

# **Affective resonance in response to others' emotional faces varies with affective ratings and psychopathic traits in amygdala and anterior insula**

**Running title:** Affective resonance to others' faces

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## **ABSTRACT**

Despite extensive research on the neural basis of empathic responses for pain and disgust, there is limited data about the brain regions that underpin affective response to other people's emotional facial expressions. Here, we addressed this question using event-related functional Magnetic Resonance Imaging to assess neural responses to emotional faces, combined with online ratings of subjective state. When instructed to rate their own affective response to others' faces, participants recruited anterior insula, dorsal anterior cingulate, inferior frontal gyrus, and amygdala; regions consistently implicated in studies investigating empathy for disgust and pain, as well as emotional saliency. Importantly, responses in anterior insula and amygdala were modulated by trial-by-trial variations in subjective affective responses to the emotional facial stimuli. Furthermore, overall task-elicited activations in these regions were negatively associated with psychopathic personality traits, which are characterized by low affective empathy. Our findings suggest that anterior insula and amygdala play important roles in the generation of affective internal states in response to others' emotional cues, and that attenuated function in these regions may underlie reduced empathy in individuals with high levels of psychopathic traits.

**Keywords:** empathy; psychopathic personality; emotional facial expression; amygdala; anterior insula

## INTRODUCTION

Empathy is a multidimensional phenomenon that involves the ability to resonate with and understand the affective states of others. Recent research suggests that this ability comprises a number of dissociable, but interacting, cognitive components. One of these components, the emotional component, involves the capacity to share or become affectively aroused by others' emotions and has been referred to as affective resonance (Decety, 2010; Decety and Cowell, 2014) or emotional contagion (Bird and Viding, 2015). Albeit using a wide range of experimental tasks and stimuli, previous studies have focused mainly on the neural basis of empathy for pain, in which the majority of the tasks involved watching another person's body parts in painful situations or a loved one about to receive an electric shock, or empathy for disgust, in which stimuli involved watching another person expressing disgust (see (see Fan et al., 2011 for a comprehensive review). Recent meta-analyses of these studies (Fan et al., 2011; Lamm et al., 2011) indicate that the observation of others' experiences of pain or disgust elicits robust activation in anterior insula, *pars orbitalis* of the inferior frontal gyrus (IFGOp) and dorsal anterior cingulate cortex (dACC). While less consistently reported in previous studies, the amygdala is also thought to participate in affective resonance with others' emotions, due to its role in detecting and responding to emotionally salient stimuli (Adolphs, 2010).

Despite the extensive literature on the neural correlates of empathy, there is limited data on the neural correlates of empathic processing for facial expressions and, to our knowledge, no study has used an experimental task explicitly probing *online* subjective affective response to facial expressions of basic emotions. Facial expressions have specific communicatory functions,

conveying information about the observed person to the observer (Blair, 2003, 2005). They thus constitute important cues to others' emotional states and, because they can be readily perceived, likely readily trigger empathic responses in humans. If the above-mentioned brain regions underlie empathic processing more generally, they should be recruited independently of the type of emotional content being empathized with, and we would thus expect them to participate in affective responses to both positive and negative basic emotional expressions. Indeed, previous research on emotional facial processing has reported that observing facial expressions of basic emotions such as sadness, anger and happiness elicits responses in visual and prefrontal brain areas, but also in limbic and temporoparietal areas, including the amygdala and the anterior insula (e.g. Kesler/West et al., 2001; Fitzgerald et al., 2006). Moreover, response in amygdala and anterior insula also appears to be positively correlated with the valence attributed to emotional stimuli in general (Phan et al., 2004). Here, we build on these previous studies and inspect whether activity in regions typically associated with empathic processing co-varies with trial-by-trial fluctuations in the intensity of *online* self-reported affective responses to a wide range of facial expressions, in a larger sample than has been used previously.

One important motivation for studying the neural basis of affective resonance in response to others' emotional cues is to better understand conditions that are characterized by apparent difficulties in empathising with other people. Callous and un-empathic behavior is the hallmark of individuals with high levels of psychopathic traits. Psychopathic traits include a constellation of affective-interpersonal traits, such as lack of consideration for others' feelings and a tendency to manipulate others, as well as impulsive lifestyle-antisocial behavior characteristics, such as impulsiveness and persistent antisocial behavior (Hare, 1993; Hare & Neumann, 2008). It has

been proposed that the absence of a robust spontaneous empathic response to others' distress explains why individuals with psychopathy find it easier to commit acts of antisocial behavior towards others (Blair, 2013; Blair et al., 2005). Behavioral and neuroimaging data are consistent with the notion that these individuals do not find other people's distress as salient as their peers do (e.g. Blair, 2013; Marcoux et al., 2013). Furthermore, individuals with high levels of psychopathic traits report reduced affective responses to others' emotional faces (Ali et al., 2009; Seara-Cardoso et al., 2012; Seara-Cardoso et al., 2013) and reduced empathic concern for other people relative to those with low levels of psychopathic traits (Seara-Cardoso et al., 2012; Seara-Cardoso et al., 2013). It has been proposed that the absence of a robust affective response to the distress cues of others is a core feature of psychopathy. Over time, this may lead to impaired moral development, making individuals high in psychopathic traits more prone to engage in antisocial behavior (Blair et al., 2005).

A recent functional neuroimaging study from Decety, Skelly, Yoder, and Kiehl (2014) investigated neural processing of dynamic facial expressions of fear, sadness, happiness and pain, in a large group of incarcerated males with varying levels of PCL-R scores. Decety et al., (2014) found that, while passively observing dynamic emotional facial expressions, inmates with highest levels of psychopathy presented significantly lower hemodynamic response than inmates with low and medium levels of psychopathy in a wide set of regions, including facial cortical processing areas such as the fusiform gyrus, and regions typically involved in affective processing like the inferior frontal gyrus. In contrast to what might be expected, given the putative role of the anterior insula in affective processing, Decety et al. (2014), found that the group with highest levels of psychopathy presented increased activity in this region in response

to negative emotional facial expressions. Additionally, three recent studies addressed the neural correlates of empathic processing in adults with psychopathy while viewing other people in painful situations. Decety, Skelly and Kiehl (2013) found that when observing stimuli depicting body parts in painful situations and stimuli with facial expressions of pain, incarcerated men with high levels of psychopathy exhibited *greater* responses in anterior insula, dACC and IFG, compared with those with low levels of psychopathy. In a follow-up study, Decety, Chen, Harenski, and Kiehl (2013) reported that the manipulation of the instruction given before the observation of body parts in painful situations had an impact on the patterns of activation observed. When inmates with high levels of psychopathic traits were instructed to imagine themselves in the pictures they also showed *increased* activity in anterior insula, dorsal anterior cingulate and inferior frontal gyrus in relation to those with low levels of these traits. But, when instructed to imagine another person in the pictures, they showed *reduced* response in anterior insula, orbitofrontal cortex and in the amygdala, as expected. These findings suggest that these individuals may present a specific deficit in regions associated with affective processing when instructed to imagine others in pain but not when imagining themselves in pain.

Meffert et al. (2013) also found that when observing videos depicting hands in emotional interactions (e.g. a hand being caressed or hit by another hand), offenders with high levels of psychopathic traits had *lower* activation relative to non-offenders in several brain regions including anterior insula, IFG, dACC and amygdala. Meffert and colleagues reported that when participants were explicitly instructed to ‘empathize’ with the actors in the video, group differences in activation related to psychopathy were reduced. Although this might suggest that top-down instruction can modulate neural responses to affective stimuli in individuals with

psychopathy, it is unclear whether their experience of empathy is itself altered. In summary, existing evidence suggests reduced engagement of brain areas typically associated with empathic processing in individuals with high levels of psychopathic traits, particularly in response to others' pain and when not explicitly instructed to empathize. These results are consistent with developmental studies where precursors of psychopathic traits (i.e. callous-unemotional traits) have been reported to be associated with reduced responses in the anterior insula, dACC and amygdala when participants viewed others in painful situations (Lockwood, Sebastian et al., 2013; Marsh et al., 2013) and add to the hypothesis that hypo-reactivity of these regions might underlie disrupted emotional and empathic behavior typically encountered in individuals with high levels of these traits.

