennis et al., 2013]. In addition, neuroticism and extraversion are not completely independent from each other and may share a common variance. Therefore, it is possible that both traits may be partly involved in the same processes, which are mirrored in neural activations. This idea is supported by the finding of a comparable inverse neural pattern. However, investigation of neural connectivity patterns of these structures in association with personality traits are lacking so far. Taken together, our results emphasize the importance of connectivity processes between remote brain areas for the understanding of higher order personality traits.

With respect to clinical implications, altered functional and effective coupling between the amygdala and the insula as well as amygdala/ACC connectivity have been directly linked to psychiatric disorders [Jacobs et al., 2016; Sutherland et al., 2012, 2013] as well as to vulnerability factors, such as functional genetic variations within the promoter region of the serotonin transporter gene [Klucken et al., 2015c; Lemogne et al., 2011; Pezawas et al., 2005; Schardt et al., 2010]. It has been assumed that the altered connectivity may mirror increased interoceptive processing and/or dysfunctional emotion regulation processes, which may in turn increase the risk for psychiatric disorders [Klucken et al., 2015c; Lemogne et al., 2011; Schardt et al., 2010]. In addition, it has been shown that decreased magnitude of coupling explained nearly 30% of variation in trait anxiety [Pezawas et al., 2005]. Consequently, altered amygdala/insula and amygdala/ACC connectivity has repeatedly been linked to psychiatric disorders like addiction and affective disorders in which emotion regulation and interoceptive processing are of importance [Jacobs et al., 2016; Sutherland et al., 2012, 2013]. However, it should be noted that it is to date not entirely clear whether increased or decreased coupling may contribute to psychiatric disorders, because results are heterogeneous and differ with respect to studies and analyses (e.g., effective vs. functional connectivity) approaches [Fedota and Stein, 2015].

CONCLUSION

In sum, we found that neuroticism and extraversion are associated with altered neural responses during human appetitive conditioning. The association of amygdala and neuroticism as well as the decreased neural coupling processes could underlie the altered processing of reward stimuli in neuroticism subjects. The positive correlations of extraversion scores with hemodynamic responses in subcortical structures could be a marker for facilitated acquisition of conditioned reward responses. In addition, the observed associations of neuroticism and extraversion with nearly inverse patterns of connectivity of the

amygdala with structures relevant for the learning and processing of emotional responses emphasize the importance of analyzing brain responses on a network level. In sum, our results point to a considerable influence of neuroticism and extraversion on neural processes and may contribute to a more sophisticated understanding of human behavior.

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