Activating the attachment system modulates neural responses to threat in refugees with PTSD

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Abstract

Social attachment systems are disrupted for refugees through trauma and forced displacement. This study tested how the attachment system mitigates neural responses to threat in refugees with posttraumatic stress disorder (PTSD). Refugees with PTSD (N = 28) and refugee trauma-exposed controls (N = 22) viewed threat-related stimuli primed by attachment cues during a functional magnetic resonance imaging scan. Group differences and the moderating effects of avoidant or anxious attachment style and grief related to separation from family on brain activity and connectivity patterns were examined. Separation grief was associated with increased amygdala but decreased ventromedial prefrontal cortical (VMPFC) activity to the attachment prime and decreased VMPFC and hippocampal activity to attachment primed threat in the PTSD (vs trauma-exposed control) group. Avoidant attachment style was connected with increased dorsal frontoparietal attention regional activity to attachment prime cues in the PTSD group. Anxious attachment style was associated with reduced left amygdala connectivity with left medial prefrontal regions to attachment primed threat in the PTSD group. Separation grief appears to reduce attachment buffering of threat reactivity in refugees with PTSD, while avoidant and anxious attachment style modulated attentional and prefrontal regulatory mechanisms in PTSD, respectively. Considering social attachments in refugees could be important to post-trauma recovery, based within changes in key emotion regulation brain systems.

Key words: PTSD; refugee; attachment; threat; fMRI

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Attachment theory proposes that when threatened, humans seek support from their secure attachment figures to co-regulate distress and facilitate coping (Bowlby, 1978; Mikulincer et al., 2003). The human attachment system develops during childhood through a secure relationship with a caregiver (e.g. parent), providing the basis for forming healthy relationships with others across a lifetime (Bowlby, 1978; Forges and Carter, 2011). As adults, effectively drawing on social attachments (e.g. parents, siblings, spouse, close friends, either explicitly via direct physical or emotional support, or implicitly via internal representations) has been shown to reduce subjective feelings of pain (Eisenberger et al., 2011), buffer stress hormone release (Bryant and Chan, 2015), enhance cardiovascular stability (Liddell and Courtney, 2018), interrupt fear acquisition processes (Toumbelakis et al., 2018), decrease functional activity in threat detection and alarm neural systems (amygdala, superior colliculus, hypothalamus) (Coan et al., 2006; Karremans et al., 2011; Norman et al., 2015) and enhance emotion regulation neural activity (medial prefrontal cortex; MPFC) (Eisenberger et al., 2011; Eisenberger, 2012; Canterbury and Gillath, 2013). These findings reflect the benefit of a secure attachment system to enhance threat coping via heightening emotion regulation processes.

Insecure attachment systems, however, can develop as a result of separation from key attachment figures in childhood (i.e. primary caregivers) or adulthood (i.e. close family) (Pinquart et al., 2013; Mikulincer and Shaver, 2016) and are associated with maladaptive responses to threat (Nash et al., 2014; Mikulincer and Shaver, 2016). Avoidant attachment style is characterized by hypoactive tendencies designed to dampen connections with others, whereas anxious attachment style evokes hyperactive behaviours focused on holding others unrealistically close (Shaver and Mikulincer, 2010). As such, insecurely attached individuals do not show the same benefit from activating attachments during threat. Instead, individuals with an avoidant attachment style tend to deactivate or deflect emotional experiences, even threatening ones, whereas those anxiously attached individuals may intensify their negative emotions (Mikulincer and Shaver, 2016). Attachment insecurity also appears to be reflected in altered neural patterns during threat-related information processing—which typically engages sub-cortical regions including the amygdala, insula and hippocampus (Mobbs et al., 2009) and activity in emotion regulation circuits—most specifically the ventromedial prefrontal cortex (VMPFC) and anterior cingulate cortex (ACC) (Ochsner et al., 2012). Attachment avoidance has been associated with less deactivation in prefrontal regions (i.e. ventral ACC and lateral prefrontal cortex) during emotional suppression (Gillath et al., 2005) and increased activity in similar prefrontal regions when judging or reappraising negative social scenes (Vrticka et al., 2012). Such findings provide neural evidence that avoidantly attached individuals may recruit top-down cognitive processes to facilitate evasion of social cues, resulting in inefficient emotion regulation processes (Vrticka et al., 2012). Anxious attachment style by contrast has been associated with greater amygdala engagement to un-primed threatening faces (Vrticka et al., 2008; Norman et al., 2015), increased amygdala activity while making judgments about social threat scenes (Vrticka et al., 2012) and greater anterior temporal pole but reduced orbitofrontal cortical activity during emotional suppression (Gillath et al., 2005). These findings point to the notion that anxious attachment may be underpinned by poorly regulated activity in threat-related neural circuits. Other studies that activated the attachment system via priming found increased amygdala activity was correlated with general attachment insecurity (Lemche et al., 2006) and that insecure attachment priming was associated with weaker recruitment of emotion regulation brain regions (Canterbury and Gillath, 2013).