The primary aim of the current study was to identify the brain regions involved in processing affective responses to both positive and negative facial expressions of others. We predicted that these would include structures that have been consistently associated with empathic responding in previous studies, in particular anterior insula, dACC and IFGOp, as well as the amygdala, which is thought to be involved in detecting emotional saliency, particularly from facial cues (Adolphs 2010; Fitzgerald et al., 2006). Critically, we tested whether activation in these regions is modulated according to trial-by-trial variation in the intensity of self-rated affective responses to facial stimuli. If these regions participate in the generation of affective states generally, then neural responses should follow a quadratic (U-shaped) function with respect to affective responses along the valence continuum (i.e. they should respond maximally to stimuli eliciting affective responses at both positive and negative extremes of valence). To this end, we adapted the *Empathy for emotional facial expressions task* (Seara-Cardoso et al., 2012; Seara-Cardoso et

al., 2013) for functional magnetic resonance imaging (fMRI). In this task, participants are asked to rate their affective state while viewing faces expressing basic emotions. The task includes realistic and naturalistic stimuli and is proposed to index affective resonance since participants are asked how the stimulus depicting another individual makes they themselves feel. The task correlates highly with other measures of empathy and related constructs, and is sensitive to individual differences in psychopathic traits in the general population (Seara-Cardoso et al., 2012; Seara-Cardoso et al., 2013; Lockwood, Bird et al., 2013). Our second aim was to test whether inter-individual variability in psychopathic traits is associated with responses in these regions during affective resonance with facial expressions. We predicted that psychopathic traits would be negatively associated with neural activity in anterior insula, dACC, IFGOp and amygdala during affective resonance, consistent with the callous-unemotional behavior commonly observed in individuals with high levels of these traits and with prior evidence of blunted affective and neural responses to others' emotions in this group.

## **MATERIALS AND METHODS**

### ***Participants***

Thirty-one right-handed male participants from the community with no reported history of psychiatric illness were recruited for this study. Of these, one was excluded due to failure to respond on >50% of trials and corrupted fMRI data due to movement, leaving 30 participants in the analysis [mean age: 26.9, range: 20-40; mean estimated intelligence quotient (IQ) 110, range: 85-125]. All participants provided written informed consent according to the guidelines approved

by UCL Division of Psychology and Language Sciences Ethics Committee who provided ethical approval for this study.

## **Materials**

### *Questionnaire assessments*

Psychopathic traits were assessed with the *Self-Report Psychopathy Scale Short Form* (SRP-SF; Paulhus et al., in press), a 29-item scale designed to measure psychopathic attributes in non-institutionalized samples. The SRP-SF assesses psychopathic traits, organized in four facets – interpersonal (e.g. “I have pretended to be someone else in order to get something”), affective (e.g. “I never feel guilty over hurting others”), lifestyle (e.g. “I rarely follow the rules”) and antisocial (e.g. “I have threatened people into giving me money, clothes, or makeup”) – consistent with recent research on the Psychopathy Checklist – Revised (PCL-R; Hare 2003). Like the PCL-R, the four facets can be modelled in terms of the traditional two-factor dimensions: affective-interpersonal and lifestyle-antisocial. The SRP has been shown to have a clear latent structure and good construct validity (Neumann and Pardini, 2012; Neumann et al., 2012), and strongly correlates with the PCL-R (Lilienfeld and Fowler, 2006; Paulhus et al., in press). Items are scored on a 5-point Likert scale (from 1 “Disagree Strongly” to 5 “Agree Strongly”). In the present sample, SRP-SF total scores varied between 31 and 109 ( $M=58.07$ ;  $SD=18.18$ ), affective-interpersonal scores varied between 14 and 61 ( $M=29.23$ ;  $SD=10.89$ ), lifestyle-antisocial scores varied between 15 and 47 ( $M=27.70$ ;  $SD=8.73$ ), thus presenting a similar distribution to a previously reported distribution from a larger sample of adults from the general population (Seara-Cardoso et al., 2012). The Matrix Reasoning subscale of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was administered to estimate level of

general intellectual ability. Participants also completed the State-Trait Anxiety Index (STAI; Spielberger et al., 1970) to assess state and trait anxiety.

#### *Empathy for emotional facial expressions task*

We adapted the *Empathy for emotional facial expressions task* previously described in Seara-Cardoso et al. (2012; 2013) for event-related fMRI. In this task, originally based on Ali et al. (2009), participants are instructed to rate their own affective state on the valence scale of the Self-Assessment Manikin (SAM; Bradley and Lang, 1994) while observing images depicting a person displaying a sad, fearful, angry, happy or neutral expression. This task has been shown to be highly correlated with other measures of empathy and related constructs, and to be sensitive to individual differences in psychopathic traits in the general population (Seara-Cardoso et al., 2012; Seara-Cardoso et al., 2013; Lockwood, Bird et al., 2013). To prevent possible confounding effects at the neural level of presenting expressive manikins (which contain emotional facial expressions) alongside the emotional stimuli of interest (emotional facial expressions), the valence scale of the SAM was replaced by a sliding scale, ranging from -4 (most negative) to +4 (most positive), with 0 as the central 'neutral' anchor. The task included a total of 40 different images, 8 images (4 male, 4 female) per emotional condition (sadness, fear, anger, neutral, and happiness), which were repeated 3 times. Immediately prior to scanning, participants were familiarized with the task and instructions. Stimuli used during practice were not used in the scanning session. Inside the scanner, participants were presented with a total of 120 trials, pseudorandomised across two runs, and were instructed to rate how the picture made them feel on the sliding rating scale (Figure 1).

Each trial lasted 8.5 s and started with the presentation of the face stimulus. After 2 s, the sliding scale appeared on the screen, below the stimuli. Participants made their ratings using three keys on a keypad. Two keys moved the cursor (initially positioned in the center of the scale) to the left or the right on the sliding scale, and a third key ‘marked’ the answer. Participants had a maximum of 4 s to make their ratings. If a rating was not made within that time, the trial was considered an error. After marking their ratings, participants received visual confirmation of their answer for 1 s. A fixation cross appeared on the screen for 1.5 s before the next trial started. Twenty-four fixation cross “baseline” trials, with the same overall duration, were also presented. Trials were presented in a pseudorandom order to prevent presentation of more than two consecutive trials of the same emotional category and more than one consecutive null trial. Stimulus presentation and response collection were carried out with Cogent (<http://www.vislab.ucl.ac.uk/cogent.php>) running in Matlab 2011b (<http://mathworks.com>).

#### *Magnetic resonance imaging acquisition*

Images were acquired using a Siemens Avanto 1.5 T MRI scanner at the Birkbeck-UCL Centre for Neuroimaging with a 32-channel headcoil. A 5.5 min 3D T1-weighted anatomical scan, and multislice T2\*-weighted echo planar images (EPIs) with blood oxygenation-level-dependent (BOLD) contrast were acquired. The T2\* EPI sequence used the following acquisition parameters: 35 2 mm slices acquired in a descending trajectory with a 1 mm gap; echo time = 50 ms; repetition time = 2.975 s; slice tilt = -30°; flip angle = 90°; field of view = 192 mm; matrix size = 64 x 64. Field maps (phase and magnitude images) were also acquired for use in the unwarping stage of data preprocessing.

