

Motivation and Pleasure Deficits Undermine the Benefits of Social Affiliation in Psychosis

Clinical Psychological Science
1–23

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DOI: 10.1177/21677026241227886

www.psychologicalscience.org/CPS



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Abstract

In psychotic disorders, motivation and pleasure (MAP) deficits are associated with decreased affiliation and heightened functional impairment. We leveraged a transdiagnostic sample enriched for psychosis and a multimethod approach to test the hypothesis that MAP deficits undermine the stress-buffering benefits of affiliation. Participants completed the social-affiliation-enhancement task (SAET) to cultivate affiliation with an experimental partner. Although the SAET increased perceived affiliation and mood, individuals with greater negative symptoms derived smaller emotional benefits from the partners, as indexed by self-report and facial behavior. We then used the handholding functional MRI paradigm, which combines threat anticipation with affiliative physical contact, to determine whether MAP deficits undermine the social regulation of distress. Individuals with greater MAP deficits showed diminished neural “benefits”—reduced dampening of threat-elicited activation—from affiliative touch in key frontoparietal nodes of the dorsal attention network. In short, MAP symptoms disrupt the emotional and neuroregulatory benefits of affiliation.

Keywords

anhedonia/avolition, interpersonal emotion regulation, negative symptoms, psychosis/psychotic spectrum, schizophrenia, social-affiliative deficits, social-baseline theory

Received 3/5/23; Revision accepted 1/5/24

Viewed through a clinical-science lens, “affiliation” can be defined as positive social interactions (Kozak & Cuthbert, 2016). From this perspective, affiliation is the behavioral manifestation of approach-oriented (“appetitive”) social motivation. Like anhedonia, anxiety, and other cross-cutting dimensional symptoms, affiliative deficits do not respect traditional diagnostic boundaries; they are evident in individuals with a range of psychiatric disorders (e.g., major depression, social anxiety disorder; Barkus & Badcock, 2019; Blay et al., 2021) and in individuals who do not meet full diagnostic criteria for any psychiatric illness (e.g., Blanchard et al., 2011; Llerena et al., 2012). Pronounced affiliative deficits—including

diminished desire for and reduced engagement in social interactions—are often evident among individuals living with schizophrenia and other psychosis-spectrum disorders. Social amotivation and anhedonia are prominent and enduring negative symptoms of psychotic disorders (Blanchard & Cohen, 2006; Horan et al., 2006, 2008; Kring et al., 2013). Individuals with psychotic disorders tend to endorse lower levels of extraversion and higher levels of detachment (Horan et al., 2008; Longenecker

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et al., 2020). These motivation and pleasure (MAP) deficits are associated with heightened social, vocational, and functional impairment (Blanchard et al., 2017; Kalin et al., 2015; Kring et al., 2013; Moe et al., 2021; Rocca et al., 2014). These negative symptoms do not fully respond to existing treatments and have been identified as a key unmet therapeutic need (Kirkpatrick et al., 2006). In short, understanding the factors that promote affiliative deficits in psychotic disorders is critically important for the development of more effective treatments.

Affiliative deficits in psychotic disorders are complex and likely multiply determined; deficient behavioral skills and cognitive impairment have been identified as core features (Blanchard et al., 2015; Fulford et al., 2018; Green et al., 2012, 2018; Miller et al., 2021; Pelletier-Baldelli & Holt, 2020). There are also questions concerning whether affiliative deficits are related to the reduced anticipation of pleasure or to reduced hedonic pleasure during social experiences (e.g., Catalano et al., 2022; Engel et al., 2016; Gard et al., 2007; Merchant et al., 2022; Moran & Kring, 2018; Zhang et al., 2020; also see Riehle et al., 2024). A key unresolved question is whether individuals with psychotic disorders are less socially motivated because they derive fewer emotional benefits from social contact (e.g., Abel et al., 2023). Among healthy individuals, affiliative drive reflects the wide range of benefits conferred by interpersonal attachments, which range from the experience of positive affect to improved health outcomes (Baumeister & Leary, 1995; Eisenberger, 2013; Farrell et al., 2018; Sbarra & Coan, 2018). From this perspective, social-motivation deficits in psychosis have typically been conceptualized in terms of aberrant responses to incentives and rewards (Catalano et al., 2018; Fulford et al., 2018; Lee et al., 2019; Moran et al., 2019; Mow et al., 2020). Beyond reward mechanisms, it may be important to consider the social regulation of stress, another potent promoter of social contact and affiliation (Coan & Sbarra, 2015; Cohen, 2004; Cottrell & Epley, 1977; Williams et al., 2018).