Attachment systems are therefore likely to play a critical role in influencing how humans respond to threatening or traumatic events (Mikulincer et al., 2015; Bryant, 2016; Barazzone et al., 2019). For example, secure attachment systems serve as a protective factor against posttraumatic stress disorder (PTSD) following trauma exposure (Barazzone et al., 2019) and enhance post-trauma adjustment (Soloman et al., 1998). The benefits of a secure attachment system in PTSD have also been demonstrated behaviourally. For example, activating the attachment system via subliminal priming reduced interference from trauma-related words on reaction times—a phenomenon typically observed in PTSD (Mikulincer et al., 2006). This suggests that secure attachments can serve to mitigate hypervigilance to threat in PTSD in accordance with attachment theory (Mikulincer and Shaver, 2016). Conversely, both anxious and avoidant attachment styles have been linked to more severe PTSD symptoms (Soloman et al., 1998; Escolas et al., 2012) and PTSD symptom maintenance over time (Franz et al., 2014; Barazzone et al., 2019). Moreover, the advantages provided by a secure attachment system may be altered following profound life events in adulthood, including the experience of interpersonal traumas such as being a prisoner of war (Dieperink et al., 2001; Mikulincer et al., 2014), torture (De Haene et al., 2010) or forcible separation (Mikulincer and Shaver, 2016). Perhaps not surprisingly, such stressful experiences can ‘erode’ secure attachment systems over time (Mikulincer et al., 2011), leading to insecure attachment and compromising the benefit of secure attachments to post-trauma recovery. Moreover, the same threat and regulation brain systems that are altered by insecure attachments also crucially underpin PTSD (Shalev et al., 2017; Ressler, 2020)—but no single study has examined the brain mechanisms of disrupted attachments in PTSD.

Liddell and Bryant (2018) have proposed that alterations to the attachment system following significant life events may represent a specific mechanism underpinning the biological effects of refugee trauma. Those who have experience forcible displacement due to persecution or conflict (UNHCR, 2016) numbered 79.5 million individuals in 2019 (UNHCR, 2020). Refugees have commonly experienced the interpersonal traumatic events such as political imprisonment and torture (Steel et al., 2009) and forced separation from loved ones (Miller et al., 2018) that have been found to be associated with the erosion of secure attachment systems (Barazzone et al., 2019). Exposure to interpersonal trauma has been associated with greater avoidant attachment insecurity in refugees (Morina et al., 2016). Refugees also commonly undergo post-migration stressors that further disrupt secure attachment systems and social networks. These may include prolonged separation from family and disintegration of social networks (Li et al., 2016; Miller et al., 2018). Unresolved grief is a common result of on-going separation or missing family (Miller et al., 2018) and prolonged grief related to bereavement in a resettled refugee cohort has been shown to be associated with both separation from family, and a history of imprisonment and torture (Bryant et al., 2019). On-going separation from social attachments could result in compromising a secure attachment system, diminishing its capacity to play its role in supporting adaptive emotional responses during threatening situations (Servaas and Hazan, 2008). Therefore, we hypothesize that feelings of grief related to separation from family members will have specific effects on how refugees with PTSD draw on attachments to assist coping with threat.
To test how attachment systems may be affected in refugees with PTSD (compared to a trauma-exposed refugee control group; TEC), we conducted a functional magnetic resonance imaging (fMRI) study that examined neural responses to threat-related cues when primed by external attachment stimuli. Priming with attachment cues is a well-evidenced paradigm for activating the attachment system (Mikulincer et al., 2002, 2006). Specifically, we were interested in how activating attachments while processing threat cues modulated threat detection and emotion regulation networks (comprising the amygdala, hippocampus, insula, ACC and VMPC). Given the novelty of this study, we considered PTSD vs TEC group differences in broader attentional and visual networks via a whole brain analysis. We were also interested in mapping the specific effects of separation grief and attachment insecurity. We predicted that separation grief would diminish the regulatory power of attachment primes over threat reactivity in refugees with PTSD, reflected in increased activity in the amygdala and insula, and deactivation in ACC and VMPC regions, relative to the TEC group. We hypothesized an increased buffering effect of the attachment prime over threat reactivity with avoidant attachment style (i.e. reflecting patterns of emotional deflection and hypervigilance) but that anxious attachment style would be associated with decreased emotion regulation neural activity (i.e. consistent with hyperactivating emotions).

Methods and materials

Participants

A total of 51 adult refugees participated in the study. Participants were partly recruited from the NSW Service for the Treatment and Rehabilitation of Torture and Trauma Survivors (STARTTS) and partly from community advertisements placed at refugee services in Sydney Australia. Inclusion criteria included >18 years old, no visual, auditory or physical impairment, no diagnostic history of a neurological condition, moderate-severe traumatic brain injury, bipolar disorder, psychosis, alcohol or substance use disorder or current suicidal intent and able to meet MRI safety criteria. Informed consent was provided as approved by the Northern Sydney Local Health District Human Research Ethics Committee. Participants were reimbursed for taking part in the study. One participant did not complete the interview component, and thus the final sample comprised 50 participants.

