Psychoneuroendocrinology 78 (2017) 48–56

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

The burden of conscientiousness? Examining brain activation and cortisol response during social evaluative stress

Anne-Sophie Dahm[a], Phöbe Schmierer[a,b,f], Ilya M. Veer[a], Fabian Streit[c], Anna Görgen[a], Johann Kruschwitz[a], Stefan Wüst[e], Peter Kirsch[d], Henrik Walter[a,b], Susanne Erk[a,*]

[a] Dept. of Psychiatry, Division of Mind and Brain Research, Charité Universitätsmedizin Berlin, Campus Mitte, Charitéplatz 1, 10117 Berlin, Germany
[b] Berlin School of Mind and Brain, Humboldt University Berlin, Unter den Linden 6, 10099 Berlin, Germany
[c] Dept.of Genetic Epidemiology in Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim/University of Heidelberg, Square J5, 68159 Mannheim, Germany
[d] Dept. of Clinical Psychology, Central Institute of Mental Health, Medical Faculty Mannheim/University of Heidelberg, Square J5, 68159 Mannheim, Germany
[e] Institute of Experimental Psychology, University of Regensburg, Regensburg, Germany
[f] Dept. of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim/University of Heidelberg, Square J5, 68159 Mannheim, Germany

ARTICLE INFO

Article history:
Received 5 September 2016
Received in revised form 19 January 2017
Accepted 20 January 2017

Keywords:
Conscientiousness
Stress
Cortisol
fMRI
Insula
Amygdala

ABSTRACT

Although conscientiousness has for a long time been considered generally adaptive, there are findings challenging this view, suggesting that conscientiousness might be less advantageous during uncontrollable stress. We here examined the impact of conscientiousness on brain activation during and the cortisol response following an uncontrollable social evaluative stress task in order to test this hypothesis.

Brain activation and cortisol levels were measured during an fMRI stress task, where subjects ($n = 86$) performed cognitive tasks containing preprogrammed failure under time pressure, while being monitored by a panel of experts inducing social-evaluative threat. The degree of conscientiousness was measured using the NEO-FFI.

We observed a positive correlation between conscientiousness and salivary cortisol levels in response to the stressful task in male subjects only. In male subjects conscientiousness correlated positively with activation in right amygdala and left insula, and, moreover, mediated the influence of amygdala and insula activation on cortisol output. This pattern of brain activation can be interpreted as a disadvantageous response to uncontrollable stress to which highly conscientious individuals might be predisposed.

This is the first study showing the effect of conscientiousness on physiology and brain activation to an uncontrollable psychosocial stressor. Our results provide neurobiological evidence for the hypothesis that conscientiousness should not just be seen as beneficial, but rather as a trait associated with either costs or benefits depending on the extent to which one is in control of the situation.

1. Introduction

Conscientiousness (C) traditionally has been seen as a protective factor, providing longevity (Kern and Friedman, 2008) and subjective well-being (Steel et al., 2008), and moderating the relationship between daily hassles and health-behavior (O'Connor et al., 2009). However, others challenge the generally protective effect of conscientiousness, suggesting that conscientiousness is rather associated with either costs or benefits, depending on the situation (Nettle, 2006).

One indication that conscientiousness is not always advantageous for well-being is provided by a study showing that highly conscientious individuals experience a 120% higher decrease in life satisfaction than those at low levels when being 3 years unemployed (Boyce et al., 2010). In the context of unemployment, often perceived as severe and chronic failure, conscientiousness thus seems to be a trait that might in some circumstances constitute a risk for well-being (Boyce et al., 2010).

Additionally, it has been reported that highly conscientious individuals experience higher tension after receiving negative feedback

* Corresponding author at: Department of Psychiatry and Psychotherapy, Division of Mind and Brain Research, Charité -Universitätsmedizin Berlin, Campus Mitte, Charitéplatz 1, D–10117 Berlin, Germany.
E-mail address: susanne.erk@charite.de (S. Erk).

http://dx.doi.org/10.1016/j.psyneuen.2017.01.019
0306-4530/

than less conscientious individuals (Cianci et al., 2010). Similar to unemployment, negative feedback can be interpreted as failure that cannot easily be changed or controlled. It appears plausible that highly conscientious individuals become more strongly affected by experiences of failure, because of being high-achievers who are not self-indulgent (McCrae and John, 1992).

Beyond that conscientiousness is not only associated with achievement-striving but also with high levels of self-regulation, persistence, impulse-control, and self-discipline (McCrae and John, 1992). Highly conscientious individuals are thus likely to be motivated to succeed and to persist until a particular goal is attained. This might result in being rigidly attached to previously defined goals (Nettle, 2006), which in turn might induce increased stress levels in the context of uncontrollable failure. In other words, as conscientiousness seems to influence the importance of, and therefore the reaction to failure as well, which clearly represents a stressful experience for highly conscientious individuals because of their personal standards, expectations, and behavior, a rather detrimental effect of conscientiousness on well-being possibly depends on the processing of uncontrollable stressful experiences.

The influence of personality on the endocrine stress reaction has been investigated by several studies (Bibbey et al., 2013). The reported null findings concerning conscientiousness (Bibbey et al., 2013) could be due to the controllability of the stressor in these studies, as the effect of conscientiousness is suggested to be dependent upon the degree of control afforded during stress exposure (Bibbey et al., 2013).

In order to investigate the influence of conscientiousness on the neural and endocrine stress reaction, we investigated subjects with different levels of conscientiousness during an fMRI task inducing social evaluative threat and the experience of uncontrollable failure (Lederbogen et al., 2011), the combination of which is known to elicit the strongest stress reaction in a laboratory setting (Dickerson and Kemeny, 2004).

We tested the following parameters: behavior (subjective experience of stress), endocrine stress reaction (cortisol output, i.e. AUCg), and brain activity (fMRI). We hypothesized that highly conscientious participants will be more stressed in response to the task than their less conscientious counterparts reflected by increased levels of behavioral, endocrine, and neural responses to stress. At the neural level, we expected to find an association between conscientiousness and changes in brain activity in those brain areas that have been previously implicated in subjective perception and appraisal of stressful situations, i.e. amygdala, insula, and dACC (Kern et al., 2008; Tillfors et al., 2001; Wang et al., 2005). In addition, as gender differences in stress processing and cortisol response are well known (Duchesne and Pruessner, 2013), we also included sex as a variable of interest.

2. Material and methods

2.1. Participants

We recruited 86 (50 female, 36 male; mean age: 27 (±6.01 years)) healthy volunteers of European descent in Berlin. All participants were screened reporting no acute or chronic diseases, no recreational drug use, no medication and neither personal nor family history of DSM-IV axis I disorders during a structured clinical interview (Wittchen et al., 1997). All subjects met the safety requirements for participation in an fMRI study. The study was approved by the local ethics committee and written informed consent was given by all participants. We also assessed handedness, intelligence, Body Mass Index and psychometric variables, such as anxiety and depression scores, to exclude possible confounds. For demographic and behavioral measures see Table 1.

Table 1
Demographic and behavioral measures.

