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Anxious attachment is associated with heightened responsivity of a parietofrontal cortical network that monitors peri-personal space

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ABSTRACT

Background: Attachment, or affiliative bonding among conspecifics, is thought to involve neural mechanisms underlying behavioral responses to threat and reward-related social signals. However, attachment-oriented responses may also rely on basic sensorimotor processes. One sensorimotor system that may play a role in attachment is the parietofrontal cortical network that responds to stimuli that are near or approaching the body, the peripersonal space (PPS) monitoring system. We hypothesized that this network may vary in responsivity to such potentially harmful stimuli, particularly those with social salience, based on individual differences in attachment styles.

Methods: Young adults viewed images of human faces or cars that appeared to move towards or away from them, while functional magnetic resonance imaging data were collected. Correlations between each of four adult attachment styles, measured using the Relationship Questionnaire, and responses of the PPS network to approaching (versus withdrawing) stimuli were measured.

Results: A region-of-interest (ROI) analysis, focused on six cortical regions of the PPS network that showed significant responses to approaching versus withdrawing face stimuli in an independent sample (n=80), revealed that anxious attachment style (but not the other 3 attachment styles) was significantly positively correlated with responses to faces (but not to cars) in all six ROIs (r=0.33-0.49, p=0.01-0.0001, n=50).

Conclusions: These findings suggest that anxious attachment is associated with over-responsivity of a sensorimotor network involved in attending to social stimuli near the body.

1. Introduction

Attachment behaviors have been defined as interpersonal relationship patterns that are intended to increase an individual's sense of safety and promote survival, particularly during times of stress or danger (Bowlby, 1969; Atzil, 2018; Ein-Dor, 2014). Fundamentally, individuals are driven to seek proximity to (and care from) a supportive other during times of need. This drive for social support is thought to reflect the output of basic biological mechanisms that aim to maintain an expected, baseline level of social connection; sustaining such a level may reduce the bioenergetic requirements of bodily functions and conserve resources (Coan and Sbarra, 2015). According to this model, deviations

from this baseline, optimal level of social contact, or "set point", will trigger behavioral responses that aim to correct such deviations (i.e., allostasis) (Matthews and Tye, 2019; Quadt, 2020).

In addition, this allostatic drive is thought to be continuously modified by experiences with others, such as those with early caregivers, giving rise to "internal working models" (IWMs) (Zimmermann, 1999) or prediction signals (Atzil, 2018), i.e., internalized expectations about the behavior of oneself and others, that, over time, form the basis of consistent strategies for meeting attachment needs (Bowlby, 1982). Although IWMs are initially shaped by early experiences, they are believed to undergo further modification at later junctures of development, in the context of specific adult relationships (Fraley, 2019).

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Consistent patterns of feelings about others and behaviors in relationships during adulthood (i.e., adult attachment "styles") have been classified as either "secure" or "insecure" based on whether the behaviors tend to be successful (secure) or not (insecure) in promoting emotional well-being and sustained and mature relationships. Hazan and Shaver described three types of insecure adult attachment styles: "anxious preoccupied", "dismissive avoidant" and "fearful avoidant" (Hazan and Shaver, 1987). According to their model, "anxious preoccupied" or anxious attachment is characterized by a lack of confidence in the sustainability of relationships and a strong desire for closeness and need for reassurance, whereas "dismissive avoidant" attachment is associated with an emphasis on self-reliance and emotional distance from others, and "fearful avoidant" attachment is linked to a fear of rejection and abandonment (Hazan and Shaver, 1987; Bartholomew and Horowitz, 1991). Other closely related models of attachment have focused on two dimensions (rather than categories) of attachment, avoidance and anxiety, with secure attachment characterized by both low avoidance and low anxiety (Brennan et al., 1998).

It is also important to note that, although insecure attachment patterns were initially characterized as "unsuccessful", potentially adaptive, desirable features of insecure attachment have also been highlighted by recent studies. For example, there is evidence that greater heterogeneity in attachment styles of members of a group is advantageous to that group in terms of survival, since the ability to rapidly detect threats (linked to anxious attachment) and to focus on action and flight from threats (linked to avoidant attachment) can each confer benefits to all members of a group (Ein-Dor, 2014). Such heterogeneity in attachment strategies among adults naturally emerges in response to a range of environmental, interpersonal pressures that are present during development. However, although such variation is expected and adaptive in specific interpersonal contexts, insecure attachment styles, particularly on the extremes of the continuum, are also associated with increased risk for the development of several neuropsychiatric disorders (Erickson et al., 1985), including autism spectrum disorders, schizophrenia and personality disorders (Myhrman, 1996; Jones, 1994; Schiffman, 2002; Gumley and Liotti, 2018; Liotti, 1992; Rutgers, 2004; Shapiro, 1987). Given these known associations, identifying the neural mechanisms of variation in attachment may provide some important clues about the etiology of these conditions (Feldman, 2017; Insel and Young, 2001), and could lead to the development of objective markers that could be targeted by treatments for these disorders.

Evidence for neurobiological distinctions among adult attachment styles (or dimensions) has emerged from a range of methodologically-varied studies (Long, 2020). Higher levels of anxious attachment have been associated with higher arousal responses (Rognoni, 2008; Vrtička et al., 2012) and attentional vigilance (Dewitte and De Houwer, 2008) to threatening social information, and greater activation of brain regions involved in threat evaluation, such as the amygdala, insula and dorsal anterior cingulate cortex, in response to negatively valenced social cues (Vrtička, 2008; Lemche, 2006) and social exclusion (Lemche, 2006). In contrast, avoidant attachment has been linked to inhibition of physiological responses to threat (Dewitte and De Houwer, 2008) and deactivation of the neural circuitry involved in threat responses (Long, 2020).