Procedure

The study took part over two sessions: Session 1 comprised an interview with a clinical psychologist, and Session 2 constituted an fMRI scan. Professional interpreters were engaged in both sessions if required. During the clinical interview, participants responded to demographic, trauma history, mental health and attachment-related questions. Trauma history was measured by the Harvard Trauma Questionnaire (HTQ) (Mollica et al., 1992), indexing lifetime exposure to 16 different types of traumatic events common to refugees. PTSD was measured by the PTSD Symptom Scale—Interview (PSS-I) (Foa and Tolin, 2000) updated for Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) to determine PTSD diagnosis. PTSD symptom severity was indexed by computing a total score of symptoms (Cronbach $\alpha = 0.94$). Depression symptoms were measured with the Hopkins’s Symptom Checklist (HSCL; Derogatis et al., 1974), which includes 15 items indexing depression symptoms over the past week ($\alpha = 0.89$). Attachment style was measured by a 12-item short-form version of the Experiences in Close Relationships Questionnaire (Wei et al., 2007), which indexes anxious attachment and avoidant attachment on items comprising a 7-point scale ($1 = $strongly disagree, $7 = $strongly agree); good internal consistency was observed for both sub-scales (avoidant: $\alpha = 0.83$, anxious: $\alpha = 0.81$).

Separation grief was measured using three items extracted from the gold standard measure of prolonged-grief disorder (PG-13) (Prigerson et al., 2009), which we adapted to reflect physical separation. The three items indexed separation distress in the form of (i) yearning for the separated person, (ii) emotional pain and (iii) shock regarding the separation as experienced in the last month on a 5-point scale ($0 =$not at all, $4 =$several times a day). Our measure initially screened for separation from close others and asked participants to identify the separated person they were most concerned about. If participants were screened out on the separation measure, they were given a score of 0. Separation grief items were summed to create a separation grief index, with strong internal consistency ($\alpha = 0.86$).

Attachment priming fMRI task. fMRI scanning took place at the Advanced Research Clinical High-Field Imaging Facility at Royal North Shore Hospital in Sydney Australia, on a 3 T Siemens Magnetom Trio scanner using echo-planar pulse sequences.

The task comprised a 2 (prime) × 2 (target) within-subjects design, which was based on validated affective priming methods (Murphy and Zajonc, 1993) and a previous attachment priming fMRI study (Canterberry and Gillath, 2013). Participants viewed a series of threat-related and neutral target stimuli, each preceded by an attachment or non-attachment prime cue. The attachment prime cues were 12 archetypal images of culturally diverse depictions (i.e. Caucasian, East Asian, South Asian, Middle Eastern, Iranian and African) of a mother and child or father and child dyad, drawn from online photograph databases (e.g. iStock). Each attachment prime cue was matched on culture, gender and positive valence to a non-attachment cue, displaying single individuals. Target threat ($N = 48$) and neutral ($N = 48$) cues were drawn from the International Affective Picture System (IAPS) (Lang et al., 2008) and the Geneva Affective Picture Database (Dan-Glauser and Scherer, 2011). There were four within-subject conditions: (i) attachment prime/threat target (AttThreat); (ii) attachment prime/neutral target (AttNeut); (iii) non-attachment prime/threat target (NAttThreat) and (iv) non-attachment prime/neutral target (NAttNeut).

During scanning, participants viewed a total of 96 trials (24 trials for each trial type) consisting of a brief 70 ms presentation of the prime cue, immediately followed by a target cue presented for 4 s. Figure 1 presents an example trial. Participants then completed a target cue rating on a negative valence dimension with a 5-point Likert scale using a button press device (3 s). Trials were separated by a fixation cross-presented for an average of 2930 ms across trials, jittered by ±500 ms on each trial, with the trial length being 10 s on average. Stimuli were delivered to participants inside the scanner via a screen viewed through a mirror connected to the head coil using Presentation software (version 16, Neurobehavioral Systems, Inc.), which also recorded the button press responses. Functional brain volumes of 29 ascending slices (5 mm thickness) across the entire brain were acquired ($TR = 2000$ ms; $TE = 40$ ms; matrix $= 64 \times 64$). Participants completed two stimulus runs of 8 min, each consisting...
Fig. 1. Example trial in attachment priming paradigm implemented in this study.

of five dummy volumes that were subsequently discarded and 240 task-related volumes.

Participants also rated the attachment and non-attachment prime cues post-scan according to the degree the cue depicted ‘closeness with others’ on a 5-point Likert scale, as per other attachment studies (Toumbelekis et al., 2018).

Data analysis
fMRI data. Data was analysed in SPM12 using Matlab 2016b. Raw data were re-oriented to the anterior commissure-posterior commissure (AC-PC) line. We first used ArtRepair toolbox (version 5b) to deal with excess head movements in two stages, conducted initially via an interpolation method to correct bad slices based on large voxel spike noise (Mazaika et al., 2007, 2009). On average, 0.7 slices were corrected in Run 1 (0.01%; s.d. = 3.0) and 7.3 slices were corrected in Run 2 (0.1%; s.d. = 31.3). Preprocessing steps were then undertaken in SPM12, including slice timing correction, normalization to standard stereotactic space using the Montreal Neurological Institute (MNI) template via linear registration, and smoothing [8 mm full width at half maximum Gaussian filter as recommended (Mikl et al., 2008)]. Additional data cleaning at the volume level was conducted, again via ArtRepair, detecting and correcting bad volumes using the interpolation method. This method corrected a mean of 26.7 volumes in Run 1 (11.1%; s.d. = 42.1) and 33.1 volumes in Run 2 (13.8%; s.d. = 46.3).