		N	mean	SD	*p*
Age	male	36	27.03	5.45	
	female	50	28.18	6.40	0.384
	all	86	27.70	6.02	
BMI	male	36	23.46	2.66	
	female	50	22.62	3.23	0.204
	all	86	22.97	3.02	
School certificate (Abitur, 10th grade)	male	36	33/3		
	female	50	47/3		0.916
	all	86	80/6		
MWTB	male	36	31.81	2.56	
	female	50	31.02	2.18	0.129
	all	86	31.35	2.37	
STAI-T	male	36	33.19	5.12	
	female	50	31.94	7.28	0.377
	all	86	32.47	6.46	
BDI-II	male	35	3.97	3.54	
	female	50	3.94	4.41	0.972
	all	85	3.95	4.05	
conscientiousness	male	36	32.03	6.95	
	female	50	34.98	5.60	0.032
	all	86	33.74	6.34	
neuroticism	male	36	13.61	5.59	
	female	50	14.22	6.41	0.648
	all	86	13.97	6.05	
extraversion	male	36	28.89	5.13	
	female	50	30.04	6.98	0.404
	all	86	29.56	6.27	
openness	male	36	32.92	6.31	
	female	50	32.76	5.73	0.918
	all	86	32.83	6.16	
agreeableness	male	36	31.81	6.49	
	female	50	35.24	5.04	0.007
	all	86	33.80	5.91	
subjective stress	male	36	1.78	0.90	
	female	49	2.14	0.71	0.039
	all	85	1.99	0.81	
AUCi	male	34	294.42	419.18	
	female	49	185.72	447.02	0.267
	all	83	230.25	436.55	
AUCg	male	34	1130.09	475.88	
	female	49	907.09	510.63	0.048
	all	83	998.44	505.91	
Responder/Nonresponder	male	34	27/7		
	female	49	28/21		0.058
	all	83	55/28		
Handedness (right/left/ambidextrous)	male	36	34/2/0		
	female	50	47/0/3		0.085
	all	86	81/2/3		

BMI, Body mass index, MWTB, Mehrfachwahl-Wortschatz-Intelligenztest, STAI-T, State-Trait-Anxiety-Inventory, BDI-II, Beck Depression Inventory, AUCi, Area under the curve with respect to increase, AUCg, Area under the curve with respect to ground. P-value refers to sex differences.

2.2. Stress task

To examine the influence of conscientiousness on brain activation and cortisol levels in response to uncontrollable stress the Scan*STRESS* paradigm was employed (Akdeniz et al., 2014; Lederbogen et al., 2011). Participants performed two runs (lasting 11:20 min per run), each consisting of four blocks of a stress condition and four blocks of a control condition. Every block lasted 60 s and was preceded by a 5 s screen indicating the specific task that had to be performed. Within each run, the order of blocks was as follows: Subjects first performed one block of mental spatial rotation and one block of arithmetic subtraction under time pressure (stress blocks), followed by a block of simple figure-matching and a block of number-matching (control blocks). This sequence of blocks was presented twice within one run, and blocks were interspersed with 20 s of rest. During stress blocks, social-evaluative threat was induced by two investigators in laboratory coats (introduced to the participants as a panel of experts), providing serious and disapproving facial expressions via live video stream after slow or incorrect responses. In addition, the investigators displayed every wrong answer with a buzzer, which prompted negative visual feedback on the task screen. The task contained preprogrammed failure as the program automatically adjusted task speed and difficulty. In the control condition, subjects performed the number- and figure-matching tasks without monitoring, time pressure, and feedback. After completing half of the task, subjects received standardized negative verbal feedback via the video stream, indicating that their performance was insufficient and that their data might not be of sufficient quality to analyze. Following task completion, subjects rated to what extent the task elicited negative emotions, including feelings of stress, on a four-level scale (Lederbogen et al., 2011). Concerning feelings of stress they rated to what extend they agreed with the statement 'I was stressed by the negative feedback on my insufficient performance' (agree at all, rather disagree, rather agree, and fully agree). At the end of the procedure subjects were thoroughly debriefed.

2.3. Conscientiousness

Conscientiousness was assessed with the German version of NEO-FFI (Borkenau and Ostendorf, 2008). Internal consistency of the NEO-FFI factors are reported to be between $\alpha = 0.72$ and $\alpha = 0.87$ and retest reliability (5 years) between $r = 0.71$ and $r = 0.82$ (Borkenau and Ostendorf, 2008).

2.4. Saliva sampling

Salivary cortisol was assessed at seven time points throughout the scanning session using Salivettes (Sarstedt, Nümbrecht, Germany). The first saliva sample was taken shortly before the beginning of the stress task, the second sample between the two runs of the task after the negative verbal feedback (approximately 15 min after the onset of the task), and the third sample immediately after finishing the task, approximately 30 min after the onset of the stress induction. Sample 4–7 were taken outside of the scanner, at about 45, 60, 75, and 90 min after the onset of the task.

The saliva samples were stored at −20 C until analysis. Cortisol concentrations in saliva (in nmol/L) were measured using a chemiluminescence-immunoassay kit (IBL, Hamburg, Germany). Inter- and intra-assay coefficients of variation were below 6%.

2.5. Procedure

The stress task took place on the second day of a two-day study protocol, created to examine the neural basis of affective disorders. Thus, on the day of scanning participants were already familiar with the MR environment as the stress task took place on the second day of the study-protocol, minimizing stress reactions independent of the task. After arrival, participants were seated in a quiet room and instructed about the protocol. Before the first saliva sample was taken they completed a test-session of the Scan*STRESS* control condition to become familiar with the task, which was introduced to them as a performance test. To keep cortisol levels as comparable as possible and free of morning cortisol elevations, scanning sessions were organized such that saliva sampling started either at 12 am or 2 pm. Subjects reported no use of medication (except for hormonal contraceptives, $n = 23$) and felt rested and healthy on the testing day. In order to reduce further unwanted effects on cortisol levels, participants were asked to wake up at least 4 h before testing, to refrain from caffeine, and not to eat 2 h before arrival. Psychological testing took place on a separate day within one week.

2.6. Behavioral and physiological statistical analysis

Analysis of demographic, psychometric, and physiological variables were performed using SPSS Statistics 22 (IBM).

Three subjects had to be excluded from cortisol analysis due to insufficient saliva. A repeated measures ANOVA was conducted to test whether stress induction was successful or not. In addition to that, the area under the curve with respect to both ground (AUCg) and increase (AUCi) were calculated for all participants for saliva samples 1–7 reflecting the total amount of hormonal output (AUCg) and changes over time (AUCi) (Pruessner et al., 2003). Responders were defined as AUCi > 0. In an additional analysis, we defined responder status as baseline-to-peak cortisol increase >1.5 nmol/l as it has been proposed recently (Miller et al., 2013). Regression analyses were conducted to test whether conscientiousness influences the cortisol response or the experience of subjective stress. For all analyses, sex was added as a covariate.

Additionally, Greenhouse-Geisser corrections were applied when the sphericity assumption was violated and non-parametric tests were done.