Although the function of basic sensorimotor circuits in relation to attachment has been less often studied, regions involved in the simulation of sensorimotor processes (e.g., mirroring) are thought to influence attachment-related perceptions and behaviors. Specifically, it has been proposed that medial and lateral frontal and parietal cortices, and the insula and anterior cingulate cortex, which are involved in representing the actions, experiences and mental states of others, contribute to an individual's capacity for empathy and attachment to others (Adolphs, 2003; Feldman, 2017).

Another sensorimotor system that may play role in social behavior and attachment, which is adjacent anatomically to the circuits involved in mirroring, is the parietofrontal cortical network involved in monitoring the space near the body (peripersonal (PPS) space) (Cléry, 2015;

di Pellegrino, G., & Làdavas, E., 2015; Graziano and Cooke, 2006). Studies in non-human primates (Duhamel JR, Colby CL, Goldberg ME, 1998; Graziano MS, Hu XT, Gross CG, 1997) and humans (Bremmer, 2001; Brozzoli, 2011) have shown that specific areas within parietal and frontal cortices are particularly responsive to stimuli within or entering PPS. Based on observations of defensive motor responses evoked by stimulating neurons in these regions, it is thought that the PPS network plays a key role in generating responses to threats in the local environment (Graziano and Cooke, 2006). However, although the central role of this network in defending against or avoiding collisions or intrusions into the space near the body has been emphasized, given that an organism's need for self-protection is balanced by an opposing drive for affiliation with others, the expression of this balance during day-to-day social behaviors (specifically those behaviors occurring within PPS during interactions with conspecifics) may represent one manifestation of a person's attachment style. Thus, managing the delicate tuning between social proximity and self-protection, including in its physical expressions, may be one important attachment-related function supported by the PPS network.

Consistent with this idea is the observation that many behaviors in children that are driven by attachment needs involve modulating (decreasing or increasing) physical distances from caregivers (Gervai, 2009). Also, individuals with neuropsychiatric disorders associated with insecure attachment have shown impairments in this type of social distance regulation (Gessaroli, 2013; Holt, 2015; Schienle, 2015). Thus, variation in the ability to maintain context-appropriate physical distances from others (and variation in the functioning of the PPS network) may reflect dimensions of adult attachment.

Based on this model, in the current study we tested the hypothesis that responsivity of the PPS network is linked to variation in adult attachment. In prior work, we found evidence that two nodes of the PPS network (the dorsal parietal cortex and ventral premotor cortex) respond to images of human faces that appear to approach (versus recede or withdraw from) participants (Holt, 2014). Thus, we predicted that the magnitude of responses of the PPS network to approaching (vs. withdrawing) faces partially reflects variation in self-reported adult attachment styles. Lastly, we also explored whether resting-state functional connectivity among nodes of the PPS network shows a similar association.

2. Methods and materials

2.1. Study participants

Participants were recruited for a behavioral assessment and MRI scanning session at the Harvard University Center for Brain Science, as part of a larger ongoing study of psychopathology in college students (Farabaugh, 2012; Shapero, 2019; Barbour, 2020). Inclusion criteria for this imaging study were designed to enrich the sample for variation in subclinical symptoms of psychopathology (i.e., a total score on the Beck Depression Inventory (BDI) (Beck, Aaron T., 1961) of 5 or greater; or a score on the BDI suicidal ideation question of greater than zero; or a total score on the Peters et al Delusion Inventory (PDI) of 7 or greater (Preti, 2007)), including variation in social functioning characteristics and attachment. See DeCross, 2019 for further details. Exclusion criteria for the neuroimaging portion of the study included contraindications to magnetic resonance imaging (MRI) (claustrophobia, mental implants, pregnancy), a history of brain injury or of recent substance abuse. Written informed consent was obtained from participants in accordance with the guidelines of the Partners Healthcare and the Harvard University Institutional Review Boards.

MRI data were collected in 130 participants. Fifty of these 130 subjects also completed the Relationship Questionnaire (RQ) (Bartholomew and Horowitz, 1991), which is a self-report questionnaire that assesses adult attachment styles. For the current analysis, the cohort of 130 participants with MRI data was divided into two groups, based on

whether RQ data were available: 1) a Reference Sample (n = 80; mean age = 19.45 \pm 1.4, 31% males), in which the regions-of-interest (ROIs) for the fMRI analyses were defined (see below), and 2) a Test Sample (n = 50; mean age = 19.6 \pm 1.4; 28% male), in which our hypotheses regarding the relationships between attachment style and responses of the PPS network were tested. Although the RQ was not administered randomly in the 130 subjects (since it was added to the assessment battery in one non-random subset of the sample, referred to as the Test Sample here), the Reference and Test samples did not differ from one another with respect to demographic variables, symptom levels, behavioral performance or average activation patterns and levels (see Table 1 and Results).

2.2. Attachment style assessment

The Relationship Questionnaire (RQ) (Bartholomew and Horowitz, 1991) is comprised of four items. Each item describes, from a firstperson perspective, the common internal experience associated with one of the four classic attachment styles ("secure", "anxious preoccupied", "fearful avoidant", and "dismissive avoidant"), in a few sentences. Subjects in the Test Sample were asked to rate the degree to which the description of each style appeared to describe them, on a scale of 1 to 7 (see Supplementary Table 1 for the items of the RQ). As defined in earlier work (Hazan and Shaver, 1987; Bartholomew and Horowitz, 1991), the RQ items reflect the model of "secure" attachment as associated with a positive self-image and an expectation that others are also accepting and responsive to them, whereas "anxious-preoccupied" (or "anxious") attachment is characterized by a negative self-image accompanied by positive feelings about others. In contrast, "fearful avoidant" attachment is thought to reflect a negative self-image accompanied by a lack of trust and a sense of being rejected by others (i.e., negative feelings about others), and "dismissive avoidant" attachment is associated with a positive self-image and a negative disposition toward other people.