Boxcar regressors modelled the four conditions over the target presentation epoch (4 s) within each trial. Six regressors representing translation and rotation movements were included in the model as nuisance covariates (subject motion summaries are provided in Supplemental Information). At the first level, individual contrasts were generated to examine (i) main effect of prime (Att > NAtt); (ii) main effect of target (Threat > Neut) and (iii) interaction effects of prime on target ([AttThreat > NAttThreat] > [AttNeut > NAttNeut]). These contrast images were brought to the second level to examine PTSD group by attachment style/separation grief moderation effects. Baseline task-related activity collapsed across groups is presented in Supplemental Information.

At the group level, we first considered the main effects of prime and target stimulus as a function of PTSD group in an independent-samples t-test and then the interaction effect to determine the specific effects of attachment primed threat. Avoidant attachment style, anxious attachment style and separation grief indices were mean centred and modelled in interaction with PTSD group to examine group by covariate (i.e. moderator) interaction effects.

We implemented a region of interest (ROI) approach to isolate processing within the threat regulation network (Williams, 2016), including the VMPFC due to its observed regulatory role in the context of attachment (Eisenberger et al., 2011). ROIs were constructed using automatic anatomical labelling masks (Tzourio-Mazoyer et al., 2002), including bilateral amygdala, hippocampus, insula, ACC and VMPFC. Given that the neural substrates of attachment priming in PTSD are currently unknown and to balance risk for Type 1 and Type II errors in our relatively modest sample size (Carter et al., 2016), we implemented a cluster-wise corrected threshold to determine significant activations via the 3DClusstim module in AFNI (Forman et al., 1995; Fournier et al., 2017). We used a cluster-wise corrected significance threshold for both ROI and whole brain analyses ($P < 0.05$ FWE-corrected), with a cluster-forming threshold set at $P < 0.002$ as recommended (Cox et al., 2017). Cluster-forming thresholds...
were set using the 3DClustSim module using ACF estimates calculated via 3dTFWHMx in AFNI and were amygdala (4 voxels), hippocampus (20 voxels), insula (35 voxels), ACC (28 voxels) and VMPCF (46 voxels) and for the whole brain (220 voxels).

Connectivity analysis. Since we were primarily interested in understanding the effects of the attachment prime on threat-related processing, we focused on functional connectivity of the amygdala. Using the generalized psychophysiological interaction (gPPI) toolbox (McLaren et al., 2012), we examined task-related connectivity within a spherical 5 mm radius seed in the left amygdala, centred on MNI coordinates [26 −6 −12] based on significant activations from the between-group analyses (see Results below). The interaction regressor between the amygdala seed and task-related activation during attachment primed threat was taken to the group level, where group comparisons were conducted with avoidant, anxious attachment style and separation grief included in the model as covariates. We applied the same ROI analysis with the same thresholds as described above.

Results

Demographics and clinical characteristics of participants

Table 1 presents demographic information. The 50 participants included 30 male and 20 female participants, with a mean age of 40.6 years (s.d. = 12.02). For the PTSD group (N = 28), we combined participants who met the full DSM-5 PTSD diagnostic criteria (N = 17) and participants who met criteria for subsyndromal (or partial) PTSD (N = 11), defined as meeting full criteria for symptom Cluster B (re-experiencing symptoms) and two of the remaining three DSM-5 PTSD symptom clusters (i.e. avoidance, alternations in mood/cognition and hyperarousal symptoms). Henceforth, the PTSD group refers to the combined full PTSD and subsyndromal PTSD participants (N = 28). The control group comprised 22 participants with a refugee background who had been exposed to trauma but did not currently meet the diagnostic or subsyndromal criteria for PTSD (i.e. TEC).

The PTSD and TEC groups did not differ on age, sex, marital status, education, employment, country-of-origin, visa status or time in Australia. The PTSD group reported more severe PTSD symptoms (t(48) = 11.78, P < 0.001), but the groups did not differ on trauma exposure (t(48) = 1.08, P = 0.29). The PTSD group was more likely to be receiving psychological treatment (χ²(1) = 7.79, P = 0.005) or prescribed a form of psychotropic medication (χ²(1) = 5.86, P = 0.015) compared to the TEC group. We note that all participants were receiving stable treatment in either form for at least 6 weeks prior to fMRI scanning. The PTSD group also reported more severe depression symptoms (t(48) = 4.95, P < 0.001). The PTSD group showed higher avoidant attachment style (t(48) = 2.11, P = 0.04), anxious attachment style (t(48) = 2.38, P = 0.022) and separation grief (t(47.9) = 2.18, P = 0.034) compared to the TEC group. The groups did not differ in regard to the category of separated person that affected them the most (χ²(9) = 7.05, P = 0.63; see Supplemental Information).

Neural responses to attachment prime: main effects

Findings are presented in Table 2A. When controlling for attachment style and separation grief, the PTSD group, relative to the TEC group, showed reduced activation in a left occipitotemporal cluster (lingual gyrus, middle temporal gyrus and hippocampus) to the attachment prime across threat and neutral targets. Avoidant attachment style appeared to be an important moderator of the effects of the attachment prime in PTSD. In interaction with an increase in avoidant attachment style, the PTSD group (vs TEC group) exhibited increased activity in the left posterior dorsomedial prefrontal cortex (DMPFC), a right parieto-occipital cluster encompassing the cuneus, precuneus and superior occipital gyrus, a left occipitotemporal cluster extending from the lingual gyrus, fusiform gyrus and into the cerebellum, and in the left amygdala (ROI (Figure 2A)). Higher levels of anxious attachment style were associated with reduced activity in the bilateral DMPFC in the PTSD compared to TEC group (Figure 2B). Separation grief was associated with increased activity in the left amygdala (ROI) but reduced activity in the VMPCF in the PTSD group compared to the TEC group (Figure 2C).