2.7. fMRI data acquisition and preprocessing

Imaging data were acquired on a 3 T scanner (Siemens Tim Trio, Erlangen, Germany) during the Scan*STRESS* task (GRE-EPI; 36 slices; axially tilted; slice thickness 2.4 + 0.6 mm gap; FoV = 192 mm; voxel size: 3 mm isotropic; TR = 1960 ms; TE = 25 ms; flip angle = 80°). Preprocessing and analysis were conducted using Statistical Parametric Mapping (SPM8, http://www.fil.ion.ucl.ac.uk/spm). Images were realigned to a mean image, slice time corrected, transformed to the Montreal Neurological Institute (MNI) EPI reference space (voxel size: 2 mm isotropic), and spatially smoothed with an 8 mm full-width at half-maximum (FWHM) Gaussian filter.

2.8. fMRI analyses

A first level fixed effects model including two session-specific partitions per subject was calculated for each participant. For each session it included six regressors (stress arithmetic subtraction, stress figure rotation, control numbers, control figures, announcement of stress, and announcement of control) and six movement parameters that were entered as covariates of no interest. Obtained t-contrast images (stress (arithmetic + figure) > control (arithmetic + figure) overall sessions, stress (arithmetic + figure) for session 1 and 2 separately and control (arithmetic + figure) for session 1 and 2 separately, see below) were subjected to second-level random effects models: The general effect of task (stress induction) was tested using a one-sample *t*-test. Further, as the social stress intervention was applied between runs 1 and 2 (see 2.5), we additionally tested for an interaction between stress and run by calculating a 2 × 2 ANOVA with the factors stress and session-number. Finally, we analyzed the influence of conscientiousness on stress related brain activation using a multiple regression analysis. Sex was added as a covariate (Duchesne and Pruessner, 2013).

Significance was defined as $p < 0.05$, family wise error (FWE) corrected, either whole brain (one sample *t*-test, 2 × 2 ANOVA) or for a priori defined regions of interest (ROI). For all predefined ROIs (i.e., amygdala, dACC and insula) we used structural ROI masks from the AAL atlas (Tzourio-Mazoyer et al., 2002) using the WFU Pickatlas toolbox (Maldjian et al., 2003).

3. Results

3.1. Behavioral results

Conscientiousness was normally distributed, the mean score (33.74 ± 6.34) was slightly below the normal mean (34.5) (Borkenau and Ostendorf, 2008), and the female subjects in our study scored slightly higher than the male subjects (males (32.03 ± 6.9), females (34.98 ± 5.6), $F(1.85) = 4.74$, $p = 0.032$, $\eta^2 = 0.053$). Conscientiousness correlated positively with subjective experience of stress ($r = 0.301$, $p = 0.003$, CI: [.06–0.50]). However, as scores for conscientiousness differed significantly between sex, we performed correlation analyses for male and female subjects separately, showing a significant association only in the female group (female $r = 0.28$, $p = 0.027$, CI: [-0.02–0.55]; male $r = 0.26$, $p = 0.072$, CI: [-0.09–0.57]). The difference in correlation between groups was not significant ($z = 0.09$, $p = 0.92$, two-tailed).

3.2. Endocrinological results

Stress induction was successful in the whole sample, as sampling time point significantly predicted cortisol levels ($F(6.00) = 57.07$ $p < 0.001$). Wilcoxon-signed-rank test revealed higher cortisol values during ($p < 0.0001$) (sample 2) and after ($p < 0.008$) the stress induction (samples 3–7) compared with cortisol values before the stress task (sample 1, for time course of cortisol concentration see supplementary figure SF1). 55 of 83 (66.3%) subjects showed a cortisol increase in response to the task (AUCi > 0) while 28 (33.7%) subjects did not. Within the group of responder 28 were female (57.1% of the female group) and 27 male (79.4% of the male group), in the non-responder group were 21 female (42.9%) and 7 male (20.6%). When grouping subjects according to a recent proposal (baseline-to-peak cortisol increase > 1.5 nmol/l), 57 (68.7%) subjects were defined as responder (30 female (61.2% of the female group), 27 male (79.4% of the male group)) and 26 (31.3%) as non-responder (19 female (39.8%), 7 male (20.6%)).

Conscientiousness did not correlate with AUCi ($r = 0.001$, $p = 0.496$, CI: [-0.20–0.23]), but did with AUCg ($r = 0.210$, $p = 0.029$, CI: [-0.01–0.41]). Again, because scores for conscientiousness differ significantly between sex, and because there are known sex differences in the endocrinological stress response, we calculated the analysis for male and female subjects separately: There was no significant correlation between conscientiousness and AUCi in both groups (male $r = 0.174$, $p = 0.162$, CI: [-0.36–0.43]; female $r = -0.087$, $p = 0.28$, CI:[-0.10–0.44]). Conscientiousness correlated significantly with AUCg in male subjects only ($r = 0.478$, $p = 0.002$, CI: [0.24–0.66]; female $r = 0.104$, $p = 0.24$, CI:[-0.26–0.39]). This difference shows a trend for significance ($z = 1.83$, $p = 0.067$, two-tailed).

3.3. fMRI results

Stress processing involved a similar network of brain structures seen in previous studies (Akdeniz et al., 2014; Lederbogen et al., 2011): A one-sample *t*-test showed increased activation during stress (compared to the control condition) in the bilateral insula ($x = -32$, $y = 22$, $z = 4$, $Z > 8$; $x = 34$, $y = 24$, $z = 0$, $Z > 8$), ventral striatum ($x = -14$, $y = -2$, $z = 0$, $Z > 8$; $x = 14$, $y = -2$, $z = 0$, $Z > 8$), dorsal anterior cingulate cortex (dACC, $x = -6$, $y = 10$, $z = 50$, $Z > 8$), and posterior hippocampus ($x = -26$, $y = -32$, $z = 8$, $Z = 7.11$; $x = 24$, $y = -28$, $z = 12$, $Z > 8$), and reduced activation in the bilateral amygdala ($x = -16$, $y = -2$, $z = -16$, $Z = 6.73$; $x = 18$, $y = -4$, $z = -18$, $Z = 6.09$), anterior hippocampus ($x = -26$, $y = -18$, $z = -20$, $Z > 8$; $x = 28$, $y = -16$, $z = -20$, $Z = 7.31$), subgenual and perigenual anterior cingulate cortex (sgACC, $x = -4$, $y = 32$, $z = -18$, $Z > 8$; pgACC, $x = -6$, $y = 54$, $z = 0$, $Z > 8$) and posterior cingulate cortex ($x = 0$, $y = -50$, $z = 32$, $Z > 8$) (all $p < 0.05$, whole brain corrected). Female and male subjects did not differ in their brain response to stress. As participants were presented with social-evaluative negative feedback in between the two runs, we additionally tested for an interaction between stress and run (see Section 2.8) using an undirected F-test. A significant interaction was observed within dACC ($x = -2$, $y = 8$, $z = 32$, $Z = 7.32$), bilateral insula ($x = -34$, $y = 14$, $z = 4$, $Z = 6.96$; $x = 38$, $y = 0$, $z = 12$, $Z = 6.75$) and sgACC ($x = -8$, $y = 30$, $z = -20$, $Z = 5.0$), all $p < 0.05$ corrected for whole brain, as well as the bilateral amygdala ($x = -28$, $y = -6$, $z = -12$, $Z = 4.35$, $x = 32$, $y = -4$, $z = -12$, $Z = 2.98$, both $p < 0.05$ corrected for region of interest). Post-hoc tests demonstrated increased stress-related activation in the dACC, insula, and amygdala, as well as reduced activation in the sgACC during the second run, following social-evaluative negative feedback. Therefore, we chose to focus on data from the second run in the following analyses. Again, we observed no significant difference between male and female subjects.