## **Data analyses**

### *Behavioral data analysis*

All behavioral analyses were conducted with IBM SPSS Statistics for Windows, Version 20.0. To investigate whether the stimuli in the different emotion (sad, fearful, angry, happy) conditions elicited significantly stronger affective responses than the stimuli in the neutral condition, we conducted a repeated-measures ANOVA. Post-hoc pairwise comparisons included Bonferroni correction for multiple comparisons. Relationships between affective response ratings and psychopathic traits were assessed using the Pearson correlation coefficient. Overall affective response was estimated by averaging ratings of all emotional stimuli (i.e. excluding neutral stimuli), with the sign of ratings of negatively valenced stimuli reversed (note that ratings were reversed only for this specific analysis).

### *Image processing and analyses*

EPI data were analyzed using SPM8 ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)) in Matlab. The first five volumes were discarded, and the data were realigned to the sixth volume, unwarped using a fieldmap, normalized to the Montreal Neurological Institute template resampling to a voxel size of 2x2x2 mm, and smoothed with an 8 mm full width at half-maximum Gaussian filter. Data were high-pass filtered at 128 s to remove low-frequency drifts, and the statistical model included an AR(1) autoregressive function to account for autocorrelations.

At the first level we estimated two models. In the first model, onsets were time-locked to the presentation of the face stimuli (one regressor per emotion condition), with duration 2-6 s, depending on the duration of the rating on the sliding scale. Where necessary, we also included a

regressor modelling any missed trials with duration 8.5 s (range of missed trials: 1-6;  $M=0.367$ ). Fixation cross trials (baseline) were also modelled in the analyses with duration 8.5 s. Regressors of interest were created by convolution of these onsets with a canonical hemodynamic response function. The six realignment parameters were included in the model to control for minor participant motion. For two participants, an extra regressor was included to model corrupted images resulting from excessive motion ( $>1\text{mm}$  or  $1$  degree between one volume and the next). These images were removed and replaced with an image created by interpolating the two adjacent images to prevent distortion of the between-subjects mask. To test whether the neural responses in the first analysis varied according to the reported level of affective response elicited by each stimulus, a second model was estimated. This model was specified and estimated in a similar manner to the first model, with the exception that all emotional stimuli were combined in a single regressor, which was parametrically modulated by a series of polynomial expansions (linear to cubic), using the subject-specific affective ratings from each trial (ranging from  $-4$  to  $+4$ ) after  $Z$ -transformation of the ratings within each subject. Using such a cubic expansion ensures that possible exponential relationships are not misinterpreted as quadratic (Winston et al., 2007). Neutral trials were modelled in a second regressor.

Second-level analyses group analyses were implemented on contrasts of interest using the standard summary-statistics approach to random-effects analysis. For the first model, whole-brain analyses were conducted using a threshold of  $P<0.05$ , FWE corrected at the voxel level, after applying an inclusive grey matter mask (segmented from the group average anatomical scan). Region-of-interest (ROI) analysis was conducted in bilateral amygdala (as a single ROI) following an initial threshold of  $P<0.005$  (uncorrected), defined using the Pickatlas toolbox with

the automated anatomical labelling (AAL) atlas (Maldjian et al., 2003), and applying small volume correction (SVC). Additional exploratory analyses were conducted using a cluster forming threshold of  $P < 0.005$  (cluster size  $> 20$ ) after applying the inclusive grey matter mask, and clusters surviving FWE correction for spatial extent across the whole brain ( $P < 0.05$ ) were considered statistically significant. For the second (parametric) model, ROI analyses were conducted in regions identified as robustly engaged by the task in the (orthogonal) first analysis: anterior insula, dACC, IFGOp and amygdala. ROIs for the anterior insula, dACC and IFGOp were defined by creating 8 mm spheres centered on activation peaks identified in the first analysis. An initial threshold of  $P < 0.005$  was applied and effects surviving SVC FWE correction ( $P < 0.05$ ) at the voxel-level were considered statistically significant.

To test whether individual differences in hemodynamic response in these regions were associated with individual differences in psychopathic traits, we used the Marsbar toolbox (Brett et al., 2002) to extract contrast estimates from 8 mm spheres centered on activation peaks identified in the first analysis (anterior insula, dACC, IFGOp and amygdala) and related these to SRP scores in SPSS. Note that these correlation analyses were orthogonal to the contrast used to identify the neural response and as such do not require correction for a voxel-wise search (Kriegeskorte et al., 2009). Contrast estimates extracted with Marsbar were also used to generate the regression plots presented in Figure 3. Residual analyses were performed to check the validity of parametric assumptions and presence of outliers.

## **RESULTS**

## ***Behavioral analyses***

### *Manipulation check*

Analysis of subjective affective ratings revealed a significant main effect of valence ( $F(1, 29) = 423.27, P < 0.001$ ), confirming that our task elicited the expected subjective states in participants. Post-hoc pairwise comparisons, with Bonferroni correction, confirmed significant differences in affective ratings between all emotional categories (all  $P < 0.001$ , except for sad < fear:  $P = 0.03$ ), with the pattern sad < fearful < angry < neutral < happy (additional descriptive statistics are presented in Supplementary Table 1).

### *Relationship between psychopathic traits and affective response to emotional facial expressions*

Psychopathic traits, specifically affective-interpersonal traits, were significantly negatively associated with overall affective responses to faces (SRP total:  $r = -0.34, P = 0.07$  (marginal); SRP affective-interpersonal:  $r = -0.41, P = 0.03$ ; SRP lifestyle-antisocial:  $r = -0.20, P = 0.30$ ). Inspecting the associations between psychopathic traits and different emotion categories, we observed that psychopathic traits, specifically affective-interpersonal traits, were significantly negatively associated with affective response to happy faces (total:  $r = -0.43, P = 0.02$ ; affective-interpersonal:  $r = -0.43, P = 0.02$ ; lifestyle-antisocial:  $r = -0.23, P = 0.23$ ). The associations between psychopathic traits, and specifically affective-interpersonal traits, with fearful and angry faces had correlation coefficients of similar magnitude to those reported in the previous studies (all  $r_s > 0.25$ ; Seara-Cardoso et al., 2012; Seara-Cardoso et al., 2013), but failed to reach statistical significance,

likely due to the lower number of participants that could be included in the present study. Associations with ratings for the neutral faces were weak and non-significant ( $r_s < .10$ ). Including IQ and trait anxiety as covariates did not change this pattern of associations (Supplementary Tables 2 and 3). Residual statistics analyses confirmed that the assumptions for parametric analysis were met and that there were no outliers.

\*\*\* Figure 1 \*\*\*

### *fMRI analyses*

#### *Activation during task performance*

We initially contrasted neural responses associated with task performance relative to baseline (fixation cross) in the first model to isolate regions recruited during face processing. Performing this task evoked responses in regions that have been consistently identified to be associated with affective empathy at  $P < 0.05$  (whole-brain FWE corrected): right IFGOp bilateral anterior insula and dACC. Activations were also observed in left parietal operculum, supramarginal gyrus, middle frontal gyrus, thalamus and cerebellum, extending to fusiform gyrus (Table 1). No regions exhibited the reverse pattern at this significance threshold. ROI analysis in bilateral amygdala identified two significant clusters of activation at  $P < 0.05$  (**FWE SVC**), one in the right amygdala (peak coordinates:  $[x=-27; y=-4; z=-11]$ ;  $k=8$ ;  $Z=4.77$ ;  $P < 0.01$ ) and one in the left (peak coordinates:  $[x=24; y=2; z=-11]$ ;  $k=1$ ;  $Z=3.26$ ;  $P=0.03$ ).