2.3. Symptoms of psychopathology

Symptoms of psychopathology were also measured in our participants. Symptoms of depression, anxiety and subclinical psychotic symptoms were measured using the BDI, the Anxiety Symptoms Questionnaire (ASQ) (Baker, 2019), and the PDI and the Launay-Slade Hallucination Scale-Revised (LSHS) (Waters et al., 2003), respectively. Scores on the RQ and LSHS were not normally distributed (Shapiro-Wilk test, p < 0.05). All of the other measures and the fMRI data were normally distributed (Shapiro-Wilk test, p > 0.1).

2.4. MRI data acquisition

All MRI data were collected using a 3 Tesla Siemens Tim Trio scanner (Siemens, Erlangen, Germany) with a 12-channel head coil. The neuroimaging session included a total of 9 scans (Holmes, 2015). The

Demographic characteristics and symptom levels of the Reference (n=80) and Test (n=50) Samples. The two samples showed no significant differences in age, gender, or levels of symptoms. P-values of Student's T-tests performed to compare these variables are listed. Three participants of the Reference Sample and no participants of the Test Sample were being treated with psychotropic medications (antidepressants) at the time of the study. SD, standard deviation; BDI, Beck Depression Inventory; PDI, Peters et al Delusion Inventory.

	Reference Sample Mean (SD)	Test Sample Mean (SD)	P-value
age	19.45 (1.4)	19.6 (1.4)	0.32
gender	31% male	28% male	0.27
BDI total score	9.8 (0.8)	10.9 (1.09)	0.23
PDI total score	5.9 (0.4)	6.5 (0.4)	0.12

analyses conducted in the current study were conducted using the following three scans with the parameters below:

- 1) An anatomical scan: One high-resolution multiecho T1-weighted magnetization-prepared gradient-echo image (MPRAGE, 1.2 mm isotropic voxels, repetition time (TR) = 2200 ms, inversion time (TI) = 1100 ms, echo time (TE) = 1.54 ms for image 1 to 7.01 ms for image 4, flip angle (FA) = 7° and field of view (FOV) = 230) was collected.
- 2) Functional MRI (fMRI) scans, during which the face and car stimuli were presented: Four 3.2-minute blood oxygenation-level dependent (BOLD) scans (with 96 time points, 3 mm isotropic voxels, $TR = 2000 \, \text{ms}$, $TE = 30 \, \text{ms}$, $FA = 90^\circ$, FOV = 200.3) were collected, during which participants viewed 1) computer generated, realistic images of human faces with neutral facial expressions, and 2) car stimuli (see Fig. 1) (Holt, 2014, 2015). Both face and car stimuli appeared to either approach or withdrawal from the participant (expanding or contracting in size; see below for details).
- 3) Resting-state fMRI scans: Two 6.2-min resting-state BOLD scans (with 124 time points, 3 mm isotropic voxels, TR = 3000 ms, TE = 30 ms, $FA = 85^{\circ}$, FOV = 216, and 47 axial slices collected with interleaved acquisition, with no gap between slices) were collected. During these scans, subjects were instructed to keep their eyes open and blink normally.

2.5. Experimental paradigm

A total of 6 different images of faces, with an equal number of males and females, and 6 different images of cars, were presented in six conditions (Female Face Approach, Female Face Withdrawal, Male Face Approach, Male Face Withdrawal, Car Approach, Car Withdrawal). The face stimuli were computer-generated (http://www.facegen.com). Photographs of cars were used as the car stimuli. Each stimulus/condition was presented in blocks of 16 s, in a counterbalanced order. A small red circle (the fixation target) was presented at the center of each stimulus, to enable central fixation during stimulus presentation. The stimulus (face or car) changed in size at a rate equivalent to a physical distance change of 112 cm/sec, a typical speed for walking. In addition, two 16-second blocks of uniform gray were presented, one at the beginning and one at the end of each run.

To reduce or eliminate attentional biases across different conditions, each subject performed a "dummy attention task" during the task-based scans (the Dot Detection Task). During this task, a blue dot appeared at a random location of the computer screen for 400 ms (three dots during each 16-sec block), every 5.3 s. Subjects were instructed to fixate on the center of the face and car images and press a button (located on the button box inside the scanner) whenever they saw a blue dot, located peripheral to the fixation target. The instructions were repeated before each task run, and the percentage of correct responses per condition/per run was calculated for each subject.

2.6. Functional MRI data analysis

Preprocessing: All functional MRI data analyses were performed with the Freesurfer v.6 analysis suite (http://surfer.nmr.mgh.harvard.edu) in three main steps: (i) cortical reconstruction, (ii) preprocessing of the functional data, (iii) first level and group statistical analyses (Dale et al., 1999; Dale and Sereno, 1993; Fischl and Dale, 2000; Fischl et al., 2001; Fischl, 2002a, 2004b, 2004c).

The automated reconstruction of the structural data included the following steps: image realignment and motion correction, non-uniform intensity normalization, skull stripping (removing the non-brain tissues), gray-white matter segmentation, reconstruction of cortical surface models and labeling of the regions on the cortical surfaces and subcortical structures based on probabilistic information derived from a manually labeled training set.

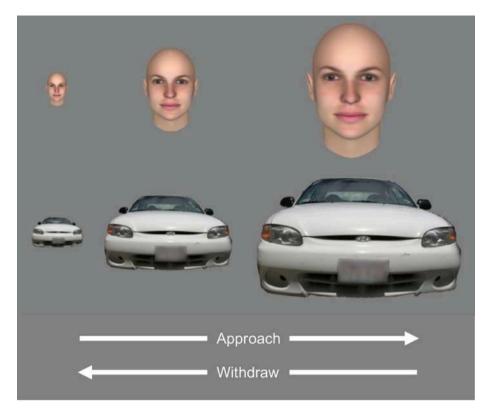


Fig. 1. Experimental stimuli. An example of each category of stimuli (faces and cars) is shown.