Similar to the behavioral analyses, we tested the influence of conscientiousness on stress related brain activation in separate analyses for male and female subjects. Here, we observed a significant positive correlation between conscientiousness and activation increase in the left insula ($x = -40$, $y = 0$, $z = 4$, $Z = 3.47$, $p_{FWE\_ROI} = 0.043$) and right amygdala ($x = 34$, $y = 2$, $z = -24$, $Z = 3.13$; $p_{FWE\_ROI} = 0.021$) in male subjects only (Fig. 1). We observed no significant effect in women.

3.4. Results of control analyses

As it is known that the five factors of the NEO-FFI are intercorrelated, we additionally ran a partial correlation analysis controlling for neuroticism, extraversion, openness and agreeableness. All results of the behavioral, endocrinological and fMRI analyses remain significant. Although we know that this does not rule out confounding effects of the other NEO-FFI-factors, we assume that our results rely mainly on individual levels of conscientiousness.

Further, we tested for associations of conscientiousness within and between female subjects taking hormonal contraceptives and those who do not. Female subjects that do not take hormonal contraceptives show no significant correlation between conscientiousness and subjective experience of stress ($r = 0.121$, $p = 0.556$), whereas the group taking contraceptives does ($r = 0.598$, $p = 0.004$). The difference between the groups is not significant, yet can be considered a trend ($z = 1.86$, $p = 0.063$). Concerning endocrinological results, both groups show no significant correlation of conscientiousness with either AUCi (with contraceptives $r = 0.239$, $p = 0.315$, without contraceptives $r = -0.186$, $p = 0.363$) or AUCg (with $r = 0.408$, $p = 0.066$, without $r = -0.138$, $p = 0.502$). Further, we also tested for a correlation between brain activation in response to stress and conscientiousness in each of the two groups. Again, no significant effect was observed. Thus, we do not see a significant difference between females taking hormonal contraceptives and those who do not in any of our analyses. However, as the groups are relatively small, this might mask underlying effects of contraceptives.

Finally, to explore the influence of responder status to our results, we split the group and tested for correlation of conscientiousness with behavioral, endocrine and neuroimaging data for each responder group separately. For the behavioral data, we observed a significant correlation of conscientiousness with subjective experience of stress only in the non-responder ($n = 28$, $r = 0.598$, $p = 0.001$), but not in the responder group ($n = 55$, $r = 0.105$, $p = 0.22$) when responders where defined as AUCi > 0. Similar results were observed when defining responder status according to baseline-to-peak cortisol increase > 1.5 nmol/l (non-responder: $n = 26$, $r = 0.593$, $p = 0.002$, responder: $n = 57$, $r = 0.103$, $p = 0.45$). Neither for the

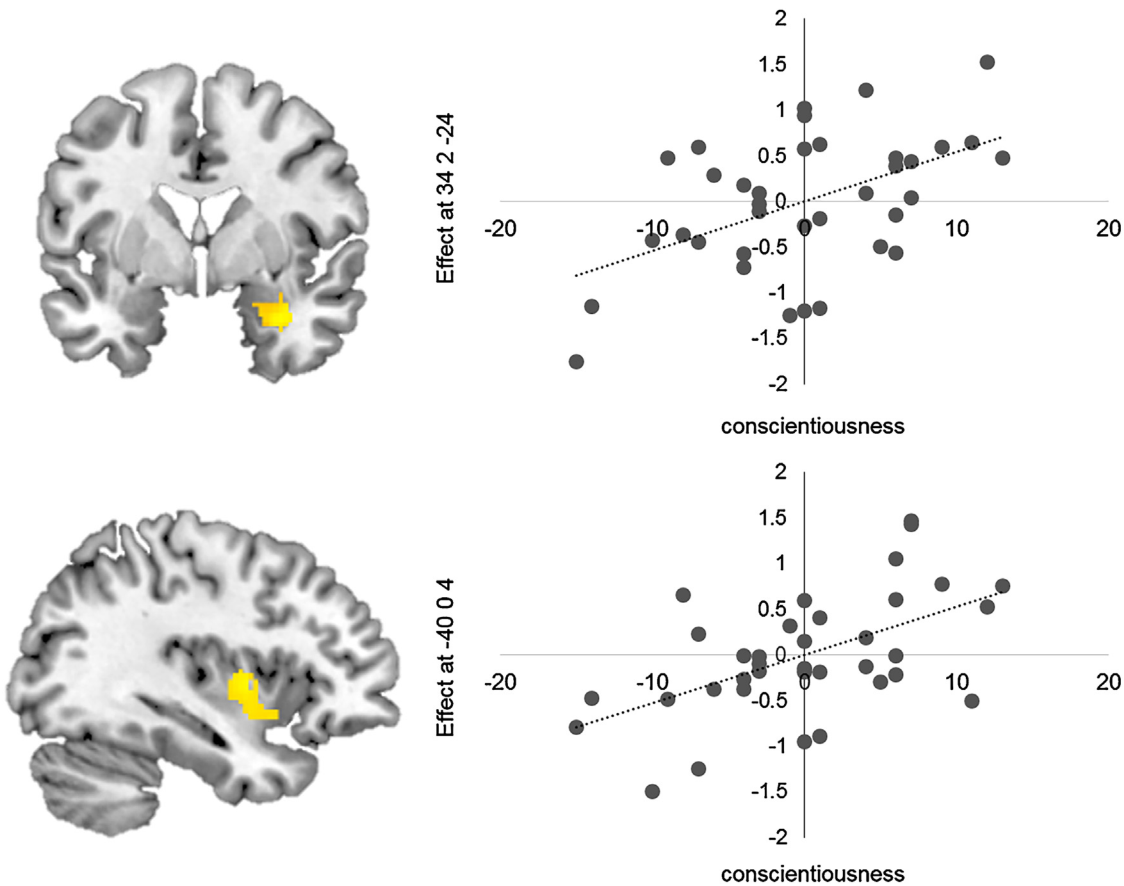

Fig. 1. Results of correlation analysis. In male subjects brain response to stress > control in the right amygdala and left insula during the second run correlated positively with conscientiousness scores ($p < 0.05$ FWE_{ROI}).

endocrine nor for the neuroimaging results we found a significant difference between responder groups (in both grouping models).

3.5. Exploratory mediation analysis

Mediation analyses, using ordinary least squares path analyses in the SPSS version of PROCESS (Hayes, 2013), were conducted across male participants to examine whether the observed amygdala and/or insula activation influenced cortisol output (AUCg) through conscientiousness (Fig. 2, Tables 2a and 2b). Data for amygdala and insula activation were extracted from peak voxel coordinates of the group-level statistical map. A bias-corrected 95% bootstrap confidence interval (CI) for the indirect effect (ab = 106.618) based on 5000 bootstrapped samples was above zero (25.878–247.946), and thus considered statistically significant. A corresponding analysis with left insula activation showed a similar effect of mediation (ab = 143.00, CI = 29.865–314.742).