Taylor (2006) noted that the most striking aspect of the human stress response is the inclination to affiliate and the resulting “tending and befriending” that buffers and ameliorates stress. Supportive social relationships can attenuate a variety of physiological stress responses (Eisenberger et al., 2007; Gunnar, 2017; Morawetz et al., 2021; Uchino, 2006; Uchino et al., 1996). A growing literature suggests that the brain circuits underlying this “neuroregulatory” effect are distinct from those responsive to primary and secondary rewards, including food, money, and addictive substances (Coan et al., 2006, 2017; Coan & Sbarra, 2015; Eisenberger, 2013; Eisenberger et al., 2007; Morawetz et al., 2021; Morriss et al., 2019). To date, the relevance of socio-emotional

regulatory systems to affiliative deficits across the psychosis continuum remains unexplored and unknown.

Here, we tested the overarching hypothesis that more severe MAP symptoms undermine the emotional benefits of social partners. To ensure a broad spectrum of social motivation, social functioning, and symptoms, we capitalized on a sampling strategy inspired by the Research Domain Criteria and focused on a mixed transdiagnostic community sample enriched for psychotic-spectrum disorders (Kozak & Cuthbert, 2016; Tiego et al., 2023). Most participants were on a stable regimen of outpatient treatment, enhancing clinical relevance.

We used a well-established handholding functional MRI (fMRI) paradigm to probe the social regulation of stress (Coan et al., 2006, 2017). The handholding paradigm combines a robust stressor—uncertain and uncontrollable threat of noxious electric shock—with varying degrees of affiliative touch: holding the hand of an affiliative partner (“partner”), holding the hand of an unfamiliar experimenter (“stranger”), or holding no hand at all (“alone”). In a preliminary report, Coan et al. (2006) demonstrated that holding a spouse’s hand dampened neural reactivity to anticipated threat (shock) across a range of cortical and subcortical brain regions. Participants reporting higher marital quality and greater spousal support evinced more extreme dampening. In a better-powered follow-up study, Coan and colleagues (2017) examined a broader range of social relationships—including opposite-gender close friends, dating partners, and spouses—and showed that holding the hand of an affiliative partner attenuated neural reactivity to uncertain shock threat in several regions, including the right dorsolateral prefrontal cortex (dlPFC; Coan et al., 2017). Paralleling the original 2006 findings, participants reporting higher levels of perceived social support derived greater neural benefits (dampened threat reactivity) in the partner condition but not the stranger condition. More recent work has extended this framework, demonstrating that affiliative handholding also dampens neural reactivity to acute nociceptive stimulation (López-Solà et al., 2019). Together, these observations provide compelling evidence that affiliative touch buffers the neural impact of laboratory stressors.

Extending Coan’s handholding paradigm—which capitalizes on naturally occurring social partnerships—to the psychosis spectrum poses a practical challenge. Individuals with psychotic disorders often have diminished social networks (lower quantity), and even when available, romantic and family relationships are often less intimate (lower quality; Cloutier et al., 2021; Green et al., 2018; Izon et al., 2018; Koutra et al., 2014, 2016). To overcome this barrier, we used the social-affiliation-enhancement task (SAET), a recently validated set of procedures for cultivating affiliation with an

