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Research paper

Attachment insecurity modulates neural responses to psychological distress in OCD and healthy individuals

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ABSTRACT

Background: Insecure attachment style has been associated with obsessive-compulsive disorder (OCD). Psychological stress is known to aggravate OCD symptoms and activate the attachment system. Here, we investigated reactivity of attachment-related neurocircuitry under psychological distress in OCD patients.

Methods: Twenty-two patients with OCD and twenty-three healthy controls underwent fMRI scanning after psychological stress induction and a control condition in a cross-over design. Neural responses were measured during presentation of negative emotional faces. Attachment insecurity was measured using the self-report experiences in close relationships scale (ECR) and the adult attachment interview (AAI).

Results: OCD participants showed higher scores on ECR attachment anxiety compared to controls. Stress was successfully induced as shown by subjective stress measurements and physiological parameters. OCD participants showed a blunted cortisol response to the stressor. However, no group differences were found in neural stress responses. Across participants, psychological distress decreased hippocampal responses. This effect was dependent on attachment style, with participants scoring high on attachment anxiety showing increased rather than decreased hippocampal activity when distressed. Participants scoring high on attachment insecurity as measured with the AAI showed increased activity in multiple attachment-related brain regions.

Conclusions: Attachment style, but not OCD status, modulated neural responses to emotionally salient information under psychological distress. These findings provide further support for the assumption that attachment insecurity may be an important transdiagnostic vulnerability factor.

1. Introduction

Attachment insecurity, referring to the constellation of personal characteristics related to the absence of a secure base in close relationships, has been associated with increased life-time vulnerability for psychopathology (M. Mikulincer and Shaver, 2007). It negatively impacts on self- and worldview, social behavior, quality of close relationships and stress- and emotion regulation (Bakermans-Kranenburg and van IJzendoorn, 2009; Mikulincer and Shaver, 2007). Two types of attachment insecurity have been distinguished, i.e., attachment anxiety and attachment avoidance, although people can also have mixed traits, referred to as fearful avoidance (Bartholomew and Horowitz, 1991). Attachment anxiety is characterized by fear of abandonment and clinging behavior, while attachment avoidance is characterized by overreliance on control and autonomy, avoiding dependency on and emotional proximity to others. Securely attached persons rely on social support while at the same time feeling autonomous (Bartholomew and Horowitz, 1991; Brennan et al., 1998).

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Obsessive-compulsive disorder (OCD) is associated with higher levels of attachment anxiety and to a lesser extent with higher levels of attachment avoidance (van Leeuwen et al., 2020). In addition, securely attached (as opposed to insecurely attached) OCD patients have a better long term outcome after seeking treatment (Tibi et al., 2020). Possible underlying mechanisms are that attachment insecurity may render OCD patients biased to negative interpretations of intrusions (Doron et al., 2009; Doron and Kyrios, 2005; Doron and Moulding, 2009; Ein-Dor et al., 2016) and OCD patients with high levels of attachment anxiety may be more prone to reassurance seeking, contributing to the maintenance of OCD (Causier and Salkovskis, 2025; Kobori and Salkovskis, 2013). In addition, attachment insecurity may accelerate the development of OCD symptomatology because of its association with impaired stress regulation (Mikulincer et al., 2003). In fact, insecurely attached OCD patients may show worsening of symptoms particularly under stressful circumstances as this typically leads to increased fears for separation and abandonment (Ein-Dor et al., 2016; Mikulincer et al., 2003). As OCD symptoms often deteriorate under stressful circumstances (Adams et al., 2018), it is worthwhile to investigate the possible moderating role of attachment insecurity in stress regulation in OCD patients.

The attachment system becomes activated under stress (Bowlby, 1969, 1980; Long et al., 2020; Mikulincer and Shaver, 2007). When adjusted well, the (mental representation of the) attachment relationship serves effective downregulation of distress and facilitates explorative behavior by turning down the attachment system. In case of attachment anxiety, the attachment system gets hyperactivated under stress: the person becomes hypervigilant for signs of threat and attachment-related cues, leading to a cascade of negative affectability and cognitions. In case of attachment avoidance, the attachment system gets deactivated under stress: attention is turned away from threat- and attachment-related cues, leading to suppression, however no resolution, of stress and negative emotions (Mikulincer et al., 2003). In line with this, a functional neuro-anatomical model of attachment has been conceptualized (Long et al., 2020; Vrtička and Vuilleumier, 2012). Although further research is needed, imaging studies show remarkable differences between attachment styles within neural networks in response to social-emotional stimuli (Long et al., 2020; Perlini et al., 2019; Vrtička and Vuilleumier, 2012). Hypervigilance for negative social cues and a tendency to exaggerate negative emotions is reflected in hyperreactivity of areas in the salience network, such as the amygdala and hippocampus, in anxiously attached individuals (DeWall et al., 2012; Gillath et al., 2005; Long et al., 2020; Redlich et al., 2015; Riem et al., 2012; Vrticka et al., 2008). In contrast, in avoidantly attached individuals, the tendency to turn away from social support is reflected in diminished reactivity in both the salience network towards social rejection cues and the ventral striatum towards positive feedback (DeWall et al., 2012; Vrticka, 2012; Vrtička et al., 2008). Although attachment avoidance is related to increased reactivity in the salience network towards negative social cues as well, simultaneous increased prefrontal activity implies the use of (ineffective) cognitive control to suppress these triggered affects (Gillath et al., 2005; Vrtička et al., 2012).

Despite the association found between attachment insecurity and OCD, the underlying mechanism and neural substrates remain elusive. Hypothetically, heightened activation of fear- and salience related neurocircuitry by attachment insecurity can affect functional parts of the limbic and cortico-striato-thalamo-cortical circuits relevant for OCD (Adams et al., 2018; van den Heuvel et al., 2016). In this study, we aimed to investigate reactivity of attachment-related neural circuitry under psychological distress in a group of OCD patients and healthy controls. Participants were submitted to a controlled stress induction paradigm using the socially evaluated cold-pressor test (Schwabe et al., 2008) in a within-subjects design. After stress induction (or neutral control condition) neural activity was recorded with fMRI in response to negative facial stimuli, as strong attachment-related cues (Antonucci et al., 2018; Bowlby, 1973). Attachment insecurity was measured with both a commonly used and well-validated self-report questionnaire, the experience in close relationships scale (ECR) (Brennan et al., 1998), and with a qualitative semi-structured interview, the adult attachment interview (AAI) (George et al., 1985). The ECR was developed to assess conscious attachment-related coping styles towards current close relationships, whereas the AAI was developed to measure subconscious mental representations about early attachment relationships. Since the AAI is labor-intensive to conduct, it has not often been used in neuroscientific research and to our knowledge this is the first study to employ the AAI in adults with OCD.