\*\*\* Table 1 \*\*\*

We next investigated the effect of the emotional face conditions contrasted against the neutral face condition, using a within-subjects ANOVA with the 5 experimental conditions (each contrasted against baseline) constituting the repeated-measures factor (F-contrast: [1 0 0 - 1 0; 0 1 0 -1 0; 0 0 1 -1 0; 0 0 0 -1 1], where the order of conditions in the design matrix was: sad, fearful, angry, neutral, happy). At an initial threshold of  $P < 0.05$  (FWE corrected), we identified significant effects in lingual gyrus bilaterally (left peak coordinates: [x=-9; y=-85 z=-11]; k=75;  $Z=6.57$ ;  $P < 0.01$ ; right peak coordinates: [x=15; y=-73 z=-14]; k=60;  $Z=5.94$ ;  $P < 0.01$ ), and in *pars orbitalis* of the IFG (IFGOB), bilaterally (left peak coordinates: [x=-45; y=44 z=-5]; k=9;  $Z=5.03$ ;  $P=0.01$ ; right peak coordinates: [x=51; y=32 z=-11]; k=3;  $Z=4.89$ ;  $P=0.02$ ), where at least one emotional condition differed from the neutral condition. Post-hoc pairwise comparisons of extracted contrast estimates (8 mm spheres centered on activation peaks) revealed that activation in left lingual gyrus was higher for sad, fearful and angry faces than for neutral faces ( $t(29)s= 3.76; 3.39; 2.38$ ;  $P_s < 0.01$ , uncorrected). In right lingual gyrus activation was only higher for happy than for neutral faces ( $t(29)=3.47$ ;  $P < 0.01$ , uncorrected), and lower for sad, fearful and angry than for neutral faces ( $t(29)s=2.49, 2.53, 2.62$ ;  $P < 0.01$ , uncorrected). In left IFGOB, activation was higher for neutral than for each emotional face category (all  $t(29)s > 2.95$ ;  $P < 0.01$ , uncorrected), and in right IFGOB, activation was higher for neutral faces than for sad, fearful and happy faces ( $t(29)s= 3.01, 2.24, 5.09$ ;  $P < 0.01$ , uncorrected). Amygdala ROI analyses did not identify significant activations for any type of emotional expression relative to neutral faces.

#### *Quadratic parametric modulation of affective response to emotional facial expressions*

Having identified the brain network recruited by this task (relative to baseline), we then tested whether these regions participate specifically in subjective affective responding. In this second

model, using an initial threshold of  $P < 0.005$  and SVC in ROIs (anterior insula, IFGOp, dACC and amygdala) defined on the basis of the results described above at  $P < 0.05$  FWE-corrected, we identified significant positive quadratic relationships (i.e. U-shaped relationships) between activation to emotional faces and trial-by-trial subjective affective responses in the anterior insula, extending to the IFGOp, bilaterally (right peak coordinates:  $[x=42; y=2; z=4]$ ;  $k=35$ ;  $Z=3.55$ ;  $P=0.01$ ; left peak coordinates:  $[x=-48; y=2; z=-2]$ ;  $k=12$ ;  $Z=3.01$ ;  $P=0.03$ ), and in amygdala (right peak coordinates:  $[x=33; y=-1; z=-20]$ ;  $k=22$ ;  $Z=3.45$ ;  $P=0.02$ ; left peak coordinates:  $[x=-27; y=-1; z=-17]$ ;  $k=32$ ;  $Z=3.50$ ;  $P=0.02$ ) (Figure 2). None of the ROIs exhibited the opposite pattern of activation. In support of the notion that anterior insula and amygdala responses vary in accordance with the intensity of affective responses along the valence continuum (i.e. respond maximally to stimuli eliciting high affective responses at both positive and negative extremes of valence) and therefore participate in affective responding *per se* as opposed to negative emotion specifically, we did not find any significant linear or cubic relationships between activation in these regions and trial-by-trial subjective affective response to emotional faces, even at a liberal threshold of  $P < 0.005$  (uncorrected). Additional exploratory whole-brain analyses are presented in Supplementary Table 4. To confirm that the observed pattern of quadratic relationships between activation to emotional faces and subjective affective responses was not driven by varying length of the modelled epochs, we estimated an additional model where trial onsets were time-locked to the presentation of the stimuli, as previously, but where durations were kept constant by fixing them to the mean trial duration within each participant. This additional model yielded a similar pattern of significant effects in anterior insula, extending to IFG bilaterally (right peak coordinates:  $[x=42; y=2; z=4]$ ;  $k=76$ ;  $Z=4.25$ ;  $P < 0.001$ ; left peak coordinates:  $[x=-42; y=2; z=-4]$ ;  $k=57$ ;  $Z=4.05$ ;  $P < 0.001$ ), and in amygdala

(right peak coordinates: [x=33; y=-1; z=-20]; k=34; Z=3.79; P=0.01; left peak coordinates: [x=-27; y=-4; z=-11]; k=34; Z=3.77; P=0.01), thus confirming that the quadratic effect we identified was not simply driven by longer epochs in trials with more extreme affective ratings. An illustrative figure of these results is presented in Supplementary Figure 1.

\*\*\* *Figure 2* \*\*\*

*Associations between neural responses during task performance and psychopathic traits*

We tested whether responses elicited during the performance of the task (all faces relative to baseline) in anterior insula, dACC, IFGOp and amygdala were associated with individual differences in psychopathic traits. Significant negative correlations with total psychopathic traits were identified in the bilateral anterior insula (right:  $r=-0.38$ ,  $P=0.04$ ; left:  $r=-0.40$ ,  $P=0.03$ ). The magnitude of anterior insula response was significantly negatively associated with levels of lifestyle-antisocial psychopathic traits (right:  $r=-0.39$ ,  $P=0.03$ ; left:  $r=-0.43$ ,  $P=0.02$ ), and with affective-interpersonal traits at trend level (right:  $r=-0.31$ ,  $P=0.10$ ; left:  $r=-0.31$ ,  $P=0.09$ ). The magnitude of response in right amygdala was also significantly negatively correlated with total psychopathic traits ( $r=-0.37$ ,  $P=0.05$ ), specifically with affective-interpersonal traits ( $r=-0.36$ ,  $P=0.05$ ), while the correlation with the lifestyle-antisocial subscale did not reach statistical significance ( $r=-0.29$ ;  $P=0.12$ ) (Figure 3). Including IQ and anxiety as covariates did not change the associations between psychopathic traits and anterior insula response, but did change the associations with right amygdala response, where the associations became stronger, achieving statistical significance for both sub-scales (affective-interpersonal:  $r=-0.38$ ,  $P=0.05$ ; lifestyle-antisocial  $r=-0.37$ ,  $P=0.05$ ). We then explored whether observed associations were driven by

shared variance between the two dimensions of psychopathic traits, or unique variance specific to individual dimensions. Entering each dimension of psychopathy as a covariate of the other rendered associations weaker and non-significant, indicating that variance shared by both dimensions likely drives the associations found (Supplementary Table 5). Furthermore, *Steiger's* *Z* tests indicated that the two dimensions did not present significantly different correlation coefficients in any of the associations described above (all  $Z < 0.89$ ;  $P > 0.38$ ). Residual statistics confirmed that the assumptions for parametric analysis were met and that there were no outliers in any of the reported analyses.