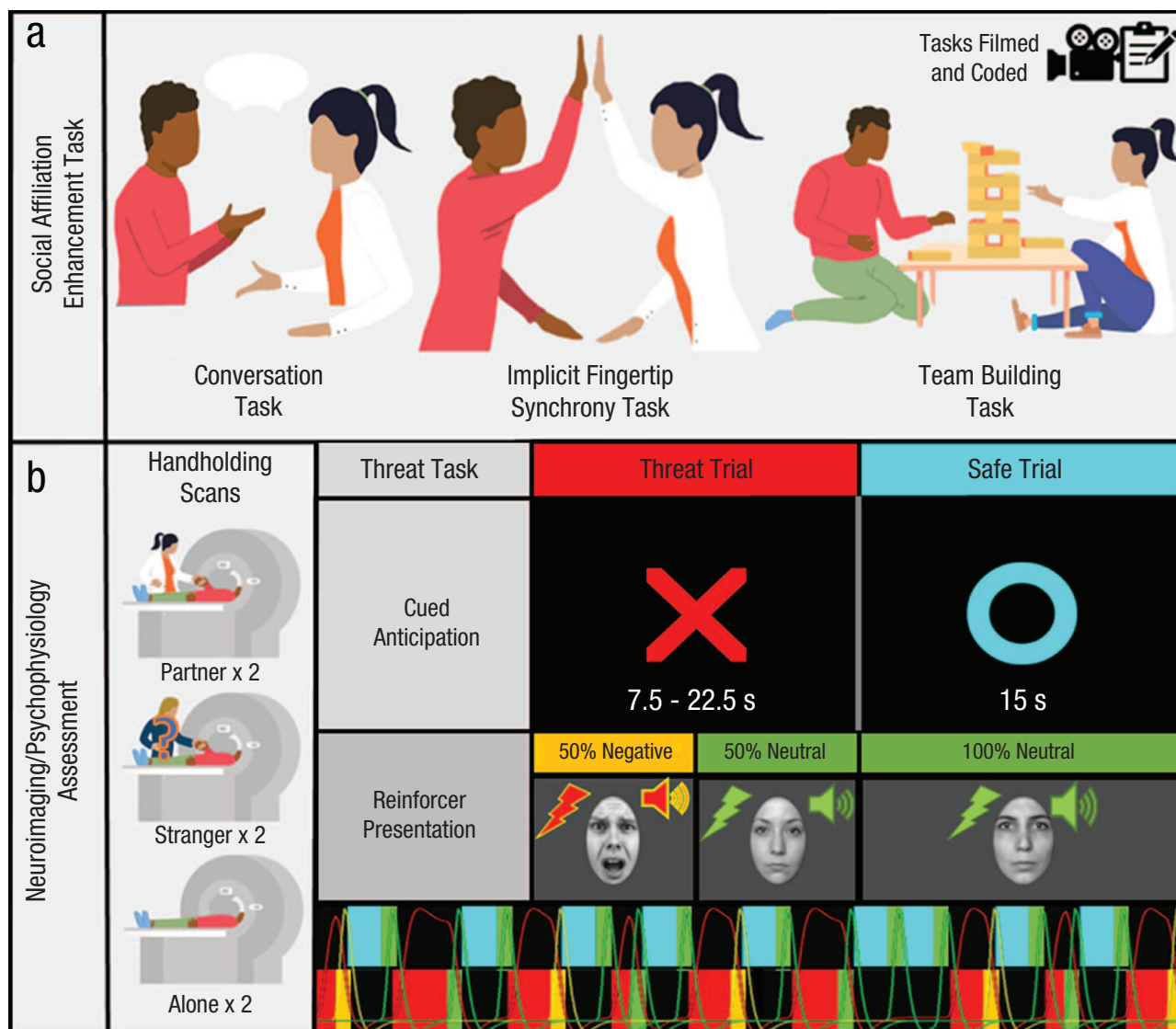


Fig. 1. Conceptual overview of the two-phase laboratory assessment. (a) The social-affiliation-enhancement task (SAET). In the first phase of the session, participants completed the SAET, which encompasses three tasks—conversation, implicit fingertip synchrony, and team building. (b) The handholding functional MRI (fMRI) paradigm. In the second phase of the session, participants completed the handholding fMRI paradigm. In each scan, participants held the hand of the experimental partner, a stranger, or no one (“alone”). Each scan included an event-related cued threat-anticipation task. To elicit robust anxiety, threat trials (red) were variable in duration and culminated in the presentation of negative reinforcers ($p = 0.50$) or neutral reinforcers ($p = 0.50$). Safe trials (blue) were fixed duration (mean duration matched across conditions) and culminated in neutral reinforcers ($p = 1.0$). Negative reinforcers included a noxious electric shock, aversive auditory clip, and a photograph of an angry or fearful face. Neutral reinforcers included a just-perceptible electrical pulse, neutral auditory clip, and a photograph of a neutral face. (Bottom right). An example of the trial structure and the expected hemodynamic responses to threat anticipation (red trace), negative reinforcers (yellow trace), and neutral reinforcers (green trace) for a representative scan. Subjects completed up to six scans in total (two scans/handholding condition).

experimental partner, de novo, in the laboratory (McCarthy et al., 2018). A key advantage of this approach is that it permits the enrollment of individuals who lack intimate social partners, enhancing generalizability, and equates the degree of partner familiarity across participants, circumventing a key confound.