Based on the research reviewed above, we hypothesized that attachment insecurity, and attachment anxiety in particular, would be positively associated with increased vigilance towards negative and threatening social cues under psychological distress. This is detectable as heightened amygdala and hippocampus activation, as part of stress-related and salience processing neurocircuitry (Herman et al., 2005). Furthermore, we hypothesized that OCD participants would show higher stress reactivity than healthy controls as well as higher attachment insecurity scores, which would subsequently moderate the neural reactivity to negative facial stimuli under psychological distress.

2. Methods

2.1. Participants

Twenty-six OCD participants were recruited from the outpatient clinic for anxiety disorders at the psychiatry department of the Amsterdam UMC (location AMC) and through advertisements on the website of the Dutch OCD patient organization. Inclusion criteria were (1) aged 18–65 years; (2) diagnosis of OCD according to the DSM-IV; (3) Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (Goodman et al., 1989) score of 12 or higher; (4) willingness and ability to understand, participate and comply with the study requirements. Exclusion criteria are reported in the Supplement.

In addition, twenty-nine healthy control participants without a psychiatric diagnosis (current and lifetime), matched according to age, sex, educational level, and handedness, were recruited through flyers and online community advertisements. All participants were assessed on anxiety, depressive and obsessive-compulsive symptoms, using the Hamilton Anxiety Rating Scale (HAM-A) (Hamilton, 1959), the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) and the YBOCS, respectively. In addition, the presence of psychiatric co-morbidities was assessed with the M.I.N.I. (Sheehan et al., 1998). After inclusion, four OCD participants and six healthy control participants dropped-out of the study. This was due to technical problems with the scanner (three OCD and one healthy control participant), insufficient brain coverage during scanning (one healthy control participant) and an incidental neurological finding (one healthy control participant). Furthermore, one OCD participant and three healthy control participants decided to discontinue the study. In total, twenty-two OCD participants and twenty-three healthy control participants were included in the data analysis.

The present study was part of a larger fMRI study, approved by the Ethical Committee of the Academic Medical Center in Amsterdam (METC 2014_168; trial ID in ISRCTN47698087). The study was conducted between February 2016 and July 2018. Beforehand, all recruited participants gave written informed consent. Other data from this study have been reported elsewhere (van der Straten et al., 2020; van Leeuwen et al., 2023).

2.2. Stress induction procedure

The study used a cross-over design with counterbalanced order of stress induction versus a control session, with a one-week interval, across participants. During the stress session, participants were exposed to the socially evaluated cold-pressor test (SECPT) (Schwabe et al., 2008). In the control session the procedure was similar, with stressful elements eliminated. The SECPT is a minimally psychologically invasive procedure that has been repeatedly shown to induce a reliable physiological and subjective stress response (Schwabe et al., 2008) (see Supplement for details).

The physiological stress response was assessed by measuring blood pressure, heart rate and salivary cortisol. Subjective stress response was measured with the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1983). Furthermore, participants were requested to rate how difficult, unpleasant, and stressful the stress (or control) procedure was using a subjective stress level questionnaire with a VAS scale (Schwabe et al., 2008). For an overview of the study design and measurement time points, see Fig. 1 and Supplement.

After stress induction and control session, participants underwent an emotional face matching task (FMT). Because this study was part of a larger set of experiments, the FMT was conducted on average 73 min after the stress (or control) procedure. Before the FMT, participants underwent a cognitive task followed by a resting state task (van der Straten et al., 2020), which were not expected to increase stress levels or to produce carry-over effects that would interact with the crossover design. At the end of the stress session, participants received a debriefing about intention of the stress manipulation.

2.3. Face matching task

The face matching task (FMT) is a short and widely used paradigm which robustly engages a network including the amygdala and hippocampus by contrasting the response to simultaneously presented angry and fearful face stimuli (pictures) with the response to geometric shapes (i.e. ellipses that consisted of scrambles of the same face stimuli) (Hariri et al., 2002). Each trial consists of three simultaneously presented stimuli, with the cue stimulus presented above the target and distractor. In the emotion condition, an angry or fearful face is presented on top as cue, and participants must indicate by an appropriate button press, which of the bottom two faces (one angry and one fearful) matches the cue in emotional expression. In the sensorimotor control (neutral) condition, the task is the same, but the stimuli consist of horizontally- or vertically oriented ellipses and the participants must select the identically oriented ellipse. Three neutral blocks were alternated with two emotion blocks with a total duration of 2.65 min. All blocks consisted of six stimuli. For an overview of the task see Fig. 2. Average response times and correct response rates were recorded.

2.4. Measurement of attachment style

Attachment style was assessed with two measures, i.e., the ECR and the AAI. The ECR is a widely used questionnaire in empirical studies that measures attachment anxiety and attachment avoidance separately as continuous variables. The self-report scale consists of 18 items assessing attachment anxiety and 18 items assessing attachment avoidance. On a seven-point scale the responder needs to indicate the extent to which a description of close relationships (with a romantic partner, close friend, or family member) corresponds to his or her experience. The total scores represent the extent of attachment anxiety and avoidance, respectively. See Supplement for additional analyses we applied on the ECR scores. Furthermore, we used the ECR scores as covariates in the fMRI analysis to investigate the correlation between attachment insecurity and neural stress responding.

The AAI is a semi-structured interview, consisting of questions about childhood experiences with attachment figures. The AAI was conducted and scored following the AAI guidelines (see Supplement). Scores are presented both categorical as well as dimensional. Categories are labelled 'Free and autonomous with respect to attachment' ('free/F'), 'Enmeshed and preoccupied with attachment' ('enmeshed/E') and 'Dismissing of attachment' ('dismissing/Ds'), related to respectively secure, anxious, and avoidant attachment styles. The dimensional score is labelled 'State of mind' (SoM) and ranks between secure and insecure poles (1–9). So, the insecure pole comprises both anxious and avoidant predispositions. We investigated if the distribution over the three attachment categories as well as dimensional scores differed between participant groups. The dimensional outcome was also used as a covariate in the fMRI analysis to investigate the correlation between attachment insecurity and neural stress responding.

2.5. Statistical analysis

Demographical and clinical data were analysed with SPSS software (version 24.0, Chicago, IL, USA). Group differences for the continuous variables age and Y-BOCS, HAMA and HDRS score were tested using Mann-Whitney *U* tests, as parametric assumptions were violated. A paired-sample *t*-test was used to compare Y-BOCS values before each visit within the patient group. For testing group differences of gender, handedness, and education, χ^2 tests were used. ECR anxiety and avoidance subscales were ^{10}log transformed to meet parametric assumptions. Dimensional attachment scores (ECR and SoM scores) were compared between patient and healthy control groups with an independent samples t-test. χ^2 test was used to test differences between groups on AAI categorization. The analysis was followed by post-hoc χ^2 tests in case of significance, with Bonferroni correction for multiple comparisons.