4. Discussion

In the current study we investigated whether conscientiousness could be less advantageous under uncontrollable stress. Highly conscientious individuals were hypothesized to show more signs of stress than less conscientious subjects in response to our social stress paradigm. Indeed, as expected, higher conscientiousness was associated with increased subjective feelings of stress, which was particularly evident in female participants. In addition, in males only, conscientiousness correlated positively with the cortisol response to the stressor and elicited stronger stress-related activity in the amygdala and insula following social stress induction. Furthermore, the trait was shown to mediate the association between the brain activity to the task manipulation within these regions and the endocrine output, as indicated by activation of the amygdala and insula and the AUCg levels, respectively.

The amygdala is involved in processing socioemotional and threatening facial information (Adolphs, 2002; Whalen et al., 2001). Moreover, activation in the amygdala has been shown to correlate positively with subjective anxiety during stress (Tillfors et al., 2001; Wang et al., 2005). Thus, increased amygdala activation among highly conscientious individuals may indicate fear of (further) negative social evaluation. This is in line with Cianci et al. (2010), who showed that individuals high in conscientiousness experience greater tension after receiving negative feedback. However, stronger amygdala activation under stressful conditions cannot only be associated with an elevated stress response, but could also represent a vulnerability pattern (Lederbogen et al., 2011), consistent with the fact that formerly depressed participants responded with greater amygdala activation to criticism (Hooley et al., 2009). Interestingly, Hooley et al. concluded that this activation might be a vulnerability marker for depression that persists even in the face of full recovery. Further, the association of greater psychological resources with lower cortisol reactivity to a stress task is supposed to be mediated by a decrease of amygdala activity during threat regulation (Taylor et al., 2008). This is consistent with findings of Urry et al. (2006) who reported intentional regulation of negative affect to be associated with amygdala deactivation, which in turn predicted a greater decrease in diurnal cortisol. Remarkably, higher threat-related amygdala reactivity has shown to predict increased risk for pathological mood and anxiety in response to common stressors (Hariri and Holmes, 2015), and the magnitude

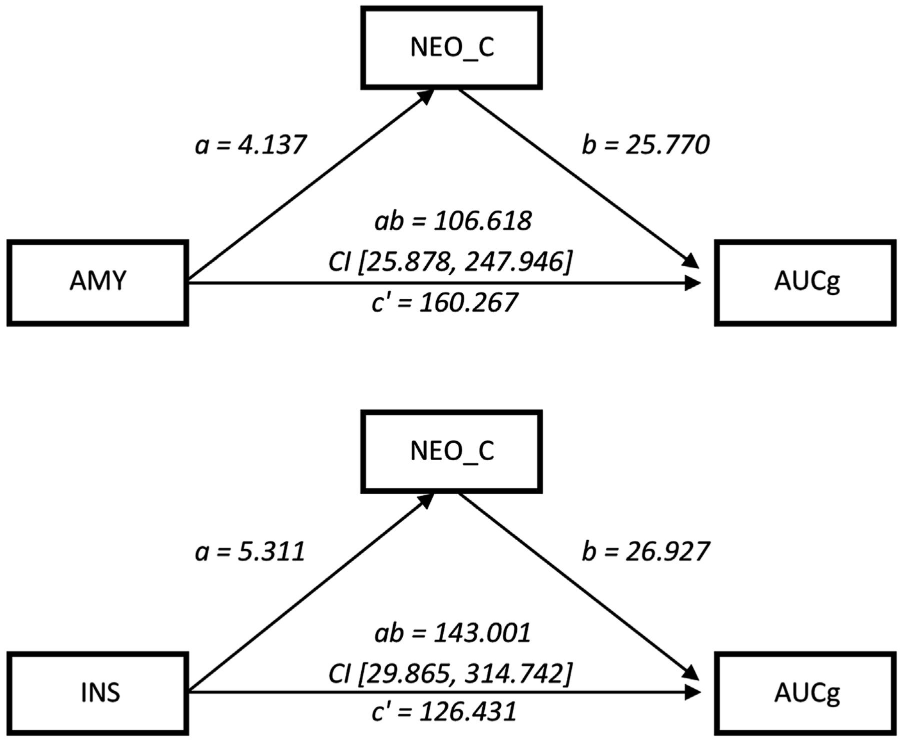

Fig. 2. Mediation Model. Pathways from amygdala/insula (AMY/INS) activation to conscientiousness (NEO_C, path a) and then from NEO_C to AUCg (path b) represent the indirect effect of AMY/INS activation on AUCg through conscientiousness (quantified as the product of path a and b). The pathway from AMY/INS to AUCg (path c') represents the direct effect of brain activation on AUCg. A 95% confidence interval (CI) for the indirect effect does not contain or go through zero, thus providing evidence that conscientiousness serves as a mediator of the effect of AMY/INS activation on AUCg.

Table 2a
Model coefficients for the mediation model of the right amygdala.

		M (NEO_C)				Y (AUCg)		
		coeff.	SE	p		coeff.	SE	p
X (right Amygdala)	*a*	4.137	1.413	0.006	*c'*	160.267	110.019	0.155
M (NEO_C)					*b*	25.770	12.221	0.043
Constant	i_1	32.402	1.036	<0.001	i_2	286.877	402.413	0.481
		$R^2 = 0.211$				$R^2 = 0.277$		
		$F(1.32) = 8.569$, $p = 0.006$				$F(2.31) = 5.953$, $p = 0.006$		

Table 2b
Model coefficients for the mediation model of the left insula.

		M (NEO_C)				Y (AUCg)		
		coeff.	SE	*p*		coeff.	SE	*p*
X (left Insula)	*a*	5.311	1.451	0.001	*c'*	126.431	128.654	0.333
M (NEO_C)					*b*	26.927	13.159	0.049
Constant	i_1	32.429	0.979	<0.001	i_2	251.795	432.926	0.565
		$R^2 = 0.295$				$R^2 = 0.251$		
		$F(1,32) = 13.395$, $p = 0.001$				$F(2.31) = 5.207$, $p = 0.011$		

of amygdala reactivity even has shown to be a better predictor of vulnerability than differences in childhood trauma, recent stressful experiences, or self-reported symptoms (Hariri and Holmes, 2015).

The part of the insula activated in our study is implicated in interoception and subjective feelings of emotion (Craig, 2004), as well as in the functional integration of these and other functional domains (Kurth et al., 2010). As activity in the insula has been reported to correlate positively with subjective experience of stress (Kern et al., 2008; Wang et al., 2005), increased activation of the insula in highly conscientious individuals in our data may also be associated with increased interoceptive perception. It might further represent a disadvantageous response to uncontrollable stress, taking into account that increased insula activation has been associated with rumination following an interpersonal provocation-task, in which participants were told they were not intelligent enough to follow simple instructions (Denson et al., 2009). This view is further supported by findings from social exclusion tasks, which indicate that people with lower self-esteem show increased activity in the bilateral insula when receiving critical evaluation about their life goals and aspirations (Eisenberger and Inagaki, 2011).