\*\*\* Figure 3 \*\*\*

## **DISCUSSION**

The aims of the study described in this paper were twofold. First, we wanted to identify the neural structures that subserve affective responding to emotional facial expressions, and verify whether these included the neural structures that have been consistently associated with empathic responding to pain and disgust and with responding to emotionally salient stimuli. Critically, we wanted to test whether responses in these regions were modulated by subjective affective responses to emotional facial expressions. Second, we wanted to test whether neural responses during affective responses to faces were associated with individual differences in psychopathic traits, which are known to reflect low empathy. Our findings indicate that, when participants rated their affective response to others' faces (relative to low-level baseline), they robustly recruited the anterior insula, dACC and IFGOp, structures consistently reported to be involved in face processing as well as in empathic processing of pain and disgust (Fan et al., 2011; Lamm et

al., 2011); and also the amygdala, a region associated with responding to emotional saliency (Adolphs, 2010). Most importantly, responses in the amygdala and anterior insula (albeit in more posterior regions of the anterior insula and nearer to the central sulcus than the peaks reported in the above-mentioned meta-analyses) were modulated by trial-by-trial fluctuations in reported subjective affective responses to facial stimuli, in line with the predicted quadratic shape. Finally, responses to faces in these regions were also negatively associated with individual differences in psychopathic traits.

While the precise roles that each of these structures play in response to others' emotional cues remains under investigation, it has been proposed that they each play separate but complementary roles in empathic processing. While the amygdala is thought to be involved in detecting emotional saliency (Adolphs, 2010) of both positive and negative stimuli (e.g. Hamann et al., 2002), as well as in the experience of arousal triggered by emotional stimuli (Decety, 2011), the anterior insula is proposed to be critical for sensory integration (Critchley et al., 2004) and interoceptive awareness of all subjective feelings (Craig 2009; Critchley and Harrison 2013). These regions therefore seem to play a crucial role in emotional awareness and understanding (Craig, 2009; Decety, 2011). Here, we demonstrated that these regions are recruited when participants rated their affective responses to others' faces. We identified a quadratic pattern in anterior insula and amygdala, bilaterally, corresponding to subject-specific trial-by-trial fluctuations in subjective affective responses to facial expressions. That is, these regions responded to more intense subjective affective states elicited by the observation of emotional faces, providing further evidence that these regions participate in the generation of emotional internal states in response to others' emotional cues.

Our findings also indicate that the dACC and the *pars opercularis* of the IFG are recruited when we respond affectively to others' faces. The dACC, with extensive connections from the somatosensory cortices, and to and from the insula, amygdala and ventral striatum, is thought to be a hub region in affective, cognitive and motor control and, ultimately, to influence motor centers responsible for expressing affect and executing goal-directed behavior (Bernhardt and Singer, 2012; Shackman et al., 2011). The IFGOp, with functional projections to the motor cortex (e.g. Greenle et al., 2004), has been found to be involved in both observation and imitation of facial expressions (Carr et al., 2003; Leslie et al., 2004; Hennenlotter et al., 2005), and is thought to be involved in motor simulation of others (Keysers and Gazzola, 2006). The IFG has been reported to form a critical part of the attention network (Corbetta & Schulman, 2002), and its *pars opercularis* region has been linked to efficient action observation and imitation (e.g. Molnar-Szakacs et al., 2005), as well as motor (e.g. Aron and Poldrack, 2006), affective (e.g. Ochsner et al., 2004) and cognitive inhibitory control (e.g. Tabibnia et al. 2011). However, the nature of the current analysis does not allow us to infer the precise role these structures play in processing others' facial cues. However, the nature of the current analysis does not allow us to infer the precise role these structures play in processing others' facial cues.

We were not able to disentangle possible distinct neural circuits involved in the affective response to different types of emotions in relation to neutral facial expressions, and only detected significant clusters of activation within the lingual gyrus, a visual cortex region thought to be engaged in early perceptual processing of facial stimuli (Adolphs 2002; Fusar-Poli et al., 2009) and in the *pars orbitalis* of the IFG, a frontal region thought to be necessary for emotional

recognition (Hornak et al., 1996). Possibly, the limited number of trials per condition, and the repetition of stimuli within conditions (which may have resulted in some habituation), meant that our task was not optimally sensitive to obtain separate parameter estimates for each emotion condition. Another possible explanation for the lack of differential neural activation between emotional and neutral conditions in our task is that the differential processing demands between the emotional and neutral conditions may have been more subtle than we expected. That is, explicitly attempting to introspect on one's own affective response to others' emotional or neutral facial expressions possibly recruits a largely overlapping set of psychological processes, regardless of the actual valence of the face. Additionally, neutral faces can be perceived as ambiguous (e.g. Russell and Fehr, 1987; Somerville et al., 2004) and it is thus possible that some degree of affective resonance takes place even with these faces, particularly if a participant is actively encouraged to reflect on their affective response. Nonetheless, we believe these difficulties were substantially mitigated by the use of a more sensitive parametric modulation analysis, which do not require a contrast. The parametric modulation analyses allowed the detection of a pattern of response in both amygdala and anterior insula which varied as a function of affective response to others' emotional expressions, as predicted. Future studies examining affective empathy for faces should include more trials per condition, without repeating stimuli, and should also employ stimuli that share visual properties with faces but that the participants are less likely to find salient, for example scrambled faces.

Previous studies have shown that variability in self-reported affective responses to emotional faces is associated with individual differences in psychopathic traits (Seara-Cardoso et al., 2012, 2013). The present findings provide insight into the neural circuits driving this association. We

found that responsivity to faces in regions previously associated with empathic responding was negatively associated with both dimensions of psychopathic traits. These findings are consistent with most of the prior work investigating empathy for pain in adults with high levels of psychopathy (Decety, Chen et al., 2013; Meffert et al., 2013) and children with high levels of callous-unemotional traits (thought to be a precursor of psychopathy) (Lockwood, Sebastian et al., 2013; Marsh et al., 2013). Our findings support the hypothesis that psychopathic traits are marked by impairments in responsivity to others, and that this is accompanied by diminished amygdala and anterior insula function in healthy individuals with higher levels of these traits.

In summary, we demonstrate that the neural structures that are most consistently reported to be involved in empathy for pain and disgust (anterior insula, dACC and IFGOp) and in detecting emotional saliency (amygdala) are robustly recruited when participants rate affective responses elicited by others' faces. Critically, we demonstrate that both anterior insula and amygdala respond more to more extreme elicited affective states (both positive and negative), providing further evidence for the involvement of these regions in affective resonance, in particular in the generation of internal affective states in response to others' emotional cues. Furthermore, we found that neural responses in anterior insula and amygdala were associated with variation in psychopathic traits in the general population, which support previous theoretical and empirical work suggesting that atypical function of these regions might represent neural markers of disrupted emotional and empathic processing for individuals with high levels of these traits.

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## Tables with captions

**Table 1.** Peak cluster activations in brain regions during response to facial expressions (relative to baseline)

Brain regions	L/R	Peak					P (FWE)	Cluster Extent (k)
		x	y	z	t	Z		
Inferior frontal gyrus, <i>pars opercularis</i>	R	54	11	7	13.63	7.56	< 0.001	659
<i>Extending to</i> Anterior insula	R	42	5	1	10.05	6.55		
Cerebellum	L	24	-49	-32	12.52	7.29	< 0.001	3583
<i>Extending to</i> Fusiform gyrus	L	39	-58	-14	12.01	7.15		
Thalamus	L	-12	-22	10	12.28	7.22	< 0.001	268
Parietal operculum	L	-45	-25	16	12.22	7.21	< 0.001	1302
<i>Extending to</i> Anterior insula	L	-42	-1	1	11.59	7.03		
Dorsal anterior cingulate cortex	R	-3	14	34	11.66	7.05	< 0.001	235
Dorsal anterior cingulate cortex	R	6	14	40	11.34	6.96	< 0.001	205
Supramarginal gyrus	L	45	-40	40	8.38	5.93	< 0.001	140
Middle frontal gyrus	R	36	41	25	8.22	5.86	< 0.001	176

Notes: Whole-brain analysis within grey matter mask, reported at a threshold level of  $P < 0.05$  (FWE corrected). Spatial coordinates (x, y, z) are in Montreal Neurological Institute space. R = Right; L = Left.