The physiological stress effects (blood pressure, heart rate and cortisol) and anxiety levels (STAI) were analysed using mixed model analysis of variance (ANOVA) with the factors group (OCD, healthy controls), session (stress, control) and time (five for physiology, four for anxiety), corrected for the order of sessions. No time factor was used for cortisol, as we calculated the area under the curve with respect to the ground (AUCg) to assess overall exposure to cortisol during the session (Pruessner et al., 2003). We compared baseline cortisol levels between sessions using paired-sample *t*-tests. Because the cortisol outcomes were positively skewed, these data were first ^{10}log transformed, after which parametric assumptions were met.

The subjective stress level questionnaire was studied using a mixed model ANOVA with the factors group (OCD, healthy controls), session (stress, control) and question type (how difficult, how stressful, how unpleasant), corrected for the order of sessions. Furthermore, response rates in the FMT were analysed using Mann-Whitney U tests for between

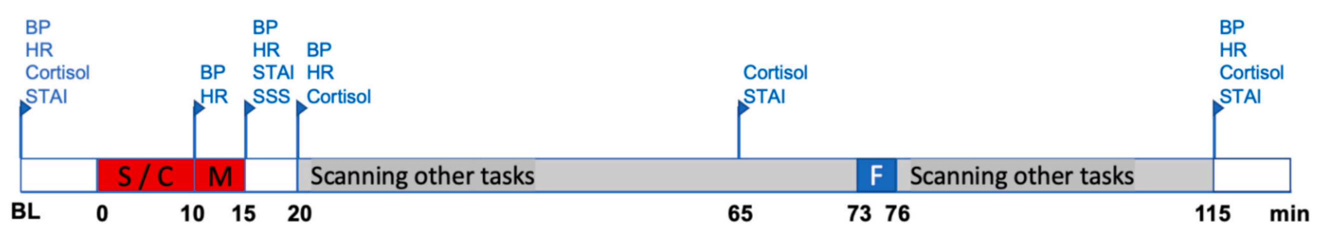

Fig. 1. Timeline of experimental procedures (bar) and assessments of psychological and physiological stress responses (upper line). Abbreviations: baseline (BL), blood pressure (BP), face matching task (F), heart rate (HR), math test (M), Socially evaluated cold-pressor test or control test (S/C), State-Trait Anxiety Inventory (STAI), subjective stress scale (SSS).

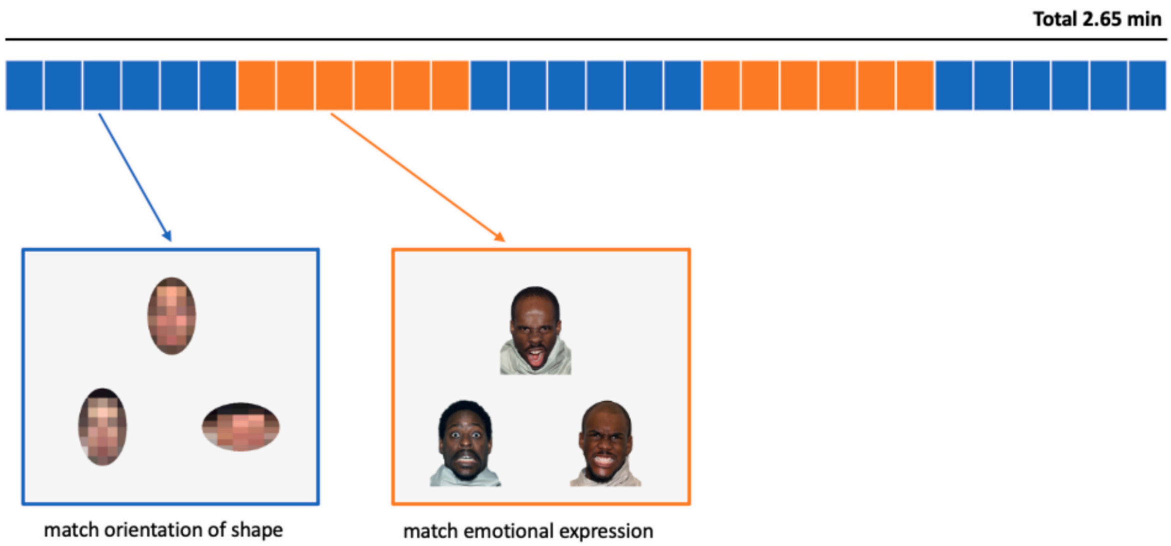

Fig. 2. Schematic overview of Face matching task.

group differences and Wilcoxon Signed Rank tests for within group differences, as parametric assumptions were violated. Response times in the FMT were entered in a mixed model ANOVA with the factors group (OCD, healthy controls), session (stress, control) and stimulus type (emotion, neutral). When the assumption of sphericity was violated, the ANOVA results were corrected with Greenhouse Geisser correction. The analyses were followed by post-hoc paired *t*-testing in case of significance, with Bonferroni correction for multiple comparisons. An online toolbox was used to calculate effect-sizes for these outcomes (psychometrica.de/effect_size.html).

2.6. Image acquisition

Imaging was performed on a 3.0 T Philips MRI scanner (Philips, Best, The Netherlands), using a 32-channel SENSE head coil. The scanning protocol included a high-resolution T1-weighted MRI (sequence parameters: repetition time = 6.9 ms; echo time = 3.1 ms; flip angle = 8°; 150 sagittal slices; voxel size = 1.1 mm isotropic, total duration = 179 s). For fMRI, multi-echo echoplanar imaging (EPI) was used to acquire T2*-weighted MRI volumes with blood oxygen level-dependent (BOLD) contrast (sequence parameters: repetition time = 2375 ms; number of echos = 3, echo time = 9, 26 and 44 ms; flip angle = 76°; field of view = 224 mm × 122 mm × 224 mm; voxel size = 3.0 mm isotropic; 37 slices; 67 volumes with a total duration of 2.65 min). Multi-echo EPI reduces signal dropout and distortion while enhancing BOLD contrast sensitivity (Poser et al., 2006). Three dummy scans were acquired to allow for equilibration of the signal. Head immobilization was established using foam pads inside the coil.