The pattern of brain activation found in our study is consistent with the concurrent positive correlation between conscientiousness and the endocrine stress response, as the amygdala is known to activate the HPA axis (Herman et al., 2005). Furthermore, there is some evidence supporting a role for the insula in psychologically mediated HPA axis activation, since the ACTH response to a challenge has been associated with activity in the insula across several emotional activation tasks (Liberzon et al., 2007). Moreover, ACTH measures, as well as cortisol levels, have been shown to correlate positively with cerebral blood flow (CBF) in the insula (Ottowitz et al., 2004). Consequently, increased insula activation among highly conscientious individuals could reflect the impact of psychological processes on HPA axis activation (Ottowitz et al., 2004). Interestingly, we could show that the association between amygdala and insula activation and cortisol output is mediated by conscientiousness. This finding further underlines the potential role of conscientiousness in the brain response to uncontrollable stress.

It is clear that stress responses are not disadvantageous in nature, but rather indicate engagement and coping (Chrousos, 2009), and the release of cortisol in response to stressors is adaptive and necessary for survival. However, prolonged or heightened activation of the HPA axis has been shown to have negative psychological and physiological effects (Seeman et al., 2001) and HPA hyperactivity, frequently reported in depression, is considered as an important risk factor in its etiology (Alexander et al., 2009).

The fact that the task used in our study contained social evaluation and explicit failure is likely to be particularly relevant for highly conscientious individuals, given that conscientiousness implies conforming to social norms (Fayard et al., 2012) and that highly conscientious individuals are supposed to be used to more successful outcomes (Byrne et al., 2005). Therefore social evaluation, especially when explicitly negative, and failure are thus particularly stressful for these individuals. We thus might speculate that highly conscientious individuals may exhibit this pattern of brain activation due to a specific attribution style. As conscientiousness is assumed to play a role in the motivation to improve performance following negative feedback (Bono and Colbert, 2005), which is a kind of active coping, but useless in the context of preprogrammed failure, the resulting repeated failure could lead to self-doubt and extreme feelings of stress. Boyce et al. (2010) interpret the greater decrease in life-satisfaction after unemployment in a way that could also apply for our context. They assumed that highly conscientious individuals are not able to attribute failure to a lack of effort (a temporary and specific cause of failure) and may attribute their failure to their own lack of ability (a stable and general cause of failure). This attribution style is likely to create stress and has been related to clinical depression (Alloy et al., 2006), anxiety (Ralph and Mineka, 1998), and negative affect (Sanjuán et al., 2008). Notably, increased activation of amygdala, the brain activation pattern exhibited by male subjects high in conscientiousness in our study, has been related to dysregulation of emotion in mood and anxiety disorders (Shin and Liberzon, 2010).

We hypothesize that the frequently reported beneficial effect of conscientiousness, such as greater well-being (Steel et al., 2008) and longevity (Kern and Friedman, 2008), could be due to the controllability and consequent effectivity of their active coping style in most situations in life, while the less beneficial side of conscientiousness will only be visible in uncontrollable situations when their strategies become ineffective and their ability to persist harmful, both causing greater stress which in turn includes several severe health impacts (Chrousos, 2009). Our findings thus highlight the importance of a more balanced perspective on this trait.

5. Limitations

Our study has several limitations. First, our sample included subjects with rather moderate levels of conscientiousness. Although conscientiousness was normally distributed, the mean score (33.7) was slightly below the normal mean (34.5) (Borkenau and Ostendorf, 2008). Further studies are needed to confirm our findings in a sample with more extreme levels of conscientiousness.

Second, albeit the responder rate in our study can be considered high, especially as the usual responder rate for this stress paradigm is 50% (Pruessner et al., 2010), the gender differences regarding the responder rate do raise some questions. Although females show a higher level of conscientiousness, only 57.1% (61.2% respectively) of the females compared to 79.4% of the males responded with an AUCi > 0 (baseline-to-peak cortisol increase > 1.5 nmol/l respectively). One possible explanation could be the panel sex composition which seems to influence the neuroendocrine stress response in both men and women (Duchesne et al., 2012). The authors observed that men and women in the follicular cycle phase presented a cortisol increase only when exposed to opposite sex panellists. Albeit we had male and female panellists, the panel in our study neither was composed of women and men in a consistent manner, nor was it composed depending on the subjects' sex. Additionally, we had more female than male panellist, which could explain the higher responder rate among the male subjects. However, yet another factor could have caused the greater cortisol response of the male as well; that is, achievement striving. The ScanSTRESS paradigm contains both social evaluation (social stress), which seems to be more relevant for women (Dedovic et al., 2009), and uncontrollable failure (achievement stress), which seems to affect men especially (Dedovic et al., 2009). It is conceivable that the women in our study perceived the achievement component as the dominant characteristic of the task, because the social evaluation appealed to their performance, and therefore had a smaller stress response than the male subjects.

In addition to this, we observed further sex differences in our analyses that need to be discussed. We did not find a significant correlation between conscientiousness and subjective feelings of stress in the male participants, although they did show an increased stress response on the endocrine and the neural level. This dissociation might be explained by emotion-suppressing coping (Campbell and Ehlert, 2012), a strategy that is assumed to be especially used by men (Avero and Calvo, 1999): As a result of mental efforts to protect the positive self-image and in order to avoid vulnerable emotional states, emotion-suppressing coping can result in decreased emotional expressiveness (Campbell and Ehlert, 2012). In light of strong evidence that men are more likely to adopt goals promoting autonomy and self-interest, as well as to keep their privacy, to present themselves in a positive light, and to control social situations (Dedovic et al., 2009), the absence of an association between subjective and objective measures of stress in our data does not seem so surprising anymore. In addition, self-report methods are very likely to be influenced by sex stereotypes and retrospective biases (Hess et al., 2000).

On the other hand, we found a significant correlation between conscientiousness and subjective feelings of stress in the female subjects, whereas the effect of conscientiousness on the endocrine and neural level was less evident. A possible explanation could be offered by hormonal influences. The current phase of the menstrual cycle has been shown to affect cortisol responses to acute stress (Dedovic et al., 2009), emotional responses (Goldstein et al., 2005), and differential activity related to the menstrual cycle has previously been reported in regions involved in stress regulation, e.g. amygdala (Bale and Epperson, 2015; Goldstein et al., 2010). Additionally, women using oral contraceptives are known to show lower levels of free cortisol in response to acute stressors (Dedovic et al., 2009). We therefore speculate, although we have not collected data on the phase of the menstrual cycle or on sex steroid levels, and did not observe significant differences between females taking contraceptives and those who do not in our analyses, that the effect of conscientiousness on stress might well have been obscured by more subtle hormonal differences in the women from our sample. It cannot be ruled out that these effects might become apparent only when testing larger samples.

Albeit the apparent impact of sex on our results, we would like to stress that we were able to provide evidence for the assumption that conscientiousness has an effect on the stress response on several levels. In addition, we hypothesize that a study controlling for this factor would be able to demonstrate the effect of conscientiousness on neural, endocrine, and subjective responses to stress both in men and women.

6. Conclusion

This is the first study providing neurobiological evidence for the assumption that conscientiousness is not universally adaptive, but rather associated with either costs or benefits, depending on the situation (Nettle, 2006). Our findings extend this view to the factor of control, which could determine the experience of stress for individuals high in conscientiousness and in this way important health outcomes as well (Chrousos, 2009), suggesting that highly conscientious individuals could be more vulnerable to develop stress-related disorders when confronted with chronic uncontrollable stressors.