Neural responses to threat target cue: main effects

Since the main effects relating to threat cue processing in both prime conditions is of secondary importance to the main aims of this study, these results are presented in Supplemental Information.

Neural responses to attachment primed threat: interaction effects

Findings are presented in Table 2B. While controlling for attachment style and separation grief, the PTSD group displayed increased activity in the posterior insula compared to the TEC group. Separation grief emerged as the only significant moderator. Specifically, higher levels of separation grief were associated with decreased activity in the right VMPCF (centred in the middle orbital gyrus) and the left hippocampus, relative to the TEC group (Figure 2C). We also observed that separation grief was associated with increased activity in the left amygdala in the PTSD group (vs TEC) at a sub-threshold level (two voxels; at P < 0.005, cluster size was 15 voxels).

Connectivity analyses with the left amygdala during attachment primed threat

Functional connectivity findings are presented in Table 3. Anxious attachment style emerged as the strongest influence on PTSD vs TEC group differences in amygdala connectivity. Specifically, anxious attachment style was associated with decreased left amygdala connectivity with a cluster including the right amygdala and right anterior insula and with a left pregenual ACC/DMPFC cluster in the PTSD vs TEC group (Figure 2B). Greater avoidant attachment style was associated with reduced connectivity between the left amygdala and two anterior insula clusters—one including the left inferior frontal gyrus and the other the left rolandic operculum in the PTSD (vs TEC) group (Figure 2A). There were no significant amygdala connectivity differences between groups in correlation with separation grief.

Behavioural data

In brief, no PTSD group differences were observed in threat or neutral target cue ratings or in the post-test attachment prime.
|                          | PTSD group (N = 28) | PTSD- group (N = 22) | Group difference |
|--------------------------|---------------------|----------------------|------------------|
|                          | N/mean %/s.d.        | N/mean %/s.d.        | P-value          |
| Age (years)              | 42.0 12.6           | 38.8 11.3            | 0.35             |
| Sex                      |                     |                      |                  |
| Male                     | 17 60.7%            | 13 59.1%             | 0.91             |
| Female                   | 11 39.3%            | 9 40.9%              |                  |
| Marital status           |                     |                      |                  |
| Married                  | 15 53.6%            | 13 59.1%             | 0.63             |
| Widow/widower            | 2 7.1%              | 0 0%                 |                  |
| Divorced/separated       | 3 10.7%             | 2 9.1%               |                  |
| Single/Never married     | 8 28.6%             | 7 31.8%              |                  |
| Education                |                     |                      |                  |
| Completed primary school  | 4 14.3%             | 4 18.2%              | 0.25             |
| Completed high school     | 4 14.3%             | 7 31.8%              |                  |
| Completed tertiary or vocational training | 20 71.4% | 11 50.0% |             |
| Employment               |                     |                      |                  |
| Employed (full or part time) or studying | 14 50.0% | 11 50.0% | 0.15             |
| Unemployed               | 4 14.3%             | 5 22.7%              |                  |
| Unable to work           | 6 21.4%             | 1 4.5%               |                  |
| Home duties or retired   | 2 7.1%              | 5 22.7%              |                  |
| Volunteer                | 2 7.1%              | 0 0%                 |                  |
| Country of origin        |                     |                      |                  |
| Iran                     | 10 35.7%            | 8 36.4%              | 0.52             |
| Iraq                     | 3 10.7%             | 6 27.3%              |                  |
| Tibet                    | 1 3.6%              | 2 9.1%               |                  |
| Othera                   | 14 50.0%            | 6 27.3%              |                  |
| Visa status              |                     |                      |                  |
| Australian citizen or permanent resident | 14 50.0% | 14 63.6% | 0.36             |
| Insecure visa including temporary or bridging visa | 14 50.0% | 8 36.4% |                  |
| Medication               |                     |                      |                  |
| Currently on psychotropic medication | 9 32.1% | 1 4.5% | 0.015             |
| Not on psychotropic medication | 19 67.9% | 21 95.5% |                  |
| Treatment                |                     |                      |                  |
| Currently receiving psychological treatment | 16 57.1% | 4 18.2% | 0.005             |
| Not receiving psychological treatment | 12 42.9% | 18 81.8% |                  |
| Time in Australia (years) | 6.05 7.55           | 6.74 9.43            | 0.78             |
| PTSD symptom severity (PSS-I; sum) | 34.39 7.95 | 34.39 7.95 | <0.001            |
| Trauma exposure (HTQ); excluding torture item (count) | 10.36 3.96 | 9.14 3.98 | 0.29             |
| Depression (HSCL; mean)  | 2.69 0.53           | 1.86 0.65            | <0.001           |
| Avoidant attachment style | 4.37 1.47           | 3.46 1.55            | 0.04             |
| Anxious attachment style  | 4.20 1.57           | 3.17 1.45            | 0.02             |
| Separation grief index   | 6.04 4.69           | 3.50 3.51            | 0.03             |

*Other countries of origin include Afghanistan, Bosnia-Herzegovia, Cambodia, Bhutan, Morocco, Myanmar, Chile, Fiji, Ghana, Kuwait, Laos, Nigeria, Tibet and Vietnam.

ratings, representing a null finding. Within subject’s findings are presented in detail as Supplemental Information.