## **FIGURE LEGENDS**

### **Figure 1. Empathy for emotional faces task**

A. Task timeline and examples of three trials (from fearful, neutral and happy conditions).

Participants were presented with each trial over two screens consisting in the presentation of the stimuli for 2 s, followed by presentation of the sliding scale where they rated how the image made them feel (0-4 s); B. Scatter-plot depicting the association between overall affective ratings (excluding ratings of neutral faces trials; ratings of sad, fearful and angry faces trials are reversed) and levels of affective-interpersonal psychopathic traits.

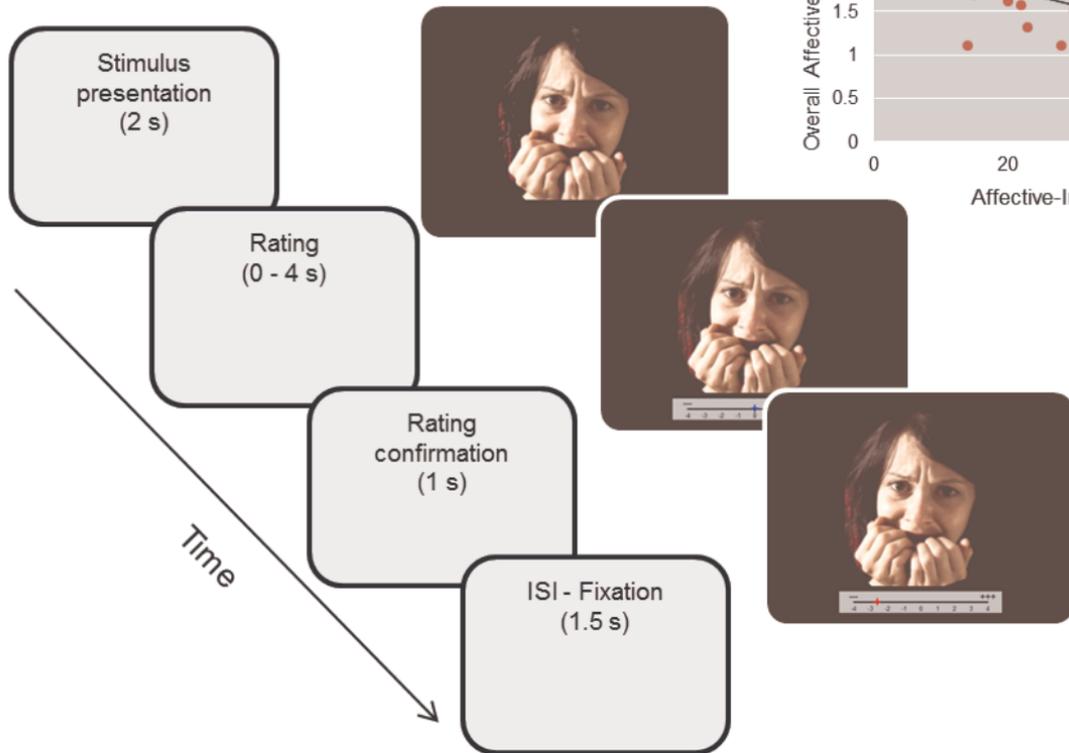
### **Figure 2. Quadratic parametric modulation of affective response to emotional facial expressions**

Results illustrate clusters of voxels in bilateral anterior insula and amygdala. Overlays are displayed at  $p < 0.005$  (uncorrected); Plots illustrate the positive quadratic effect of affective response in anterior insula and amygdala, bilaterally. All regions show a quadratic response to ratings of affective state, with trials eliciting extremes of affective ratings generating greater activation than trials eliciting medium affective ratings. Data for illustrative plots were derived from a subsidiary model in which stimuli were divided into quartiles of intensity of affective ratings for each subject and contrasted against baseline. Contrast estimates were extracted from peak coordinates identified in the quadratic parametric modulation analysis (Error bars represent standard error of the mean).

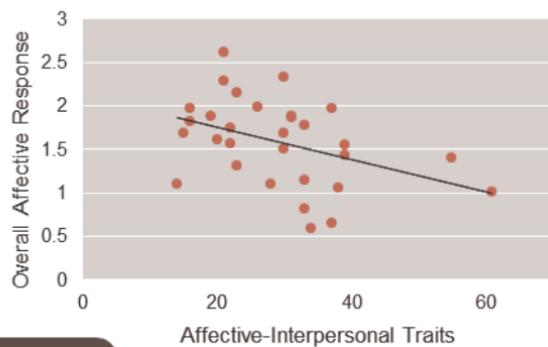
**Figure 3. Associations between neural response and psychopathic traits**

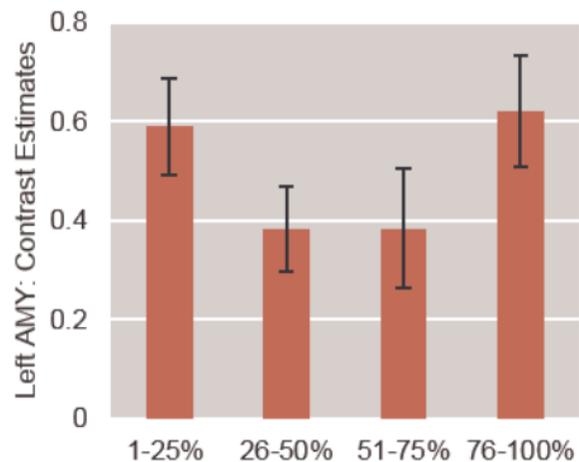
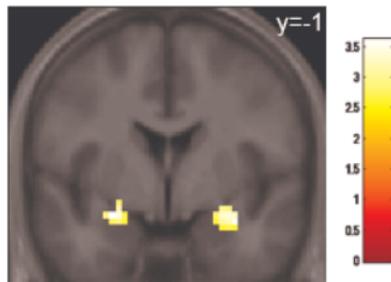
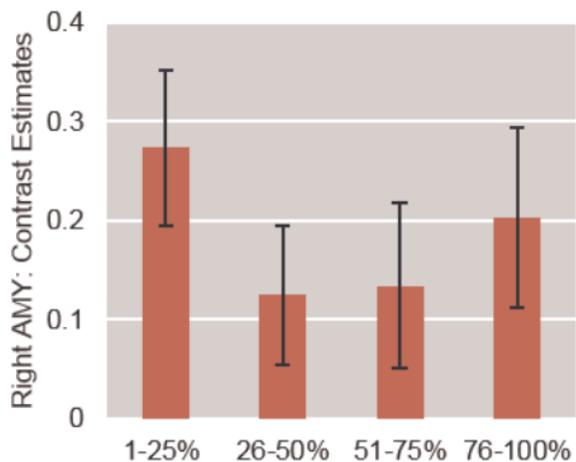
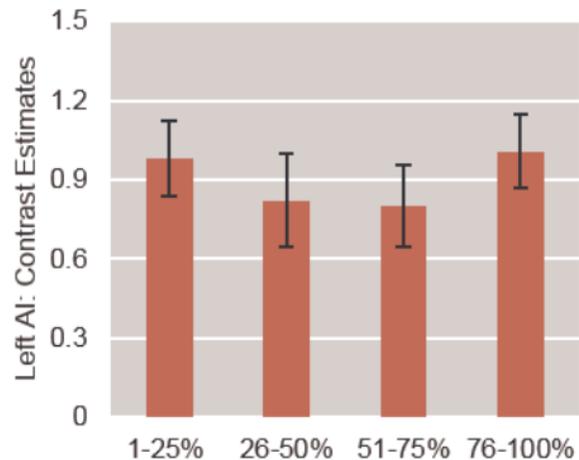
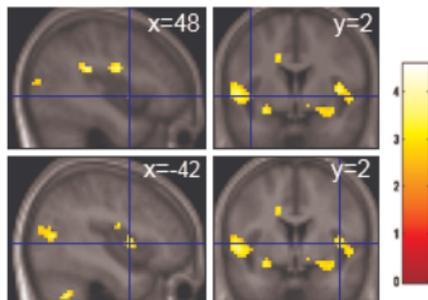
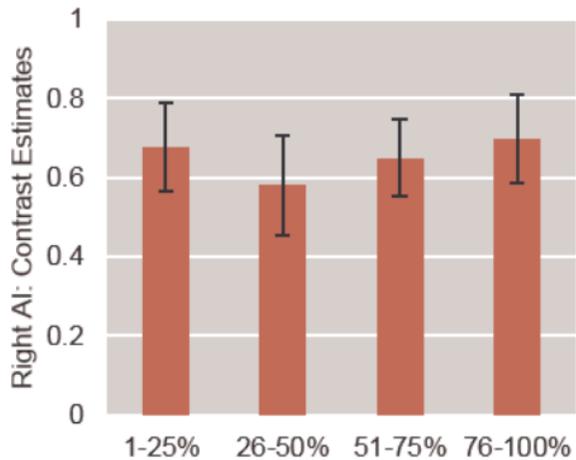
Regression plots depicting associations between contrast estimates of task elicited (relative to baseline) anterior insula (8 mm sphere centered at peak coordinates [45 5 1; -42 -1 1]) and amygdala (8 mm sphere centered at peak coordinates [24 2 -11]) response and levels of psychopathic traits.