BOLD data were preprocessed as follows: cortical surfaces of individual subjects were registered to an average reference surface; functional data were registered onto the same-subject anatomical data and corrected for head motion and normalized; and spatial smoothing was applied using a 3D Gaussian kernel (5 mm FWHM). The statistical analysis was performed by fitting a univariate general linear model (GLM) to the fMRI data. Nuisance regressors, accounting for head motion and temporal and scanner drift, were included in the model. Hemodynamic responses were estimated by fitting the SPM hemodynamic response function to the data. In the group-level analyses, the parameters estimated from the GLM were used to create linear contrast images of the predefined conditions.

Quality control: All brain images were visually inspected for brain coverage, registration quality and anatomical defects. One subject was excluded due to a structural abnormality identified in the T1 scan. Quality assurance of the remaining imaging data was performed using QA_tools in Freesurfer v.6 (https://surfer.nmr.mgh.harvard.edu). These scripts were used to verify that steps involved in reconstruction and registration of the data were conducted in the correct order. Also, the signal to noise ratio (SNR) and white matter intensity values used to detect outliers were calculated. A quality assurance (QA) value was generated using the 'tkregister-sess' command which varied between 0 and 1, with 0 indicating perfect functional to anatomical registration. All subjects' fMRI data passed the quality control criteria (QA value < 0.4, SNR > 125). The FSL motion outlier algorithm was used to eliminate time points showing excessive head motion across volumes (Power, 2012), by using a confound matrix of outlier timepoints as a regressor in GLM. There are several metrics for defining the outlier time points (Power, 2012; Bastiani, 2019). We used the DVARS metric (D referring to temporal derivative of time courses, VARS referring to RMS variance over voxels) (Smyser, 2010), which reflects the rate of change of the BOLD signal across the entire brain in comparison to the previous time point (Power, 2012). The threshold used to define an outlier was set to the default value suggested by Power et al (Power, 2012) (75th percentile + 1.5 times the Inter Quartile Range of the DVARS metric).

Any timepoint with a value larger than this threshold was eliminated from further analysis, as an outlier. Also, any run in which the number of excluded timepoints comprised more than half of the total number of timepoints was excluded. In addition to time point motion correction, the six rigid-body motion parameters within each volume were used as regressors, to account for absolute motion.

In the behavioral data, outliers were defined as a dot detection score less than two standard deviations from the mean. However, no subjects' data met this criterion.

Whole brain fMRI analysis: In both samples, BOLD responses to the two independent contrasts ('Approach vs. Withdrawal' for the face and car stimuli) were measured. In these analyses, the six rigid motion parameters and time point exclusion files were included as nuisance regressors modelled with a SPM hemodynamic response function. A threshold of 0.01 for high pass filtering was applied, to exclude frequencies that oscillate with a rate slower than 0.01 Hz, such as scanner drift and physiologic noise. This cutoff of 0.01 was chosen based on the formula of Matthews and Jezzard (Matthews and Jezzard, 2004) = $1/\{1.5 * [\text{the period of stimulation}]\}$. Mean activation maps were corrected for multiple comparisons using Monte-Carlo simulations with a voxel-wise p-value threshold of 0.001.

Region-of-interest (ROI) analysis: To define the ROIs used in the primary analyses, a map of responses to the Faces Approach vs. Withdrawal contrast was generated using the data collected from the Reference Sample (n = 80). The ROIs were constructed using these data by defining the border of each significant cluster of activation, at a threshold of p = 0.001, corrected for multiple comparisons using FDR < 0.05, in the group template (fsaverage) space. Each of these template labels was then mapped onto each of the individual Test Sample subjects (n = 50) using the mri_labeltolabel command.

For the primary analysis, the BOLD signal in response to the Approach vs. Withdrawal Face or Car contrast was measured in the ROIs for each Test Sample subject. Spearman's correlation coefficients were computed for correlations between the average BOLD signal response and the RQ score for each of the four attachment styles. A Bonferroni-

Table 2

PPS network activation in response to faces (Approach vs. Withdrawal) in the Reference (n = 80) and Test (n = 50) samples. This table lists the location (based on the FreeSurfer aparc atlas), size, and significance level (z score and p value of the peak vertex) of clusters of activation (meeting a whole-brain-corrected level of significance of p = 0.001) to the Faces Approach vs. Withdrawal contrast. Hemi, hemisphere; CWP, cluster-wise p-value; NVtxs,number of vertices in each cluster.

	Region	Hemi	Size (mm ²)	X	Y	Z	CWP	NVtxs
Reference Sample (n = 80)						<u>—</u>		
Faces: Approach > Withdrawal	Paracentral	Left	2920.9	-15.9	-19.9	41	0.0003	6686
		Right	397.61	14.9	-19.3	43.9	0.0003	1109
	Superior parietal	Right	1521.36	17.8	-61.6	61.7	0.0003	3766
		Right	492.86	19.6	-80.6	37.3	0.0003	739
	Precentral	Right	349.79	26.7	-10.3	46.4	0.0006	869
	Superior frontal	Left	250.32	-20	-5.1	53.2	0.00808	596
	Supramarginal	Left	188.55	-49.8	-29.5	33.1	0.03645	506
$Faces:\ With drawal > Approach$	Cuneus	Right	245.08	5.6	-82.4	30.2	0.00748	366
Test Sample (n = 50)								
Faces: Approach > Withdrawal	Superior parietal	Left	801.03	-19.8	-63	61.4	0.0003	1937
		Left	530.07	-21.6	-79.8	33.1	0.0003	878
		Right	964.87	16.7	-60.5	63.3	0.0003	2389
		Right	223.76	22	-81.4	41.4	0.00629	350
	Superior frontal	Left	629.1	-19.1	-1.2	55.7	0.0003	1262
	-	Right	471.83	22.1	-2.1	60.9	0.0003	1040
	Posterior cingulate	Right	184.83	14.8	-16.8	39.8	0.02528	541
Faces: With drawal > Approach	Superior parietal	Right	635.11	9.6	-88	22.7	0.0003	881

corrected alpha of 0.0125 was used to correct for the number of attachment styles examined (0.05/4). This alpha was not corrected for the number of ROIs examined (six), since all of these ROIs are members of a co-activated single network of regions (the PPS network) known to be functionally linked (i.e., non-independent) (Cléry, 2015; Culham, 2008; Holt, 2014).