**Additional analyses.** While moderate–severe traumatic brain injury was an exclusion criterion, one participant with possible mild TBI was included in the study. To ensure that their inclusion did not affect the results, we re-ran the analysis with this participant (from the PTSD group) excluded. The findings from these additional analyses revealed that excluding the possible mTBI participant did not affect the key findings reported above. A summary of these additional analyses is provided in the Supplemental Information.

We were also interested in the relationship between attachment insecurity and dissociative symptoms given the finding that avoidant attachment style in particular moderated enhanced activity in dorsal frontoparietal regions in the PTSD group. This over-regulation pattern has been consistently reported in dissociative PTSD subtype (Lanius et al., 2012). Dissociative symptoms were measured in the interview by administering the Dissociative Experiences Scale Taxon (DES-T) (Waller and Ross, 1997), an 8-item measure derived from the original DES-II (Carlson and Putnam, 1993) that specifically considers pathological dissociative symptoms. Internal consistency was satisfactory (α = 0.78). Using bivariate correlations, we observed that dissociative symptoms were positively associated with avoidance attachment style (r = 0.394, P = 0.005) and anxious attachment style (r = 0.368, P = 0.009); no significant relationship was observed with separation grief (r = 0.244, P = 0.087).

**Discussion**

This study investigated the neural underpinnings of the attachment system’s capacity to buffer threatening experiences in a refugee sample with PTSD compared to a refugee trauma-exposed sample. We additionally examined whether attachment insecurity or grief relating to family separation played a moderating role. In accordance with our hypotheses, we observed that attachment priming in general elevated neural dysregulation in PTSD in association with higher levels of separation grief (compared to controls)—a pattern that was also observed to threat cues. This was reflected in left amygdala hyperactivity (at trend level for attachment primed threat; Table 2) and hypoactivity in the VMPC and hippocampus. Findings for the moderating effect of avoidant attachment style were also consistent with hypotheses, where we observed associations with elevated activity in dorsal frontoparietal attention regions in the PTSD (vs TEC group). We also observed neural indicators of decreased emotion regulation in association with...
Table 2. Neural activations for (A) main effect of attachment prime on negative and neutral target and (B) effect of attachment prime on threat target processing for PTSD vs TEC groups

| Group contrasts | Region | Hem | Size | x | y | z | t  | P  | Cohen’s d |
|----------------|--------|-----|------|---|---|---|----|----|-----------|
| PTSD > TEC group differences controlling for attachment style and separation grief | Occipitotemporal cluster: LG/MTG cluster incl hippocampus | L   | 898  | −28| −54| 6  | 4.85| <0.01| 1.50      |
| PTSD < TEC | | | | | | | | | |
| PTSD > TEC group differences moderated by avoidant attachment style | Amygdala | L   | 23   | −32| 2  | −12| 3.34| <0.01| 1.03      |
| | Posterior DMPFC (MFG/PreG) | L   | 222  | −28| 0  | 48 | 4.30| <0.05| 1.33      |
| | Parieto-occipital cluster: Cuneus/Precuneus/SOG | R   | 639  | 28  | −64| 34 | 4.65| <0.01| 1.44      |
| | Occipitotemporal cluster: LG/FG/Cereb | L   | 599  | −12| −68| −8 | 4.41| <0.01| 1.36      |
| PTSD < TEC | | | | | | | | | |
| PTSD > TEC group differences moderated by anxious attachment style | | | | | | | | | |
| PTSD < TEC | DMPFC (SupMedG/SFG) | R   | 22   | 38  | 44 | 4.31|         | |
| PTSD vs TEC group differences moderated by separation grief | | | | | | | | | |
| PTSD > TEC | Amygdala | L   | 77   | −26| −8 | −8 | 3.78| <0.01| 1.17      |
| PTSD < TEC | VMpFC (MOG) | R   | 94   | 28  | 36 | −8 | 4.89| <0.02| 1.51      |

Notes: No significant activations denoted by (—). Cohen’s d is computed from t-values.

Abbreviations: Cereb, cerebellum; FG, fusiform gyrus; LG, lingual gyrus; MFG, middle frontal gyrus; MOG, middle orbital gyrus; PreG, precentral gyrus; SFG, superior frontal gyrus; SOG, superior occipital gyrus; SupMedG, superior medial gyrus.

*Cluster-level FWE-corrected P-values are reported; italics represent ROI analyses.
Fig. 2. Neural activation and connectivity patterns comparing PTSD and TEC groups by moderator variable. (A) PTSD group differences moderated by avoidant attachment style; (B) PTSD group differences moderated by anxious attachment style; and (C) PTSD group differences moderated by separation grief. Increased activity in PTSD group vs TEC group shown in red, decreased activity in the PTSD relative to the TEC groups shown in blue. Connectivity (gPPI) results are presented in the grey box. Abbreviations: AI = anterior insula; Amyg = amygdala; Hipp = hippocampus; MOG = middle orbital gyrus; RO = rolandic operculum; SupMedG = superior medial gyrus.