2.7. fMRI analysis

Standard preprocessing of functional MRI data was conducted in SPM12 (www.fil.ion.ucl.ac.uk/spm/) in Matlab version 2014b (http://www.mathworks.com). First, realignment was performed, and the three echoes were combined using in-house software. This was followed by slice-time correction, co-registration of the mean EPI to the T1-weighted structural scan, normalization of the functional images to Montreal Neurological Institute (MNI) space and spatial smoothing with a 3D Gaussian kernel of 6 mm at FWHM. A cut-off for scan-to-scan movement exceeding 3 mm translation on the x-, y-, or z-axis was used, which did not result in exclusion of participants.

Emotion and neutral conditions of the FMT were modelled as box-car regressors in a general linear model and were convolved with the canonical HRF. Realignment parameters were added as regressors to account for head movement during scanning, and a high-pass filter was set at 128 s to account for low frequency noise. Voxel-wise activation maps were obtained by contrasting the emotion condition against the neutral condition. A random effects mixed model ANOVA with the factors group (OCD and control) and session (stress and control) was used for statistical inference at the group level. Age, gender and order of sessions were added as covariates. To analyse if these outcomes were modulated by attachment insecurity, a dimensional attachment score (anxiety or avoidance from the ECR or SoM from the AAI) was added as covariate to three separate models. As the main aim of the study was to probe activation of main stress- and attachment related neurocircuitry, we performed a region of interest (ROI) analysis for the amygdala and hippocampus using a combined anatomical mask as provided by the AAL atlas. To optimize sensitivity to localized effects within this ROI, we corrected the voxel-wise family-wise error (FWE) rate based on Gaussian random field theory on the peak level using a small volume correction ($p < 0.017$, corrected for three models). In addition, we corrected voxel-wise tests across the whole brain on the cluster level using a height-threshold of $p < 0.001$ to optimize sensitivity to less focal and strong effects (Worsley et al., 1996).

3. Results

3.1. Demographic and clinical data

Demographic and clinical data are presented in Table 1. There were no significant differences between OCD participants and healthy controls in age, gender distribution, handedness, education, and civil status. As expected, ratings on the YBOCS, HAM-A and HDRS were significantly higher in OCD participants than in healthy controls. No significant differences in YBOCS scores existed between testing days in the OCD group. OCD participants had various current comorbid disorders, including panic disorder (9 %), agoraphobia (4,5 %), hypochondria (4,5 %), generalized anxiety disorder (4,5 %), social anxiety disorder (4,5 %), past major depressive disorder (27 %) and past alcohol abuse (4,5 %). Furthermore, sixteen OCD participants used a constant dose of antidepressant medication during the two visits, including SSRIs (55 %), SNRIs (4,5 %) and TCAs (14 %).

3.2. Attachment outcome

As further shown in Table 1, OCD participants scored higher on

Table 1
Demographic and clinical data presented as the mean ± SD.

	Patients ($n = 22$)	Controls ($n = 23$)	*P* value
Age (years)	35.00 (9.89)	33.43 (14.69)	$p = 0.376$[1]
Gender (male/female)	11/11	12/11	$p = 0.884$[2]
Handedness (left/right)	3/19	4/19	$p = 0.728$[2]
Education (low - high)	3/6/6/2/5	0/4/10/4/5	$p = 0.283$[2]
Civil status (single/ married)	11/11	9/12	$p = 0.763$[2]
YBOCS baseline:			
- total	22.50 (5.89)	0.13 (0.46)	$p < 0.001$[1]*
- obsessions	11.86 (2.98)	0.13 (0.46)	
- compulsions	10.64 (4.10)	0.00 (0.00)	
YBOCS total:			
- before stress	22.50 (6.08)		$p = 0.369$[3]
- before control	22.81 (6.70)		
HAM-A	12.95 (7.31)	1.39 (1.64)	$p < 0.001$[1]*
HDRS	8.64 (6.16)	0.65 (0.93)	$p < 0.001$[1]*
Medication status (yes/no)	16/6	NA	
ECR anxiety	1.81 (0.13)	1.69 (0.11)	$p = 0.002$[4]*
ECR avoidance	1.74 (0.16)	1.66 (0.13)	$p = 0.068$[4]
Corr with ECR anx			$p = 0.092$[5]
AAI State of Mind	4.05 (1.48)	4.22 (1.60)	$p = 0.72$[4]
Corr with ECR anx			$p = 0.22$[5]
Corr with ECR avoi			$p = 0.014$[5]*
AAI (F/E/Ds)	14/2/5	13/2/8	$p = 0.726$[2]

* Significant between groups, $p \leq 0.05$, tested with [1] Mann Whitney U test, [2] chi-square test, [3] paired t-test, [4]independent samples t-test and [5]Pearson Correlation, one-tailed. Scales: Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression Rating Scale (HDRS), Experiences in Close Relationships (ECR) attachment anxiety subscale (scores ^{10}log transformed) and ECR attachment avoidances subscale (scores ^{10}log transformed), Adult Attachment Interview (AAI) State of Mind score and classification (F = Free and autonomous, E = Enmeshed and preoccupied, D = Dismissing). Corr with ECR anx/avoi = correlation with ECR anxiety and avoidance.

attachment anxiety measured with the ECR than healthy controls ($t(43) = 3.25$, $p = 0.002$, $d_{Cohen} = -1.0$), with a mean score of respectively 67.23 (SD = 19.98) and 50.57 (SD = 13.67). Although there was a numerical difference, attachment avoidance scores were not significantly higher for OCD participants than healthy controls ($t(43) = 1.88$, $p = 0.068$, $d_{Cohen} = -0.55$), with a mean score of respectively 59.23 (SD = 21.24) and 47.91 (SD = 14.56). Pearson's correlation analysis showed that the ECR subscales were not correlated across groups. One OCD participant did not complete the AAI. When analysing attachment scores of the AAI, OCD participants and healthy controls did not significantly differ on the continuous variable SoM nor on distribution into the categories Free, Enmeshed and Dismissing. Most participants were securely attached (64 % in the OCD group and 57 % in the healthy control group). The State of Mind scores were significantly correlated with ECR avoidance scores across groups, but not with ECR anxiety scores.

3.3. Stress response

Physiological and subjective stress responses have been reported previously (van der Straten et al., 2020; van Leeuwen et al., 2023). Results for this slightly different sample are presented in Fig. 3 and reported in the Supplement. In summary, these results show that the stress session successfully increased systolic blood pressure and psychological stress measures (STAI and subjective stress level questionnaire) in both groups. STAI scores remained elevated during scanning. OCD participants reported higher STAI scores than healthy controls overall, regardless of the session. Healthy controls showed significantly higher cortisol levels in the stress session than in the control session, which was not seen for OCD participants.