Control ROIs: In secondary analyses, we also measured responses of three regions which are not part of the PPS network: the amygdala, anterior insula and primary visual cortex (V1). The amygdala and anterior insula were chosen because of their known role in top-down attentional processing and salience detection (Menon and Uddin, 2010; Santos, 2011) and prior findings of links between adult attachment styles and responses of these regions (Riem, 2012; DeWall, 2012). The visual cortex was also examined because bottom-up (implicit) attentional effects could manifest as greater V1 activation to the more salient stimuli.

The amygdala and insula were anatomically-defined in each subject using the FreeSurfer v.6 automated segmentation procedure (http://surfer.nmr.mgh.harvard.edu). The primary visual cortex (V1) ROI was constructed based on the boundaries of V1 defined by the Harvard-Oxford atlas within FSL (https://fsl.fmrib.ox.ac.uk/fsl).

Resting state functional connectivity analysis: The ROIs defined using the Approach vs. Withdrawal contrast map of the Reference Sample were also used as seeds in a functional connectivity analysis. In this analysis, six rigid motion parameters, time point exclusion files, white matter intensity, ventricular cerebral spinal fluid intensity, and global signal waveform were included as nuisance regressors. Seed-to-seed correlations of these values were calculated by generating Pearson's r values. These r values were transformed to z scores using the r-to-z Fisher transformation formula (Fisher, 1915, 1921), and further statistical analyses were performed using these z scores.

3. Results

3.1. PPS network responses in the Reference and Test Samples

In the Reference Sample (n = 80), clusters within the bilateral superior parietal, medial parietal and superior frontal cortices showed significantly greater activation in response to the Face Approach versus Withdrawal contrast (corrected p values < 0.001). Thus, a total of 6 ROIs were defined in this sample: the right and left superior frontal cortex

(SFC), which included portions of the right and left superior frontal gyrus, precentral gyrus and caudal middle frontal gyrus; and the right and left medial parietal cortex (MPC), which included portions of the right and left paracentral gyrus, precuneus and posterior cingulate cortical regions; and right and left superior parietal cortex (SPC), which included the dorsal intraparietal sulcus. We conducted the same analyses in the Test Sample (n = 50); comparison of the maps revealed patterns of activation that were consistent in location across the Test and the Reference Samples (see Table 2 and Fig. 2). Responses in the control, non-social condition (to the Car Approach versus Withdrawal contrast, including significant activation in the bilateral SFC, bilateral MPC and bilateral SPC regions) were also similar in the two samples (see Supplementary Table 2 and Supplementary Fig. 1).

We also examined the average time courses of the BOLD signal during the Approach and Withdrawal conditions in the two samples (see Fig. 2 and Supplementary Fig. 1). The time course plots (corrected for hemodynamic response and stimulus delay) show the BOLD signal changes over time in the PPS network (responses of all 6 ROIs combined) during the Approach and Withdrawal conditions. In these plots, the location of a typical personal space boundary was also estimated, using a standard behavioral measurement of personal space (Kaitz, M., Bar-Haim, Y, 2004) collected in an independent sample of 49 healthy subjects. Comparisons of the average PPS network responses inside vs. outside the personal space boundary showed that there was significantly higher activation inside compared to outside the personal space boundary in both conditions, in both samples (Reference Sample: Approach, p = 0.003, Withdrawal, p = 0.009; Test Sample: Approach, p = 0.002, Withdrawal, p = 0.044), see Fig. 2). Thus, these analyses show that the PPS network responds to a greater extent to stimuli perceived as close to (versus farther away from) the body, regardless of the direction of apparent movement of those stimuli.

3.2. Behavioral performance of subjects in the scanner

To investigate whether these patterns of activation could result from differential allocation of attention to the approaching vs. withdrawing stimuli (a potential confound), we examined the behavioral responses (the rates of dot detection) during data collection using a 2 (condition: Approach, Withdrawal) \times 2 (stimulus type: faces, cars) ANOVA. We found no significant main effects of stimulus type (F(1,49) = 0.0001, p = 0.99) or condition (F(1,49) = 0.085, p = 0.77) or interaction between