Acknowledgments

The authors thank Jonas Leppig, Katharina Demin, Mascha Roth, and Luisa Balzus for their assistance in data acquisition as well as Caroline Wackerhagen for her valuable comments

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.psyneuen.2017.01.019.

References

Adolphs, R., 2002. Recognizing emotion from facial expressions: psychological and neurological mechanisms. Behav. Cogn. Neurosci. Rev. 1, 21–62.
Akdeniz, C., Tost, H., Streit, F., Haddad, L., Wüst, S., Schäfer, A., Schneider, M., Rietschel, M., Kirsch, P., Meyer-Lindenberg, A., 2014. Neuroimaging evidence for a role of neural social stress processing in ethnic minority-associated environmental risk. JAMA Psychiatry 71, 672–680, http://dx.doi.org/10.1001/jamapsychiatry.2014.35.
Alexander, N., Kuepper, Y., Schmitz, A., Osinsky, R., Kozyra, E., Hennig, J., 2009. Gene-environment interactions predict cortisol responses after acute stress: implications for the etiology of depression. Psychoneuroendocrinology 34, 1294–1303, http://dx.doi.org/10.1016/j.psyneuen.2009.03.017.
Alloy, L.B., Abramson, L.Y., Whitehouse, W.G., Hogan, M.E., Panzarella, C., Rose, D.T., 2006. Prospective incidence of first onsets and recurrences of depression in individuals at high and low cognitive risk for depression. J. Abnorm. Psychol. 115, 145–156, http://dx.doi.org/10.1037/0021-843X.115.1.145.
Avero, P., Calvo, M.G., 1999. Emotional reactivity to social-evaluative stress: gender differences in response systems concordance. Pers. Individ. Dif. 27, 155–170, http://dx.doi.org/10.1016/S0191-8869(98)00229-3.
Bale, T.L., Epperson, C.N., 2015. Sex differences and stress across the lifespan. Nat. Neurosci. 18, 35–42, http://dx.doi.org/10.1038/nn.4112.
Bibbey, A., Carroll, D., Roseboom, T.J., Phillips, A.C., de Rooij, S.R., 2013. Personality and physiological reactions to acute psychological stress. Int. J. Psychophysiol. 90, 28–36, http://dx.doi.org/10.1016/j.ijpsycho.2012.10.018.
Bono, J., Colbert, A., 2005. Understanding responses to multi- source feedback: the role of core self-evaluations. Pers. Psychol. 58, 171–203.
Borkenau, P., Ostendorf, F., 2008. NEO-Fünf-Faktoren Inventar Nach Costa Und McCrae (NEO-FFI) Manual (2., Neu Normierte Und Vollständig überarbeitete Auflage). Hogrefe, Göttingen.
Boyce, C.J., Wood, A.M., Brown, G.D., 2010. The dark side of conscientiousness: conscientious people experience greater drops in life satisfaction following unemployment. J. Res. Pers. 44, 535–539, http://dx.doi.org/10.1016/j.jrp.2010.05.001.
Byrne, Z.S., Stoner, J., Thompson, K.R., Hochwarter, W., 2005. The interactive effects of conscientiousness, work effort, and psychological climate on job performance. J. Vocat. Behav. 66, 326–338, http://dx.doi.org/10.1016/j.jvb.2004.08.005.
Campbell, J., Ehlert, U., 2012. Acute psychosocial stress: does the emotional stress response correspond with physiological responses? Psychoneuroendocrinology 37, 1111–1134, http://dx.doi.org/10.1016/j.psyneuen.2011.12.010.
Chrousos, G.P., 2009. Stress and disorders of the stress system. Nat. Rev. Endocrinol. 5, 374–381, http://dx.doi.org/10.1038/nrendo.2009.106.
Cianci, A.M., Klein, H.J., Seijts, G.H., 2010. The effect of negative feedback on tension and subsequent performance: the main and interactive effects of goal content and conscientiousness. J. Appl. Psychol. 95, 618–630, http://dx.doi.org/10.1037/a0019130.
Craig, D.B., 2004. Human feelings: why are some more aware than others? Trends Cogn. Sci. 8, 239–241, http://dx.doi.org/10.1016/j.tics.2004.04.004.
Dedovic, K., Wadiwalla, M., Engert, V., Pruessner, J.C., 2009. The role of sex and gender socialization in stress reactivity. Dev. Psychol. 45, 45–55, http://dx.doi.org/10.1037/a0014433.
Denson, T.F., Pedersen, W.C., Ronquillo, J., Nandy, A.S., 2009. The angry brain: neural correlates of anger, angry rumination, and aggressive personality. J. Cogn. Neurosci. 21, 734–744, http://dx.doi.org/10.1162/jocn.2009.21051.
Dickerson, S., Kemeny, M., 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol. Bull. 130, 355–391, http://dx.doi.org/10.1037/0033-2909.130.3.355.
Duchesne, A., Pruessner, J.C., 2013. Association between subjective and cortisol stress response depends on the menstrual cycle phase. Psychoneuroendocrinology 38, 3155–3159, http://dx.doi.org/10.1016/j.psyneuen.2013.08.009.
Duchesne, A., Tessera, E., Dedovic, K., Engert, V., Pruessner, J.C., 2012. Effects of panel sex composition on the physiological stress responses to psychosocial stress in healthy young men and women. Biol. Psychol. 89, 99–106, http://dx.doi.org/10.1016/j.biopsycho.2011.09.009.
Eisenberger, N., Inagaki, T., 2011. The neural sociometer: brain mechanisms underlying state self-esteem. J. Cogn. Neurosci. 23, 3448–3455.
Fayard, J.V., Roberts, B.W., Robins, R.W., Watson, D., 2012. Uncovering the affective core of conscientiousness: the role of self-conscious emotions. J. Pers. 80, 1–32, http://dx.doi.org/10.1111/j.1467-6494.2011.00720.x.
Goldstein, J.M., Jerram, M., Poldrack, R., Ahern, T., Kennedy, D.N., Seidman, L.J., Makris, N., 2005. Hormonal cycle modulates arousal circuitry in women using functional magnetic resonance imaging. J. Neurosci. 25, 9309–9316, http://dx.doi.org/10.1523/JNEUROSCI.2239-05.2005.
Goldstein, J.M., Jerram, M., Abbs, B., Whitfield-Gabrieli, S., Makris, N., 2010. Sex differences in stress response circuitry activation dependent on female hormonal cycle. J. Neurosci. 30, 431–438, http://dx.doi.org/10.1523/JNEUROSCI.3021-09.2010.
Hariri, A.R., Holmes, A., 2015. Finding translation in stress research. Nat. Neurosci. 18, 1347–1352, http://dx.doi.org/10.1038/nn.4111.
Hayes, A.F., 2013. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach. The Guilford Press, New York.
Herman, J.P., Ostrander, M.M., Mueller, N.K., Figueiredo, H., 2005. Limbic system mechanisms of stress regulation: hypothalamo-pituitary-adrenocortical axis. Prog. Neuropsychopharmacol. Biol. Psychiatry 29, 1201–1213, http://dx.doi.org/10.1016/j.pnpbp.2005.08.006.
Hess, U., Sene, S., Kirouac, G., Philippot, P., Kleck, R.E., 2000. Emotional expressivity in men and women: stereotypes and self-perceptions. Cogn. Emot. 14, 609–642.
Hooley, J.M., Gruber, S., Parker, H., Guillaumot, J., Rogowska, J., Yurgelun-Todd, D., 2009. Cortico-limbic response to personally challenging emotional stimuli after complete recovery from depression. Psychiatry Res. 171, 106–119, http://dx.doi.org/10.1016/j.pscychresns.2008.04.001.
Kern, M.L., Friedman, H.S., 2008. Do conscientious individuals live longer? A quantitative review. Health Psychol. 27, 505–512, http://dx.doi.org/10.1037/0278-6133.27.5.505.
Kern, S., Oakes, T.R., Stone, C.K., McAuliff, E.M., Kirschbaum, C., Davidson, R.J., 2008. Glucose metabolic changes in the prefrontal cortex are associated with HPA axis response to a psychosocial stressor. Psychoneuroendocrinology 33, 517–529, http://dx.doi.org/10.1016/j.psyneuen.2008.01.010.
Kurth, F., Zilles, K., Fox, P.T., Laird, A.R., Eickhoff, S.B., 2010. A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis. Brain Struct. Funct. 214, 519–534, http://dx.doi.org/10.1007/s00429-010-0255-z.
Lederbogen, F., Kirsch, P., Haddad, L., Streit, F., Tost, H., Schuch, P., Wüst, S., Pruessner, J.C., Rietschel, M., Deuschle, M., Meyer-Lindenberg, A., 2011. City living and urban upbringing affect neural social stress processing in humans. Nature 474, 498–501, http://dx.doi.org/10.1038/nature10190.
Liberzon, I., King, A.P., Britton, J.C., Phan, K.L., Abelson, J.L., Taylor, S.F., 2007. Paralimbic and medial prefrontal cortical involvement in neuroendocrine responses to traumatic stimuli. Am. J. Psychiatry 164, 1250–1258, http://dx.doi.org/10.1176/appi.ajp.2007.06081367.
Maldjian, J., Laurienti, P.J., Kraft, R., Burdette, J.H., 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. Neuroimage 19, 1233–1239, http://dx.doi.org/10.1016/S1053-8119(03)00169-1.
McCrae, R., John, O., 1992. An introduction to the five-factor model and its applications. J. Pers. 60, 175–215.
Miller, R., Plessow, F., Kirschbaum, C., Stalder, T., 2013. Classification criteria for distinguishing cortisol responders from nonresponders to psychosocial stress. Psychosom. Med. 75, 832–840, http://dx.doi.org/10.1097/PSY.0000000000000002.