3.4. Behavioural responses in FMT

There were no significant differences in correct responses and reaction times between groups and between sessions, indicating comparable

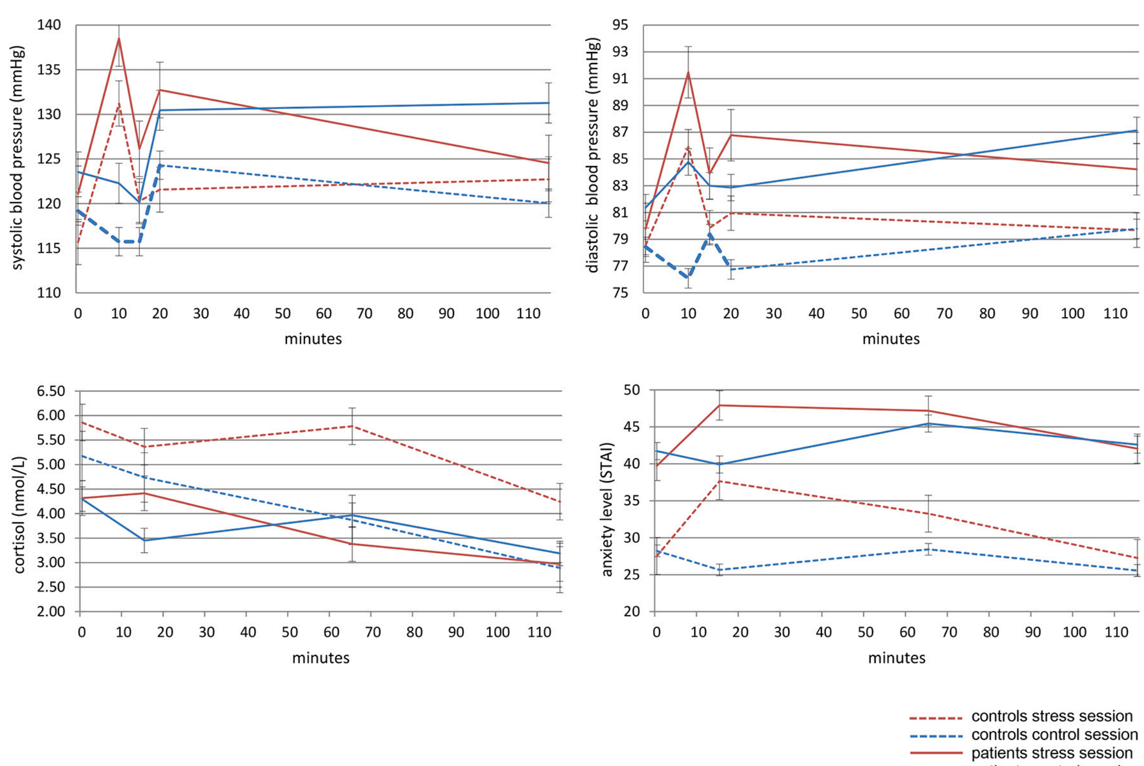

Fig. 3. Physiological and subjective stress response, time points: baseline (0 min), after water procedure (10 min), after math task (15 min), before scanning session (20 min), before face matching task (65 min) and after scanning (115 min) reported as the mean with standard error.

levels of attention (see Supplement).

3.5. fMRI results

Voxel-wise activation maps of the FMT were entered in a random effects mixed model ANOVA with the factors group (OCD and healthy controls) and session (stress and control). The main effect of task showed that the emotion condition elicited more activity than the neutral condition in a large network of brain regions, including the fusiform gyrus, occipital cortex, amygdala and hippocampus (p(FWE) < 0.05), see Table 2. The main effect of group showed more activity in the cuneus in healthy controls than OCD participants (MNI: −14, −72, 32, p(FWE) = 0.002). The main effect of stress showed lower activity in the stress session than control session in the posterior hippocampus (MNI: 24, −36, 8, p(SVC) = 0.018), see Fig. 4 and Table 2. Importantly, the group × stress interaction effect was not significant.

Next, we investigated the influence of attachment insecurity by adding the ECR subscales anxiety and avoidance as well as the AAI SoM scale as covariates in the above-described analysis. The group × stress × attachment interactions were not significant. We therefore assessed whether there was a stress × attachment interaction, regardless of group membership. This analysis showed that higher ECR attachment anxiety was associated with a stress-related increase of activation in the right posterior hippocampus (MNI: 22, −38, 6, p(SVC) = 0.015), see Fig. 4 and Table 2. Thus, whereas stress decreased hippocampal activity across participants, this effect was dependent on attachment style, as higher attachment anxiety scores were correlated to increased hippocampal activation instead. There was no significant interaction effect between attachment avoidance and stress. In addition, we found neural stress responses in several brain areas outside the ROI in relation to attachment insecurity, as measured with the AAI. Higher attachment insecurity, measured as SoM, was associated with a larger stress effect in the dorsal anterior cingulate cortex (dACC), left inferior parietal lobe (IPL), right putamen, right pallidum and right middle frontal gyrus (MFG) (p (FWE) < 0.017) (see Fig. 5 and Table 2).

Table 2
Brain activations during the face matching task.

Brain regions	*T*-value	MNI coordinates x y z
Task activation[1]		
Amygdala L	4.73[a]	−26 −4 −22
Hippocampus R	4.59[a]	16 −8 −14
Fusiform gyrus R	8.02[a]	42 −48 −18
Occipital cortex R	5.94[a]	26 −96 0
Occipital cortex L	5.73[a]	−24 −96 −2
Main effect of group[2]		
Cuneus L	4.19[a]	−14 −72 32
Main effect of stress[3]		
Hippocampus R	4.11[b]	24 −36 8
Stress × ECR Anxiety[4]		
Hippocampus R	4.17[b]	22 −38 6
Stress × AAI SoM[5]		
Dorsal ACC L	5.53[a]	−12 36 6
Inferior parietal lobe L	4.87[a]	−18 −34 36
Putamen R	4.73[a]	24 14 6
Pallidum R	4.17[a]	24 −2 −2
Middle frontal gyrus R	4.18[a]	28 40 44

Brain activations towards the face matching task (1), between OCD patients and healthy controls (2), across participants between stress and control session (3), across participants between stress and control session in interaction with attachment insecurity, measured with ECR Anxiety scale (4) and AAI State of mind scale (5). Only brain regions significant at $p < 0.05$ are reported. [a]$p < 0.05$, whole-brain correction, at cluster-level. [b]$p < 0.05$, small volume correction within ROI, at peak-level.