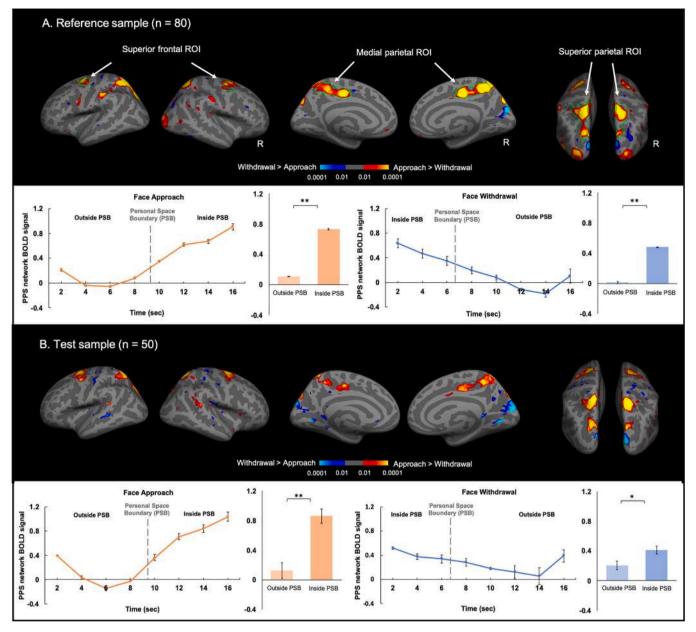


Fig. 2. Cortical surface maps and time courses of PPS network responses to face stimuli. Cortical surface maps for the Face Approach vs. Withdrawal contrast (upper panel) and time courses for the Face Approach and Withdrawal conditions (lower panel) in the Reference (A) and Test (B) Samples are displayed. In the maps, vertices labeled red/yellow are those showing significantly (p < 0.01) greater activation in response to the Approach compared to the Withdrawal condition. Vertices labeled blue are those showing significantly (p < 0.01) greater activation in response to the Withdrawal compared to the Approach condition. The time course plots (corrected for HRF and stimulus delay) show the BOLD signal changes of the PPS network (bilateral SFC + SPC + MPC) over time during the Face Approach condition (orange plots) and Face Withdrawal condition (blue plots) in the Reference and Test Samples, in relation to an average personal space boundary. The personal space boundary was derived from an independent sample of 49 healthy subjects. The bar plots reveal that there is significantly higher PPS network activation inside the personal space boundary compared to outside the personal space boundary, in both the Approach and Withdrawal conditions, in both samples (Reference Sample: Approach, p = 0.003, Withdrawal, p = 0.009; Test Sample: Approach, p = 0.002, Withdrawal, p = 0.044). SFC, Superior Frontal Cortex; MPC, Medial Parietal Cortex; SPC, Superior Parietal Cortex; p < 0.05, ** p < 0.01. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

stimulus type and condition (F(1,49) = 0.61, p = 0.43), suggesting that there were no differences in the allocation of attention across the conditions.

3.3. Hypothesis testing in the Test Sample: PPS network responses vs. RQ scores

Using the six ROIs of the PPS network defined in the Reference Sample (right and left SPC, right and left SFC, and right and left MPC),

we extracted the BOLD responses for each of these ROIs in the Test Sample and measured correlations between PPS network responses to the Face Approach vs. Withdrawal contrast and RQ scores. Significant positive correlations were found between responses of all six ROIs and levels of the anxious-preoccupied attachment style (left SPC: r=0.42, p=0.002; right SPC: r=0.47, p=0.0001; left SFC: r=0.36, p=0.01; right SFC: r=0.34, p=0.012; left MPC: r=0.33, p=0.017; right MPC: r=0.49; p=0.0001; see Fig. 3). However, no significant correlations were found between responses of any of the PPS ROIs and levels of the

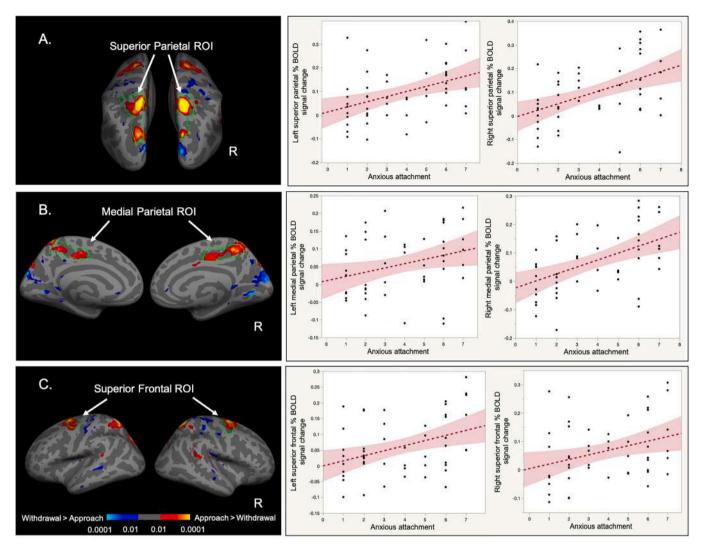


Fig. 3. Correlations between anxious attachment and responses of the PPS network in the Test Sample. The cortical surface maps on the left show the average activation (p < 0.001, whole brain corrected) produced by the Face Approach vs. Withdrawal contrast in the 50 Test Sample subjects. The three regions-of-interest (ROI) used in the analyses are outlined in green: superior parietal (A), medial parietal (B) and superior frontal (C) cortices. In the maps, vertices labeled red/yellow are those showing significantly (p < 0.001) greater activation in response to the Approach compare to the Withdrawal condition. Vertices labeled blue are those showing (p < 0.001) greater activation in response to the Withdrawal compared to the Approach condition. The middle and right panels in each row show scatter plots displaying the correlations between the responses of the corresponding ROI (of the left and right hemispheres, respectively) with anxious attachment levels. Responses of left and right superior parietal cortices (left: r = 0.42, p = 0.002; right: r = 0.47, p = 0.0001); left and right medial parietal cortices (left: r = 0.33, p = 0.017; right: r = 0.49, p = 0.0001) and left and right superior frontal cortices (left: r = 0.36, p = 0.010; right: r = 0.34, p = 0.012) were positively correlated with anxious attachment style. The red shaded areas indicate the 95% confidence interval of the fitted line. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

other three attachment styles (all p>0.2; see Supplementary Table 3). Also, there were no correlations between responses of the 6 ROIs to the Face Approach vs. Withdrawal contrast and any of the measures of depression, anxiety or psychosis (all p>0.1). Lastly, no correlations were found between responses of these 6 ROIs to the Cars Approach vs. Withdrawal contrast and levels of any attachment style (all p>0.2; see Supplementary Table 4).

3.4. Tests of specificity of the main findings

Single PPS network ROI. Since the 6 ROIs are members of a well-established PPS network and are consistently co-activated (Bremmer, 2001; Cléry, 2015; di Pellegrino, G., & Làdavas, E., 2015; Holt, 2014), we conducted an additional confirmatory analysis using a single combined ROI representing the PPS network, measuring the above correlations using this ROI. As expected, there was a significant correlation between activation of this ROI and anxious attachment style (r = 0.43, p =

= 0.002) but no significant correlations with the other 3 adult attachment styles (all p > 0.44).