As shown schematically in Figure 1, we adopted a comprehensive multimethod approach that encompassed baseline measures of clinical diagnoses and

symptoms; self-reported symptoms and functioning; subjective self-report and objective behavioral (video coding) measures of positive mood and affiliation during the SAET, just before fMRI scanning; and fMRI captured during the handholding task.

These data enabled us to extend our preliminary work in schizophrenia and test the hypothesis that individuals with more severe appetitive MAP deficits—indexed by “gold-standard” clinician ratings—would

show diminished symptoms and signs of affiliation with the experimental partner (McCarthy et al., 2018). The fMRI allowed us to test the corresponding prediction that individuals with more severe MAP deficits would derive diminished neural benefits (less dampening of threat-related activation) from holding the experimental partner's hand.

Transparency and Openness

Preregistration

This study was not preregistered.

Data, materials, code, and online resources

De-identified raw data are publicly available via the National Institute of Mental Health Data Archive (https://nda.nih.gov/edit_collection.html?id=2480).

Reporting

We report how we determined our sample size, all data exclusions, all manipulations, and all measures in the study. Other measures and procedures conducted as part of the larger parent grant will be presented in separate reports.

Ethical approval

The protocol was approved by the University of Maryland, Baltimore Institutional Review Board.

Method

Overview

The present article stems from a parent project focused on the nature and neurobiology of affiliative deficits in psychosis (R01-MH110462). Participants completed two assessments: a baseline clinical session and a two-phase laboratory session (Fig. 1). At the baseline clinical session, eligibility was confirmed, participants provided informed written consent, and demographic, diagnostic, symptom, and other self-report data were acquired. Eight participants had active prescriptions for sedatives and/or benzodiazepines at the time of enrollment and were instructed to abstain from taking these medications for at least 12 hr before the MRI assessment. None of these individuals disclosed or exhibited noteworthy withdrawal effects. During the two-phase laboratory session, participants completed (a) the SAET outside the scanner and (b) the handholding paradigm inside the scanner. Latency between the two sessions was less

Table 1. Sample Characteristics

Characteristic	Mean or <i>N</i>
Age (years)	43.87 (12.07)
Sex	
Male	69 (63.9%)
Female	39 (36.1%)
Race	
Black/African American	72 (66.7%)
White	26 (24.1%)
Asian	4 (3.7%)
Biracial/multiracial	5 (4.6%)
Not reported	1 (0.9%)
Ethnicity	
Not Hispanic/Latino	99 (91.7%)
Hispanic/Latino	8 (7.4%)
Not reported	1 (0.9%)
Marital status	
Married	8 (7.4%)
Divorced/separated	15 (13.9%)
Never married/single	85 (78.7%)
Education (years)	13.12 (2.45)
Has a paying job	
Yes	35 (32.4%)
No	73 (67.6%)
Diagnosis	
Schizophrenia	35 (32.4%)
Schizoaffective bipolar type	17 (15.7%)
Schizoaffective depressive type	15 (13.9%)
Delusional disorder	1 (0.9%)
BPD I with psychotic features	10 (9.3%)
MDD with psychotic features	9 (8.3%)
No diagnosis (healthy control subject)	21 (19.4%)
Medications (clinical participants)	
Atypical antipsychotic	56
Typical antipsychotic	9
Atypical and typical antipsychotic	8
Antipsychotic (chlorpromazine) dose equivalent	297.57 (383.97)
Antidepressant	45
Mood stabilizer	29

Note: *N* = 108. Parenthetical entries indicate standard deviation or percentage, as appropriate. BPD = bipolar disorder; MDD = major depressive disorder.

than 2 weeks ($M = 6.4$ days, $SD = 3.1$). Following the scan, participants were debriefed, compensated, and discharged.