4. Discussion

The aim of this study was to investigate neural reactivity of attachment-related neurocircuitry under psychological distress in OCD patients. We submitted participants to a controlled stress paradigm after which we measured neural responses to negative facial stimuli, which we correlated to level of attachment insecurity. Psychological distress was successfully induced in both participant groups, as confirmed with blood pressure and subjective stress measurements. In line with our expectations (Gustafsson et al., 2008; Kellner et al., 2020), OCD participants showed a blunted cortisol response to the stressor. Attachment insecurity was assessed with two constructs, the ECR and AAI. Only ECR attachment anxiety was significantly higher in OCD compared to healthy controls. The OCD and healthy controls did not differ on fMRI outcomes related to the stress manipulation, nor on its correlation with attachment insecurity. When combining groups, the results showed hippocampal deactivation towards negative facial stimuli after participants underwent stress induction. This effect was modulated by attachment style, as higher attachment anxiety scores were correlated to increased hippocampal activation instead. Furthermore, participants with higher general attachment insecurity, as measured with AAI SoM scores, showed greater BOLD responses towards negative facial stimuli under psychological distress in several cortical and subcortical brain regions. No association was found between ECR attachment avoidance and fMRI outcomes.

4.1. Attachment insecurity and OCD

Our finding of higher ECR attachment anxiety scores in the OCD group compared to the healthy control group was congruent to our earlier meta-analysis (van Leeuwen et al., 2020). In that study, we found a positive correlation for both insecure attachment styles to OCD symptom severity, although larger for attachment anxiety. In the current study, having OCD was not associated with higher ECR attachment avoidance or general attachment insecurity as measured with AAI SoM scores. Given the likely subtle role of attachment insecurity in OCD pathophysiology, our number of participants may have been too low to detect this association. In addition, heterogeneity in symptom subtype could have played a role. A recent study in a large OCD sample found that only specific facets of attachment insecurity, assessed with the *Attachment Style Questionnaire*, were associated to specific OCD subtypes (Pozza et al., 2021). The only other study we are aware of that has used the AAI in an OCD sample found an association between OCD and the dismissive classification (Ivarsson et al., 2010). That study was applied in an adolescent sample and therefore difficult to compare to our adult sample. Our findings thus partly support the idea that attachment insecurity is a predominant factor in the etiology of OCD.

4.2. OCD and neural stress response

We did not find evidence for our hypothesis that OCD participants, in comparison to healthy controls, showed altered neural reactivity within the amygdala or hippocampus towards emotional facial stimuli after psychological stress induction. Psychological distress is assumed to form a trigger for OCD symptom onset or deterioration, possibly due to hypothalamus-pituitary-adrenal (HPA) axis dysfunction (Raposo-Lima and Morgado, 2020). So far there have been no studies showing an increased or altered fMRI stress response in OCD patients vs healthy controls. With the FMT we probed the reactivity of the amygdala and hippocampus as markers of the intensity of the stress response (Hermans et al., 2014). As the FMT was conducted 73 min after stress onset, this might reflect the recovery phase rather than the acute phase of the stress response (Hermans et al., 2014). The results could therefore indicate

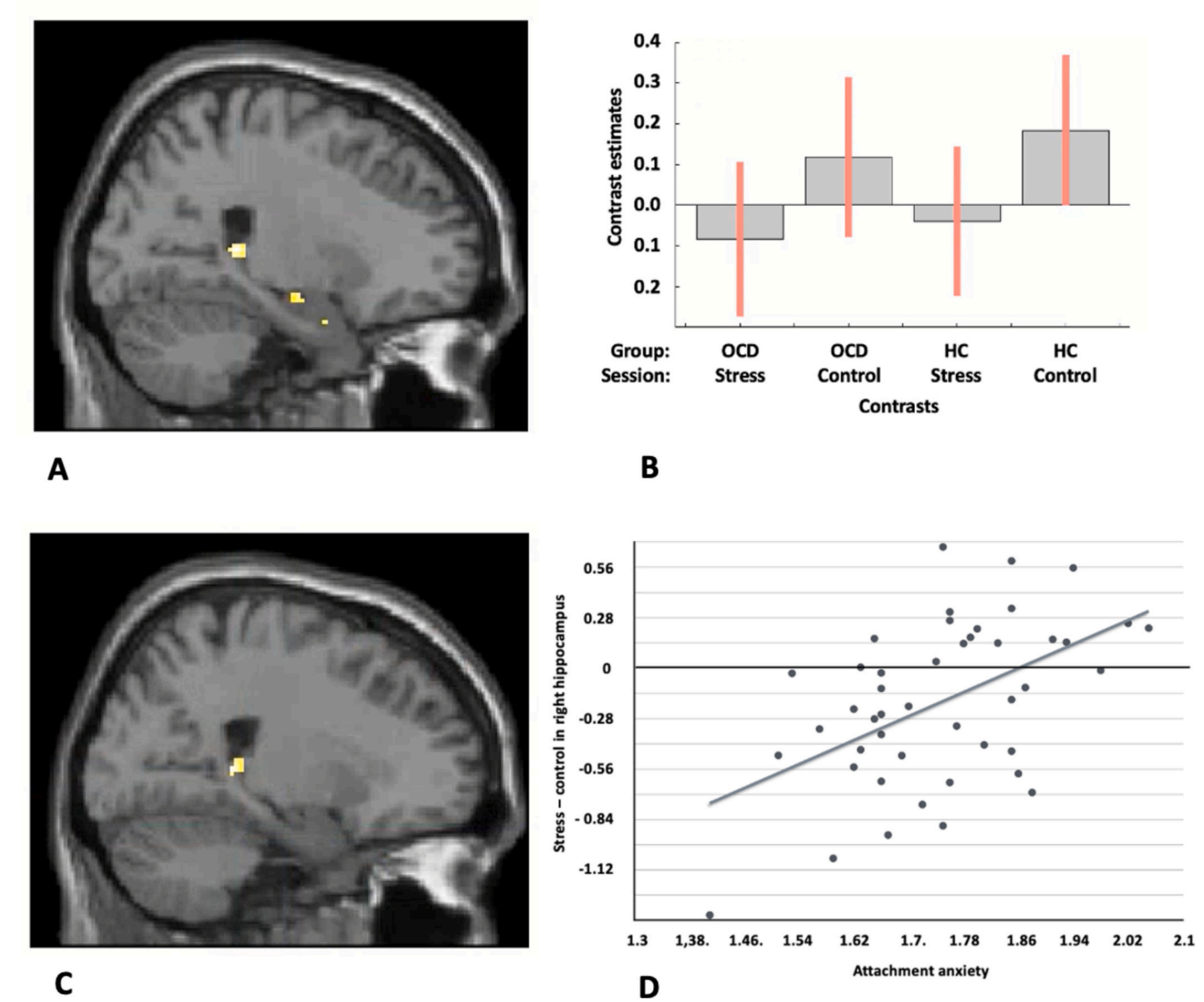

Fig. 4. A Sagittal slice illustrating the significant main effect of stress in the hippocampus while viewing negative emotional versus neutral pictures. Both healthy control and OCD participants showed blunted hippocampus activity under psychological stress when compared to the control session. The figure illustrates activity at $p < 0.001$, uncorrected within the region of interest, overlayed on a group average T1-weighted image. B Peak-voxel contrast estimates and 90 % confidence interval of separate contrasts consisting of the factors (from high to low): group (OCD, HC = healthy control participants), session (stress, control). C Sagittal slice illustrating the significant main effect of stress in the hippocampus correlated to attachment anxiety, measured with the ECR, while viewing negative emotional pictures. Both healthy control and OCD participants showed increased hippocampus activity under psychological stress when compared to the control session when their level of attachment anxiety was higher. The figure illustrates activity at $p < 0.001$, uncorrected within the region of interest, overlayed on a group average T1-weighted image. D Correlation between attachment anxiety scores (ECR, 10log transformed) and peak-voxel contrast estimate differences between stress and control session of the hippocampus of both groups combined.