Specificity of the findings to anxious attachment. To measure the contribution of anxious attachment style to responsivity of the PPS network to face stimuli when other variables (the other 3 attachment measures, the 4 symptom measures and gender) were accounted for, a multiple regression was performed, using the single PPS ROI. Together, these variables significantly predicted activation of the PPS network to the Face Approach vs. Withdrawal contrast (F (9, 38) = 2.6, p = 0.040, $\rm R^2=0.33$). However, of the variables included in the model, only anxious attachment style had a significant effect (p = 0.001).

Specificity of the findings to social (versus non-social) stimuli. To further examine the specificity of the observed effects of PPS network responses to face (compared to car) stimuli, we conducted a multivariate repeated measure ANOVA analysis to test for interactions of stimulus type (faces vs. cars), condition (approach vs. withdrawal) and attachment style (secure, anxious preoccupied, fearful, avoidant). In this analysis,

condition and stimulus type were fixed factors and attachment style was included as a covariate. A significant three-way interaction among stimulus type, condition and anxious attachment style (F (1,45) = 4.49, p = 0.040), but no significant three-way interactions with any of the other three attachment styles (p = 0.08, 0.27 and 0.87 for avoidant, fearful and secure attachment styles, respectively), was found. Followup, simple main effects analyses showed that the PPS network response to faces was significantly higher than the PPS network response to cars during the Approach condition (p = 0.047), but there were no significant differences between responses to the two types of stimuli in the Withdrawal condition (p = 0.31). Importantly, there was a significantly higher correlation between anxious attachment style and responses of the PPS network to the Face Approach > Face Withdrawal, than to the Cars Approach > Cars Withdrawal, contrast (z = 2.15, p = 0.016). Thus, these findings provide evidence for a specific relationship between anxious attachment and PPS network responses to social (faces), compared to non-social (cars), stimuli.

3.5. Resting-state functional connectivity analysis

Using the ROIs defined in the Reference Sample, seed-to-seed connectivity values were extracted from the six ROIs and correlated with RQ scores. No significant correlations were found (all p>0.1; see Supplementary Table 5).

4. Additional, secondary analyses

Other networks. To explore whether our findings may have resulted from secondary effects of over-activity of limbic areas, or from a general increase in attention to the stimuli, BOLD responses to the Faces Approach versus Withdrawal contrast of the Test Sample were extracted from two selected limbic areas (the amygdala and anterior insula) and the primary visual cortex (V1). We tested for correlations between the responses of these ROIs and 1) levels of anxious attachment and 2) performance on the Dot Detection Task. There were no significant correlations (all p > 0.1; see Supplementary Table 6).

A categorical analysis. To reproduce our main findings using an alternative analytic approach, we compared the responses of the PPS network of two subgroups of participants who represented the two ends of the continuum of anxious attachment in the Test Sample: those with low (scores = 1–2, n = 20) and those with high (scores = 6–7, n = 16) levels of anxious attachment. As expected, higher responses in the "high" compared to the "low" group were found in all ROIs (left frontal cortex (p = 0.017), right frontal cortex (p = 0.051), left medial parietal cortex (p = 0.037), right medial parietal cortex (p = 0.001), left superior parietal cortex (p = 0.004) and right superior parietal cortex (p = 0.001)). Also, consistent with the findings of the primary analysis, there were no differences between the two groups in functional connectivity among these ROIs (all p > 0.3; see Supplementary Fig. 3).

Gender and symptom effects. Lastly, in light of gender differences previously found in PPS-related behaviors (Hayduk, 1983; Iachini, 2016; Masson, 2020), we also tested for gender differences in PPS network responses and found no significant effects. Also, there were no significant correlations between levels of anxious-preoccupied attachment style and symptoms of depression, anxiety, or psychotic experiences or performance on the Dot Detection Task (see Supplementary Table 7).

5. Discussion

5.1. Summary of findings

In this study, we found that the bilateral superior parietal, superior frontal and medial parietal cortex showed significant responses to face stimuli that appeared to approach the body, intruding into personal space, replicating previous findings in other samples (Holt, 2015, 2014).

The network engaged by these stimuli corresponds to the peripersonal space (PPS) monitoring network, as previously identified in humans (Bremmer, 2001; Brozzoli, 2011; Holt, 2014) and non-human primates (Graziano and Cooke, 2006). In the current study, we found that a self-reported "anxious preoccupied" attachment style was associated with the magnitude of responses of this PPS network to social (faces), but not to non-social (cars), stimuli. The other three attachment styles studied, and symptoms of psychopathology, did not show a relationship with responsivity of this network. Moreover, functional connectivity of this network was not linked to variation in attachment.

5.2. Relationship of these findings to prior work

Our findings can be considered generally consistent with prior observations of over-responsivity of a range of brain regions to socially salient information (including potential social threats or ambiguous social cues in the environment) in individuals with higher levels of anxious attachment (Vrtička, 2008; Lemche, 2006; DeWall, 2012; Redlich, 2015; Norman, 2015). The current findings extend this work by showing that such over-responsivity to potential social threat may originate at a relatively early stage of information processing, i.e., at a mid-level stage (unimodal and multi-modal association cortex). However, our data cannot definitively resolve whether the observed effect is due to a greater sensitivity of the PPS network to social threat (or to intrusions into personal space) in those with greater attachment anxiety, or to a general consequence of heightened arousal and attentional vigilance to social information in these individuals.

In support of the first possibility, our measure of attention to the stimuli (performance on a low-level attentional task) did not correlate with response magnitudes of the PPS network or with levels of anxious attachment. In addition, we did not find any correlations between activation of primary visual cortex to approaching vs. withdrawing faces and anxious attachment style. If we had, this relationship might have suggested the presence of an overall effect of greater allocation of attention to the approaching face stimuli, with a non-specific increase in activation of visual cortex (Noudoost, 2010; Theeuwes et al., 2000; Bressler, 2008). In addition, responses of limbic areas such as the amygdala and insula were not correlated with levels of anxious attachment, which is inconsistent with some prior findings (Long, 2020). However, the experimental paradigm used in the current study does not consistently recruit these two regions so may not provide a reliable measure of attachment-related effects on their function. Future studies can use several, complimentary tasks to comprehensively assess the role of a range of brain networks in adult attachment patterns.