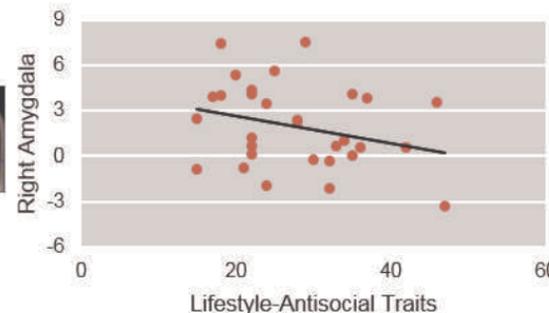
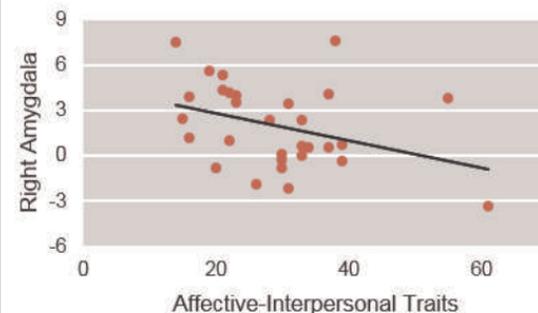
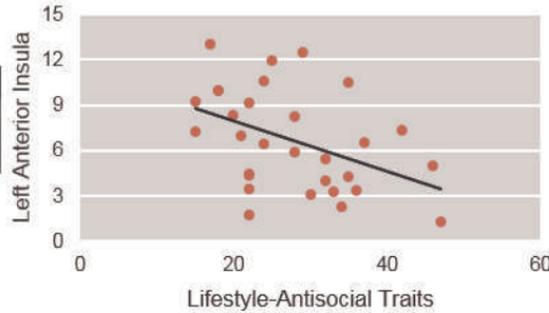
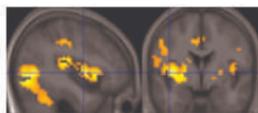
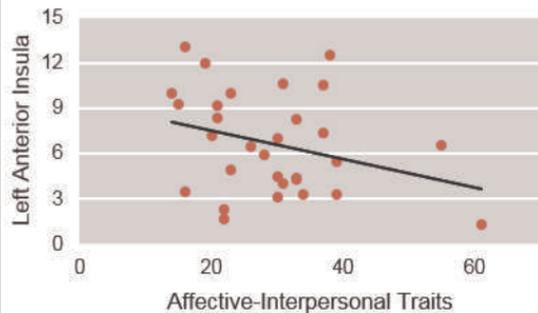
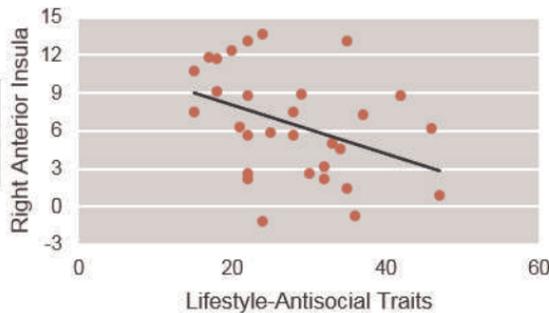
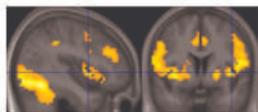
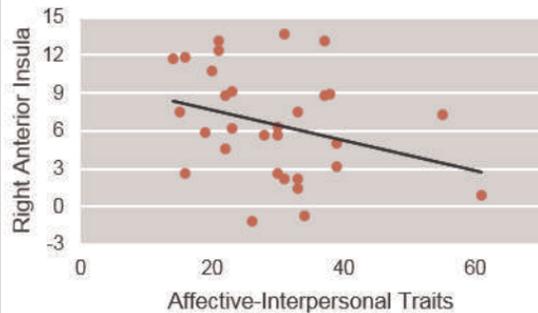
A.



B.







**Affective resonance in response to others' emotional faces varies with affective ratings and psychopathic traits in amygdala and anterior insula**

**Supplementary Materials**

**Supplementary Table 1. Descriptive statistics**

	<b>Min</b>	<b>Max</b>	<b>Mean</b>	<b>SD</b>
<b>Affective ratings</b>				
Sad faces	-3.4	-0.91	-1.93	0.55
Fearful faces	-2.85	0.04	-1.54	0.64
Angry faces	-2.22	0.67	-1.15	0.77
Neutral faces	-0.18	1.34	-0.39	0.34
Happy faces	0.52	3.34	1.70	0.65
<b>Psychopathic traits</b>				
Total	31	109	58.07	18.18
Affective-Interpersonal	14	61	29.23	10.90
Lifestyle-Antisocial	15	47	27.70	8.73

**Supplementary Table 2. Correlations between psychopathy scores, Age, IQ and Anxiety measures**

	SRP Total	SRP AI	SRP LA	Age	IQ
	r	r	r	r	r
SRP Affective-interpersonal	.94**	-			
SRP Lifestyle-Antisocial	.90**	.70**			
Age	0.20	0.31	0.05		
IQ	0.15	0.01	0.29	-0.13	
Anxiety	-0.02	-0.06	0.04	-0.12	-0.25

Notes: Pearson correlation coefficients are reported; \*  $P < 0.05$  (2-tailed).

**Supplementary Table 3. Correlations between psychopathy scores and ratings of affective response to emotional facial expressions**

	<i>Bivariate Correlations</i>			<i>Correlations controlling for IQ &amp; Anxiety</i>		
	Total	Affective-Interpersonal	Lifestyle-Antisocial	Total	Affective-Interpersonal	Lifestyle-Antisocial
	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>
Sad faces	0.09	0.11	-0.11	0.09	0.16	-0.01
Fearful faces	0.25	0.27	0.13	0.25	0.28	0.16
Angry faces	0.26	0.26	0.09	0.26	0.30	0.17
Neutral faces	-0.11	-0.03	0.01	-0.16	-0.13	-0.16
Happy faces	-0.43*	-0.43*	-0.23	-0.44*	-0.47*	-0.34
Overall affective ratings <sup>1</sup>	-0.34	-0.41*	-0.20	-0.36	-0.42*	-0.23

Notes: Pearson correlation coefficients are reported; \*  $P < 0.05$  (2-tailed); <sup>1</sup>Excludes ratings of neutral faces trials; ratings reversed on sad, fearful and angry faces trials.