Nettle, D., 2006. The evolution of personality variation in humans and other animals. Am. Psychol. 61, 622–631, http://dx.doi.org/10.1037/0003-066X.61.6.622.
O'Connor, D.B., Conner, M., Jones, F., McMillan, B., Ferguson, E., 2009. Exploring the benefits of conscientiousness: an investigation of the role of daily stressors and health behaviors. Ann. Behav. Med. 37, 184–196, http://dx.doi.org/10.1007/s12160-009-9087-6.
Ottowitz, W.E., Dougherty, D.D., Sirota, A., Niaura, R., Rauch, S.L., Brown, W.A., 2004. Neural and endocrine correlates of sadness in women: implications for neural network regulation of HPA activity. J. Neuropsychiatry Clin. Neurosci. 16, 446–455, http://dx.doi.org/10.1176/appi.neuropsych.16.4.446.
Pruessner, J.C., Kirschbaum, C., Meinlschmid, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28, 916–931, http://dx.doi.org/10.1016/S0306-4530(02)00108-7.
Pruessner, J.C., Dedovic, K., Pruessner, M., Lord, C., Buss, C., Collins, L., Dagher, A., Lupien, S.J., 2010. Stress regulation in the central nervous system: evidence from structural and functional neuroimaging studies in human populations – 2008 Curt Richter Award Winner. Psychoneuroendocrinology 35, 179–191, http://dx.doi.org/10.1016/j.psyneuen.2009.02.016.
Ralph, J., Mineka, S., 1998. Attributional style and self-esteem: the prediction of emotional distress following a midterm exam. J. Abnorm. Psychol. 107, 203–215.
Sanjuán, P., Pérez, A., Rueda, B., Ruiz, Á., 2008. Interactive effects of attributional styles for positive and negative events on psychological distress. Pers. Individ. Dif. 45, 187–190, http://dx.doi.org/10.1016/j.paid.2008.03.004.
Seeman, T.E., McEwen, B.S., Rowe, J.W., Singer, B.H., 2001. Allostatic load as a marker of cumulative biological risk: macArthur studies of successful aging. Proc. Natl. Acad. Sci. U. S. A. 98, 4770–4775, http://dx.doi.org/10.1073/pnas.081072698.
Shin, L.M., Liberzon, I., 2010. The neurocircuitry of fear, stress, and anxiety disorders. Neuropsychopharmacology 35, 169–191, http://dx.doi.org/10.1038/npp.2009.83.
Steel, P., Schmidt, J., Shultz, J., 2008. Refining the relationship between personality and subjective well-being. Psychol. Bull. 134, 138–161, http://dx.doi.org/10.1037/0033-2909.134.1.138.
Taylor, S.E., Burklund, L.J., Eisenberger, N.I., Lehman, B.J., Hilmert, C.J., Lieberman, M.D., 2008. Neural bases of moderation of cortisol stress responses by psychosocial resources. J. Pers. Soc. Psychol. 95, 197–211, http://dx.doi.org/10.1037/0022-3514.95.1.197.
Tillfors, M., Furmark, T., Marteinsdottir, I., Fischer, H., Pissiota, A., Långström, B., Fredrikson, M., 2001. Cerebral blood flow in subjects with social phobia during stressful speaking tasks: a PET study. Am. J. Psychiatry 158, 1220–1226.
Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 15, 273–289, http://dx.doi.org/10.1006/nimg.2001.0978.
Urry, H.L., Reekum, C.M., Johnstone, Van, Kalin, T., Thurow, N.H., Schaefer, M.E., Jackson, H.S., Frye, C.A., Greischar, C.J., Alexander, L.L., Davidson, A.L., 2006. Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. J. Neurosci. 26, 4415–4425, http://dx.doi.org/10.1523/jneurosci.3215-05.2006.
Wang, J., Rao, H., Wetmore, G.S., Furlan, P.M., Korczykowski, M., Dinges, D.F., Detre, J.A., 2005. Perfusion functional MRI reveals cerebral blood flow pattern under psychological stress. Proc. Natl. Acad. Sci. U. S. A. 102, 17804–17809, http://dx.doi.org/10.1073/pnas.0503082102.
Whalen, P.J., Shin, L.M., McInerney, S.C., Fischer, H., Wright, C.I., Rauch, S.L., 2001. A functional MRI study of human amygdala responses to facial expressions of fear versus anger. Emotion 1, 70–83.
Wittchen, H.-U., Zaudig, M., Fydrich, T., 1997. SKID Strukturiertes Klinisches Interview für DSM-IV Achse I Und II Handanweisung. Hogrefe, Göttingen.