Table 3. Neural activations for gPPI analysis examining left amygdala connectivity in attachment prime on negative target for PTSD vs TEC groups

| Left amygdala connectivity [-26 -6 -12] (AttThreat > NAttTheat) | MNI Region | H | Size | x | y | z | t | P* | Cohen's d |
|---------------------------------------------------------------|-------------|----|------|---|---|---|----|-----|-----------|
| PTSD vs TEC group differences controlling for attachment style and separation grief | PTSD > TEC | — | — | — | — | — | — | — | — |
| PTSD < TEC | — | — | — | — | — | — | — | — | — |
| PTSD vs TEC group differences moderated by avoidant attachment style | PTSD > TEC | IFG/AIns | L | 38 | -46 | -14 | 18 | 4.23 | <0.05 | 1.31 |
| PTSD < TEC | — | — | — | — | — | — | — | — | — |
| PTSD vs TEC group differences moderated by anxious attachment style | PTSD > TEC | AIns | R | 164 | 32 | 12 | -14 | 4.21 | <0.01 | 1.30 |
| PTSD < TEC | — | — | — | — | — | — | — | — | — |
| PTSD vs TEC group differences moderated by separation grief | PTSD > TEC | — | — | — | — | — | — | — | — |
| PTSD < TEC | — | — | — | — | — | — | — | — | — |

*Cluster-level FWE-corrected P-values are reported. Italics represent ROI analyses.

PTSD (vs TEC) group. Refugees are typically exposed to significant interpersonal trauma and on-going stressors, which may undermine the attachment system’s capacity to effectively regulate responses to threat in those with PTSD. Our findings suggest

anxious attachment style, via decreased activity in the DMPFC to the attachment prime and reduced connectivity between the left amygdala and other left pregenual anterior cingulate cortex (pgACC)/DMPFC to attachment primed threat cues in the PTSD (vs TEC) group. Refugees are typically exposed to significant interpersonal trauma and on-going stressors, which may undermine the attachment system’s capacity to effectively regulate responses to threat in those with PTSD. Our findings suggest
that the specific nature of these disruptions on brain circuits is dependent on insecure attachment style and separation grief.

Separation grief appears to mitigate the advantages of the attachment system, including coping with processing threat, in refugees with PTSD compared to refugees without PTSD. Theoretical models suggest a strong interaction between psychological and biological consequences of attachment figure loss (Sbarra and Hazan, 2008). Previous fMRI studies have shown that the presence of a social attachment figure served to increase activity in down-regulation neural systems (i.e. VMPFC) when exposed to physical pain, thus reducing the subjective experience of pain (Eisenberger, 2012). Another study revealed that poor relationship quality attenuated the benefits of direct social support on reduced threat reactivity in the brain in healthy participants (Coan et al., 2006). Our findings have particular relevance to understanding the refugee experience, where forcible separation from family is common and often prolonged (Miller et al., 2018). Family separation has been previously associated with elevated mental health symptoms in refugees, including PTSD (Steel et al., 2002; Schweitzer et al., 2006; Nickerson et al., 2010; Savic et al., 2013), an effect that is independent from overall trauma exposure (Miller et al., 2018; Liddell et al., 2021). These findings highlight a potential underlying mechanism as to why family separation affects psychological recovery from trauma in refugees. On-going forced separation from key attachment figures, and the sense of loss and grief this entails, may diminish the capacity of the attachment system to operate effectively, leading to altered neural regulation processes when exposed to perceived threat and stress.

Avoidant attachment moderated PTSD group differences in response to the attachment prime in general. Specifically, PTSD participants with greater levels of avoidant attachment style showed increased activity in dorsal frontoparietal regions—often termed the dorsal attention network (dAN) (Corbetta et al., 2008)—consisting of dorsal parietal regions Superior Parietal Lobule (SPL), frontal regions (posterior DMPFC encompassing the frontal eye fields and supplementary motor area) and sensory areas [middle temporal gyrus (MTG)]. The dAN underpins selective attention processes: by aligning attentional resources to internal goals, this network utilizes frontoparietal top-down signals to direct sensory processing towards relevant information in the environment (Corbetta et al., 2008). Recent studies show that the dAN works harder when having to suppress irrelevant information (Lanssens et al., 2020). Increased activity in regions within the dAN for those with stronger avoidant attachment style in the PTSD group could reflect hyperactive selective attention processes to the salient attachment prime. This is supported by findings in the attachment literature that avoidantly attached individuals are also more likely to engage in top-down inhibitory (Gillath et al., 2005; Vrticka et al., 2012) or suppressive emotion regulation strategies (Vrticka and Vuilleumier, 2012) in response to negative situations. This is also consistent with attachment theory that suggests that avoidant individuals suppress their attachment systems when confronted with threat, thereby reducing its regulatory benefits (Mikulincer and Shaver, 2016). We observed that activation in these frontoparietal attention networks were stronger in the PTSD group in correlation with avoidant attachment style, who may be more predisposed to engaging in these secondary coping processes such as top-down emotional suppression strategies (Vrticka et al., 2012; Vrticka and Vuilleumier, 2012). This ‘protective’ mechanism may have limited efficacy in our study, as we also observed increased left amygdala activity in PTSD, suggesting unsuccessful inhibition of the threat response. A further possibility that we examined in additional post hoc analyses is that increased activity in regulatory prefrontal regions in PTSD is similar to the over-regulatory neural pattern observed in the dissociative subtype of PTSD (Lanius et al., 2012). We found positive correlations between avoidant and anxious attachment style with dissociative symptoms in our sample. These findings suggest that the moderating effect of avoidant attachment style on prefrontal regulatory activity in PTSD may be partially explained by dissociative symptoms. However, such a neural pattern was not observed in association with anxious attachment style, even though it was also positively correlated with dissociative symptoms. More research will be required to tease out the underlying reasons for elevated prefrontal neural activity in refugees with PTSD during attachment activation, and how this relates to dissociative symptoms.