**Supplementary Table 4. Peak clusters of regions showing linear and quadratic relationships with affective responses to emotional faces**

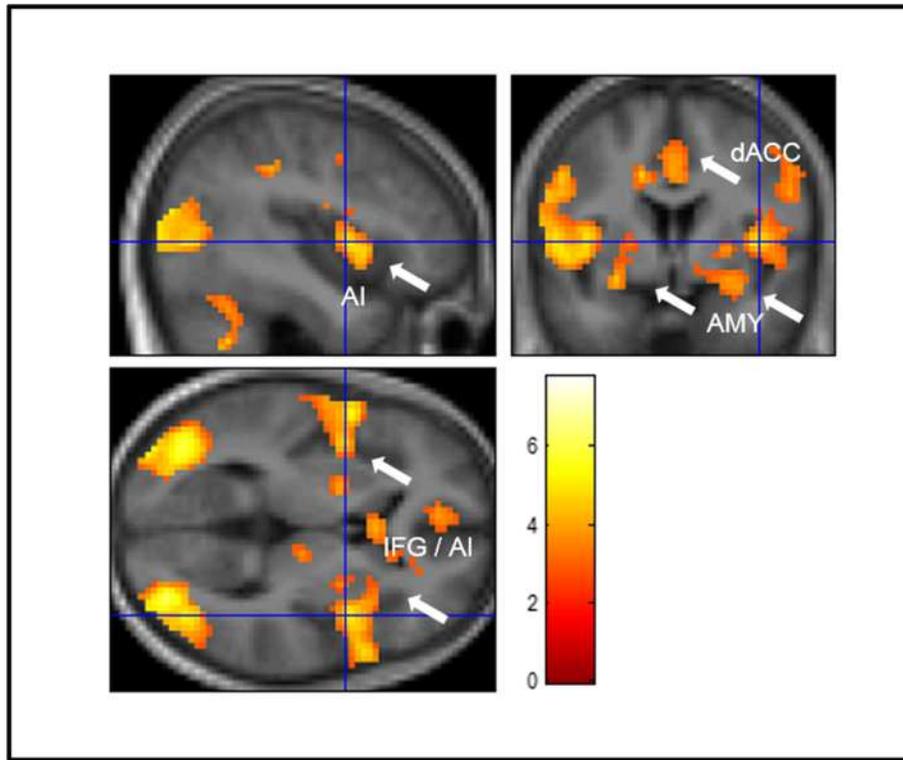
Brain regions	Peak						Cluster	
	L/R	x	y	z	t	Z	Extent (k)	P (FWE)
<i>Linear</i>								
<i>Positive</i>								
Lingual gyrus	R	15	-79	-14	9.73	6.44	1467	<0.01
Putamen	L	-27	-16	1	4.38	3.81	31	0.98
Cerebellum	L	-36	-67	-38	4.33	3.77	165	0.05
Precentral gyrus	L	-57	8	4	4.05	3.58	35	0.96
Anterior cingulate gyrus	R	3	53	1	4.05	3.57	69	0.57
Inferior frontal gyrus	R	51	44	10	3.69	3.32	57	0.73
Superior rostral gyrus	L	-3	56	4	3.60	3.25	55	0.76
Middle temporal gyrus	R	12	14	34	3.51	3.18	27	0.99
Middle frontal gyrus	L	-33	53	19	3.48	3.16	27	0.99
<i>Negative</i>								
Lingual gyrus	L	-9	-82	-11	7.25	5.43	303	<0.01
<i>Quadratic</i>								
<i>Positive</i>								
Superior frontal gyrus	L	-21	29	49	5.01	4.22	163	0.04
Supramarginal gyrus	L	-45	-37	25	4.90	4.15	48	0.82
Anterior cingulate gyrus	R	15	41	10	4.65	3.99	42	0.89
Anterior cingulate gyrus	L	-9	41	-2	4.44	3.85	385	<0.01
Inferior frontal gyrus	L	-57	5	1	4.43	3.84	100	0.23
Middle occipital gyrus	L	-33	-79	7	4.30	3.75	21	1.00
Caudate	L	-9	17	-5	4.07	3.59	51	0.78
Cerebellum	R	42	-55	-44	4.06	3.58	21	1.00
Anterior insula	R	42	2	4	4.02	3.55	42	0.89
Amygdala	L	-27	-1	-17	3.94	3.50	77	0.43
Middle temporal gyrus	L	-57	-19	-17	3.93	3.49	109	0.18
Middle temporal gyrus	R	42	-70	10	3.88	3.45	83	0.37
Amygdala	R	33	-1	-20	3.88	3.45	28	0.98
Inferior temporal gyrus	L	-54	-61	-11	3.53	3.20	21	1.00

**Notes:** Exploratory whole-brain analyses within grey matter mask, reported at a threshold level of  $P < .005$  (uncorrected, cluster size  $> 20$  voxels). Spatial coordinates (x, y, z) are in Montreal Neurological Institute space. R = Right; L = Left.

**Supplementary Table 5. Correlations between psychopathy scores and neural responses during the performance of the task (all faces relative to baseline)**

	<i>Bivariate Correlations</i>			<i>Correlations controlling for corresponding dimension</i>	
	Total	Affective- Interpersonal	Lifestyle- Antisocial	Affective- Interpersonal	Lifestyle- Antisocial
	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>	<i>r</i>
Right Anterior Insula	-0.38*	-0.31 <sup>†</sup>	-0.39*	-0.06	-0.25
Left Anterior Insula	-0.40*	-0.31 <sup>†</sup>	-0.43*	-0.17	-0.32 <sup>†</sup>
Right Amygdala	-0.37*	-0.36*	-0.29	-0.23	0.06

Notes: Pearson correlation coefficients are reported; \*  $P \leq 0.05$  ; <sup>†</sup>  $0.05 < P < 0.1$ (2-tailed)



**Supplementary Figure 1. Quadratic parametric modulation of affective response to emotional facial expressions**

Results illustrate significant quadratic parametric effects in anterior insula and amygdala, bilaterally. Overlays are displayed at  $p < 0.005$  (uncorrected),  $k > 20$ ,  $[x=42; y=2; z=4]$ . Data derived from a subsidiary model in which trial onsets were time-locked to the presentation of the stimuli and durations were kept constant by fixing them to the mean trial duration within each participant. ROI analyses with SVC (FWE) indicate a pattern of significant parametric effects in anterior insula, extending to IFG bilaterally (right peak coordinates:  $[x=42; y=2; z=4]$ ;  $k=76$ ;  $Z=4.25$ ;  $P < 0.001$ ; left peak coordinates:  $[x=-42; y=2; z=-4]$ ;  $k=57$ ;  $Z=4.05$ ;  $P < 0.001$ ), in amygdala (right peak coordinates:  $[x=33; y=-1; z=-20]$ ;  $k=34$ ;  $Z=3.79$ ;  $P=0.01$ ; left peak coordinates:  $[x=-27; y=-4; z=-11]$ ;  $k=34$ ;  $Z=3.77$ ;  $P=0.01$ ), and dACC (peak coordinates:  $[x=0; y=8; z=37]$ ;  $k=53$ ;  $Z=4.07$ ;  $P < 0.001$ ).