that OCD patients do not experience an increased or prolonged hypervigilant state under psychological distress in comparison to healthy controls in the aftermath of stress. This is in line with the results of the symptom provocation task in this same study which showed that OCD participants after psychological distress did not show enhanced hypervigilance towards OCD-specific stimuli compared to healthy controls (van Leeuwen et al., 2023). Additionally, our hypothesis was partly based on the prediction that attachment insecurity, as possible potentiator of the stress response, would be higher in OCD participants compared to healthy controls. The fact that we found only modest association between OCD and attachment insecurity in our study, could then additionally explain why OCD and healthy control participants did not differ in their neural responses under stress. Finally, although we aimed to study the effect of general stress induction on OCD, stress responses in OCD may have been more pronounced with OCD-specific stressors, for instance triggering interpersonal functions of OCD such as reassurance seeking (Causier and Salkovskis, 2025). This may explain why the fMRI findings were dependent on attachment style, but not on OCD status.

Healthy control participants showed heightened activation in the cuneus compared to OCD participants, independent of stress induction. As the cuneus is involved in visual processing this might indicate that healthy controls were more inclined to attentively focus on the task (Palejwala et al., 2021). However, as mentioned above, behavioural outcomes did not point towards different attention levels. Importantly, it was not related to increased vigilance. To further study the role of attachment style in stress regulation, independent of OCD status, we combined results of OCD and healthy control participants. Then, we

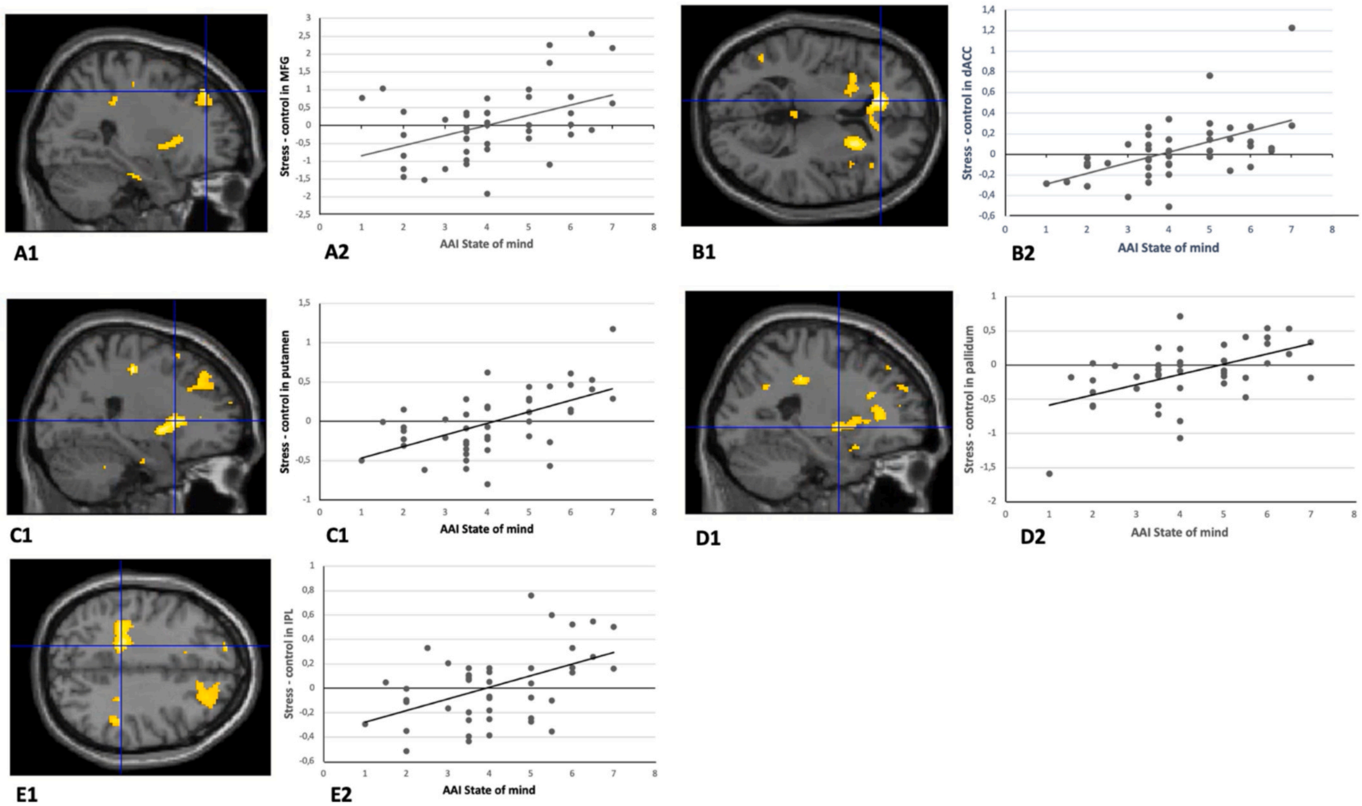

Fig. 5. Sagittal (A1, C1, D1) and horizontal (B1, E1) slices illustrating the significant main effects of stress (by distracting contrasts of control from stress session) in the A1 middle frontal gyrus (MFG), B1 dorsal anterior cingulate cortex (dACC), C1 putamen, D1 pallidum and E1 inferior parietal lobe (IPL), correlated to attachment insecurity, measured with the AAI, while viewing negative emotional pictures versus neutral pictures. Both healthy control and OCD participants showed increased activity in these areas under psychological stress when compared to the control session when their level of attachment insecurity was higher. The figures illustrate activity at $p < 0.001$, uncorrected within the region of interest, overlayed on a group average T1-weighted image. A2, B2, C2, D2, E2 Correlations between attachment insecurity scores (State of Mind scores from the AAI) and peak-voxel contrast estimate differences between stress and control session of corresponding areas.

found that psychological distress induction reduced hippocampal reactivity to negative facial stimuli. Interestingly, this effect was modulated by type of insecure attachment. Since attachment insecurity can be seen as a transdiagnostic vulnerability factor we discuss these stress-related fMRI findings in more detail below, separately for ECR and AAI attachment.