5.3. Relevance to neuropsychiatric disorders

Several neuropsychiatric conditions, including autism or autism spectrum disorders (ASD) (Rutgers, 2004; Shapiro, 1987), are associated with abnormalities in social behavior. Abnormalities in basic sensorimotor processing have also been well-documented in ASD, and links between these sensorimotor abnormalities and the changes in social behavior and attachment associated with ASD have been proposed (Rutgers, 2004; Shapiro, 1987). Several studies have found abnormalities in personal space-related behaviors (Gessaroli, 2013; Kennedy and Adolphs, 2014; Asada, 2016) and in the function of the parietal cortex (Martineau, 2010; Haas, 1996) in ASD. However, these findings have not been linked with one another, or to disruptions in attachment in these patients. Future studies could investigate whether the PPS network is altered in ASD and if so, whether such a change is linked to behavioral abnormalities in ASD.

Individuals diagnosed with schizophrenia also exhibit higher rates of insecure attachment (Harder, 2014; Berry et al., 2007; Couture et al., 2007). Some of these findings have been linked to impairments in day-to-day functioning and decreased quality of life in schizophrenia (Couture et al., 2007). Although schizophrenia has been characterized

classically by mild-to-moderate deficits in higher cognitive functions (Brenner, 1992; Bryson et al., 2001; Zihl et al., 1998; Lesh, 2011), a growing number of studies have identified abnormalities in basic sensorimotor processes (Wynn, 2005; Robson, 2016; Javitt, 2009), some of which have been linked to impairments in social functioning and other symptoms (Bortolon et al., 2015; Norton D, McBain, R, 2009; Turetsky, 2007; Whittaker et al., 2001), including abnormalities in personal space (Holt, 2015; Schoretsanitis, 2016; Delevoye-Turrell et al., 2011). Previously, we observed a significant increase in activation of the dorsal parietal cortex in response to approaching versus withdrawing face stimuli in a sample of individuals with schizophrenia, when compared to a group of demographically-matched healthy control subjects (Holt, 2015). Also, in that study, the average size of personal space was significantly greater in the schizophrenia sample compared to the controls, and this enlargement in personal space was positively correlated with the responses of the dorsal parietal cortex in the schizophrenia group. Given that schizophrenia has been associated with elevated rates of insecure attachment styles (Berry et al., 2007, 2008; Ponizovsky et al., 2007), we speculate that altered function of the PPS network and changes in personal space regulation in schizophrenia could be linked to greater levels of anxious attachment. Based on this model, in future work, therapeutic interventions for schizophrenia and related conditions could be tested which target basic sensorimotor processes that influence social behavior. Such interventions could have upstream benefits on social functioning.

6. Limitations

There are several limitations of this study. First, to optimize feasibility and our sample size, the measure of adult attachment employed in this study was a brief self-report measure, the validated Relationship Questionnaire (Bäackström and Holmes, 2001). In future work, interview-based instruments, such as the adult attachment interview (Ravitz P, Maunder R, 2010), could also be administered to assess adult attachment style, to determine whether anxious attachment measured using a narrative method also shows a relationship to the function of the PPS network.

Second, we did not assess participants for diagnoses of psychiatric illnesses; thus, it is possible that some of the observed effects attributed to anxious attachment were related to the presence of such illnesses. However, none of the participants were taking psychotropic medication at the time of the study, and all were enrolled in college, suggesting that this was primarily a non-clinical sample.

Third, we did not collect behavioral measures related to PPS network function, such as personal space size, also for reasons of feasibility. In future studies, it would be helpful to include personal space measurements and other measures of parietofrontal circuit functioning, e.g. 3D eye position (Hadjidimitrakis, 2012), to determine whether variations in levels of attachment and PPS network activity have quantifiable behavioral manifestations. Such additional findings could provide confirmatory evidence for the specificity of this association.

Fourth, in this study, only faces with emotionally neutral expressions were presented to the participants. Prior fMRI studies have suggested that face stimuli with neutral expressions elicit a greater range (in magnitude) of neural responses (Cuthbert, 2000; Hajcak et al., 2010; Schupp, 2004); thus such neutral stimuli may be particularly useful for capturing individual differences in brain function linked to behavioral characteristics. However, future work could also test whether or not modulation of the PPS network by negatively valenced (compared to positively valenced and neutral) social stimuli has a stronger association with anxious attachment.

7. Future directions

In future work, animal models could be used to determine whether individual patterns of responses of the PPS network are influenced by the development of social bonds in early post-natal life. In addition, longitudinal fMRI studies conducted in children who vary in attachment dimensions could identify progressive changes in neural systems such as the PPS network, that could be linked to emerging variation in adult attachment behaviors.

8. Summary

In this study, consistent correlations between levels of anxious attachment and responses of a network of brain regions involved in monitoring the space near the body were found. Such an association may have implications for the role of lower/mid-level sensorimotor processes in complex forms of social cognition and behavior, such as those related to attachment.

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10. Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

CRediT authorship contribution statement

Zahra Nasiriavanaki: Data curation, Formal analysis, Writing original draft. Tracy Barbour: Visualization, Formal analysis. Amy H. Farabaugh: Conceptualization, Investigation, Methodology, Supervision. Maurizio Fava: Conceptualization, Methodology, Resources. Avram J. Holmes: Investigation, Methodology. Roger B.H. Tootell: Methodology, Writing - review & editing. Daphne J. Holt: Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nicl.2021.102585.

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Z. Nasiriavanaki et al. NeuroImage: Clinical 30 (2021) 102585

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