Anxious attachment style was also linked to a pattern of neural dysregulation to threat cues in the refugee PTSD group compared to TECs: the PTSD group showed reduced DMPFC activity to the attachment prime and reduced connectivity between the left amygdala and left prefrontal regulatory regions. These findings support the notion that anxious attachment is associated with hyperactivating emotional reactions, resulting in poor regulatory responses to threat (Shaver and Mikulincer, 2010). These neural patterns are somewhat inconsistent with previous studies conducted in healthy participants, where a pattern of hyperactivation was observed in threat detection networks (Gillath et al., 2005; Vrticka et al., 2008; DeWall et al., 2012), thought to reflect increased sensitivity to social threats in anxiously attached people (Vrticka and Vuilleumier, 2012). Since this is the first fMRI study of attachment in PTSD to our knowledge, we can only suggest that anxious attachment style enhances the threat dysregulation neural signature commonly observed in PTSD (Shaley et al., 2017), resulting in poor threat responsivity. A left laterality effect was also evident, with decreased coupling observed between left amygdala and left prefrontal regions in the PTSD compared to TEC groups—including pgACC/DMPFC (moderated by anxious attachment style) and inferior frontal gyrus (IFG) (avoidant attachment style). While the right hemisphere is typically aligned with processing of negative affect and avoidance behaviours, the left hemisphere has been mostly implicated in positive emotion processing and approach behaviours (Davidson et al., 2000). Attachment and non-attachment cues are positively valenced, and disruptions to predominantly left hemispheric emotion regulation systems in PTSD during attachment activations may reflect this valence effect. This idea is supported by a previous study that found that attachment-related and positive words were prioritized by left hemispheric processing (Cohen and Shaver, 2004). Research focused on implementing paradigms to target lateralization effects will be required to investigate these effects further.

Limitations

We note the limitations of the study. First, given the study is cross-sectional, causal inferences are necessarily speculative. For instance, it is not possible to know for certain whether greater levels of attachment insecurity preceded trauma exposure or separation or whether they were consequential to these experiences. Second, our sample size is modest, and findings will need to be replicated in larger samples. This restricted our capacity to examine the role of specific traumatic experiences (e.g. torture). Our PTSD group consisted of participants...
who met DSM-5 criteria for full-PTSD and a smaller group who met criteria for subsyndromal PTSD; we did not analyse these participants separately due to the small sample size. Third, some of our participants were on psychotropic medications and were receiving psychotherapeutic treatment at the time of study. We note that treatment was stable at the time of test—i.e. that participants had not altered their treatment regime in the preceding 6 weeks (or longer). Fourth, our study found a disconnection between fMRI patterns and behavioural results. Attachment primed threat was not rated as less threatening than non-attachment primed threat targets as we expected, and we did not observe group differences in the behavioural ratings to parallel the fMRI findings (see Supplemental Information for full results). Fifth, while separation grief may reflect the specific experiences of refugees, it is difficult to ascertain whether our findings are specific to refugees or generalize to non-refugee samples with PTSD as we did not include a non-refugee sample. One advantage of this study, however, is that we compare refugees with PTSD to a healthy refugee sample with comparable trauma exposure, enabling us to pinpoint the specific effects of PTSD in the refugee group. Nevertheless, future research would benefit from examining these processes in other trauma-exposed and non-refugee healthy samples. Sixth, we did not include an assessment of prolonged grief in this study, which may contrast with the effects of unresolved grief related to family separation in terms of its impact on the attachment system. These relationships will need to be examined in future studies.

Conclusions
Our findings highlight that the secure attachment system’s capacity to modulate neural responses to threat is compromised in refugees with PTSD. This is underpinned by specific changes in threat detection, regulation and attention systems according to grief in relation to separation from significant attachment figures, and anxious or avoidant attachment style. As such, disruptions to the attachment system via experiencing significant trauma or enduring family separation could represent a key mechanism underpinning the adverse effects of these events on long-term emotional outcomes and social adjustment of refugees with PTSD. If the attachment system is compromised because of insecurity or the unavailability of key attachment figures due to forced separation, a refugee with PTSD may be less equipped to deal with daily pressures (Mikulincer et al., 2015). This likely has significant implications for how refugees with PTSD symptoms recover from trauma, particularly in the context of on-going family separation (Li et al., 2016; Liddell and Bryant, 2018).

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Conflicts of interest
Authors B.J.L., G.S.M., K.L.M. M.L.D., P.D., T.O., A.N. report no potential conflicts of interest. Authors M.A., M.C. and J.A. are employees of the NSW Service for the Treatment and Rehabilitation of Torture and Trauma Survivors, which provides counselling and psychological services for torture survivors and refugees. Author J.A. is also the President of the International Rehabilitation Council for Torture Victims.

Supplementary data
Supplementary data are available at SCAN online.

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