4.3. ECR attachment anxiety and neural reactivity under stress

In contrast to the overall effect of stress induction, high attachment anxiety was associated with increased (rather than decreased) posterior hippocampal reactivity when viewing negative faces under psychological distress. Contrary to our expectations, as attachment insecurity is related to HPA-axis modification (Long et al., 2020), we did not detect attachment-related modification in the anterior hippocampus, responsible for negative feedback to the HPA-axis (Herman et al., 2016; Hermans et al., 2014; Karst and Joëls, 2005). The posterior part of the hippocampus is associated with memory function (Herman et al., 2016). As overall participants showed suppression of hippocampal activity, this could indicate that memory functions were still dampened due to the stress response (van Ast et al., 2013). We speculate then, that for persons higher on attachment anxiety, activation of the attachment system under psychological distress reverses this effect, as hyperactivating (anxious) attachment strategies are assumed to increase access to the episodic memory system (Kennedy and Shapiro, 2004; Strange et al., 2014). This might implicate that social cues are easily biased by negative memories (or its associations) that could enlarge emotional arousal (Gillath et al., 2005). Of importance, our results show that the attachment (anxiety) system is activated under psychological distress. We did not find an association between attachment anxiety (or avoidance) and amygdala activity as did Redlich and colleagues (Redlich et al., 2015). They however, used the face matching task without stress induction, indicating that the robustness of the task for amygdala activation might have reached a ceiling effect for stress manipulation.

4.4. AAI attachment insecurity and neural reactivity under stress

General attachment insecurity, as measured with the AAI, was related to increased BOLD-responses to negative facial stimuli in the dACC, IPL, putamen, pallidum and MFG under psychological distress. In our study most insecure participants were AAI categorized as dismissive (avoidant), corresponding to the positive correlation between SoM and avoidance score. We explain our results as that increased activation in the MFG and dACC may reflect a strive for emotion down-regulation, whereas increased activation in the IPL and dorsal-striatal areas may reflect increased effortful processing of facial expressions to interpret possible threatening motives. The MFG is associated, among other functions, with emotion regulation (Frank et al., 2014; Ochsner et al., 2002) and cognitive control when (emotional) distractors exist (Compton et al., 2003; Milham et al., 2003). The dACC is associated with detecting threats and steering cognitive and affective control (Heilbronner and Hayden, 2016). Activity in the dorsal striatum could reflect encoding of stimulus-response associations to facilitate automatic responding under stressful circumstances (Colibazzi et al., 2010; Hermans et al., 2014; Steidl et al., 2006), as well as facial mimicry, contributing to emotion recognition (Binelli et al., 2014; Czekóová et al., 2019; Kinoshita et al., 2012; Liu et al., 2021). Activity within the IPL is associated with perspective taking (Fogassi et al., 2005). We speculate that avoidant persons, normally prone to distract themselves from facial expressions (Dan and Raz, 2012; Zhang et al., 2008) to avoid emotional involvement (Suslow et al., 2009), might activate these systems under psychological distress (while feeling threatened) to obtain optimal understanding of the circumstances by grasping someone else's motives. For instance, to make inferences about an upcoming assault. Meanwhile, this could be arousing and trigger an urge to control or dampen emotion-induction by negative facial cues under psychological distress for insecurely attached individuals. This parallels the preferred stress- and emotion regulation strategy of suppression for avoidantly attached persons (Long et al., 2020; Mikulincer et al., 2003; Vrtička and Vuilleumier, 2012). The AAI appeared to be more sensitive to detect neural activity related to attachment insecurity (presumably avoidance) than the ECR. We assume that the design of the task, consisting of a passive viewing task (i.e., without active reappraising or mentalizing requirements), more easily triggers sub-conscious aspects of emotion regulation strategies instead of conscious higher-order coping styles. This might be better captured with the AAI than with the ECR (Yaseen et al., 2016).

4.5. Limitations and strengths

This study has several limitations. Of importance, a high percentage of OCD participants was on medication, predominantly SSRIs. Although OCD participants still suffered from clinical OCD symptoms, it could have biased our findings. For example, this could have contributed to an absence in group differences in neural stress responding as it has been shown in healthy subjects that antidepressant medication use reduces amygdala, insula and dACC reactivity in emotional paradigms (De Almeida et al., 2010; van Marle et al., 2011). Furthermore, our sample size could have been too small to detect an interaction effect of attachment, group and stress condition.

Our study also has important strengths. First, the controlled stress design made it possible to trace stress effects on the attachment system. Second, the combination of ECR and AAI measurements made it possible to compare these two distinct assessments of attachment. Third, our study was the first study that conducted the AAI in an OCD sample. Finally, we implemented an intricate within-subject design generating a host of both clinical, stress-related and neural outcome measures.

5. Conclusion

To our knowledge, this is the first study that investigated neural reactivity of attachment-related neurocircuitry under psychological distress in OCD patients. We assessed attachment style with the ECR as well as with the AAI, thereby combining insights from two different psychological schools. Besides a blunted cortisol response in OCD participants, no differences were found between OCD patients and healthy controls in stress response or in neural reactivity to emotionally salient information under psychological distress. We did find that, independent of OCD-status, the reactivity of diverse attachment-related neurocircuitry under stress was driven by type of insecure attachment, with ECR anxious attachment being correlated with increased hippocampal activation and AAI SoM scores, mainly representing avoidant attachment, being correlated to increased activation of dACC, IPL, putamen, pallidum and MFG. This is respectively interpreted as sustained accessibility to associated negative memories, reflecting a hyperactivating attachment strategy, and an increased effort to process emotional expressions and the need to downregulate emotional arousal, reflecting a deactivating attachment strategy. Further research could investigate the role of attachment insecurity in stress regulation by comparing subgroups of secure and insecure OCD patients, and relating it to therapy-effect, or long-term course of the disorder, thereby clarifying its importance as a potential vulnerability factor.

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CRediT authorship contribution statement

W. van Leeuwen: Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. **A. van der Straten:** Writing – review & editing, Software, Data curation. **S. Bögemann:** Writing – review & editing, Software, Methodology, Formal analysis, Data curation. **P. Luyten:** Writing – review & editing. **D. Denys:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **G. van Wingen:** Writing – review & editing, Supervision, Software, Project administration, Methodology, Funding acquisition, Conceptualization. **H. van Marle:** Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.02.055.

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