Participants

Recruitment. This study adopted a transdiagnostic approach informed by the Research Domain Criteria (RDoC) framework (Cuthbert, 2014; T. Insel et al., 2010; T. R. Insel, 2014). To capture a broad spectrum of MAP deficits, maximizing range and statistical power, a mixed transdiagnostic adult sample—including both clinical and community participants—was recruited (Tiego et al.,

2023). A modest number of psychiatrically healthy community participants was included (19.4%; Table 1) to ensure that the full range of affiliative function was captured (Tiego et al., 2023). Clinical participants were recruited from outpatient community mental-health clinics in the Baltimore/D.C. metropolitan region with the approval of their provider. Community participants were recruited via online advertisements (e.g., Craigslist).

Enrollment criteria. General inclusion criteria included 18 to 60 years of age, English fluency, and normal or corrected-to-normal vision. General exclusion criteria included moderate or severe substance use disorder in the past 6 months or mild substance use disorder in the past month, as determined by the Structured Clinical Interview for DSM-5 Research Version (SCID-5-RV; First et al., 2015); standard MRI contraindications (e.g., claustrophobia); lifetime neurological, developmental, or cognitive disorder (indexed by medical history or cognitive testing); or a lifetime history of serious head injury. Clinical inclusion criteria included a lifetime psychotic disorder (e.g., schizophrenia/schizoaffective disorder, delusional disorder), a bipolar disorder with psychotic features or major depression with psychotic features, and clinical stability (i.e., no inpatient hospitalizations in the past 3 months and no changes in psychoactive medication in the past month; indexed by medical history). Community inclusion criteria included absence of current psychiatric diagnoses or medication and lifetime psychotic or mood disorders. Absence of psychiatric diagnoses was determined using the SCID-5. Absence of excluded psychiatric medications (past 6 months) was determined via self-report. A total of 16 community members were deemed ineligible during screening and were excluded.

Complete sample. A total of 120 participants completed the baseline clinical assessment. Of these participants, 12 did not attend the neuroimaging session because of psychiatric hospitalization ($n = 1$), study withdrawal ($n = 10$), or inclement weather ($n = 1$). As shown in Table 1, the remaining 108 participants included a mixture of clinical ($n = 87$, 80.6%) and community ($n = 21$, 19.4%) participants.

MRI sample. Of the 108 participants, 28 were excluded from fMRI because of safety concerns ($n = 6$), poor fit in the scanner ($n = 3$), technical problems ($n = 5$), study withdrawal ($n = 6$), fatigue or inadequate compliance ($n = 2$), or incidental neurological findings ($n = 2$). Volume-to-volume (“framewise”) displacement was used to assess residual motion artifact. Scans with excessively frequent artifacts ($> 3 SD$) were discarded. Participants with fewer than six usable scans were excluded from analyses ($n = 4$). In total, 80 participants provided usable MRI data ($M =$

43.9 years, $SD = 11.7$; 36.2% female; 77.5% clinical; 63.7% African American, 25.0% White, 5.0% Asian, 5.0% biracial/multiracial, 1.3% race not reported; 91.3% not Hispanic/Latino, 7.5% Hispanic/Latino, 1.3% ethnicity not reported; $M = 13.2$ years of education, $SD = 2.3$).

Skin-conductance sample. Skin conductance was measured during scanning to confirm that the threat-anticipation component of the handholding task evoked signs of arousal. Of the 80 participants in the MRI sample, 11 were excluded from skin-conductance analyses because of either technical problems ($n = 5$) or inadequate signal quality ($n = 6$; indexed by a nonpositive mean response to the multimodal negative reinforcer). In total, 69 participants provided usable skin-conductance data.

Clinical assessments

Diagnostic interview. Diagnoses were determined using the SCID-5-RV. Assessments were conducted by well-trained master’s-level interviewers supervised by doctoral-level clinical psychologists.

Symptoms. The Clinical Assessment Interview for Negative Symptoms (CAINS; Horan et al., 2011; Kring et al., 2013) is a 13-item interview indexing deficits in MAP (nine items; e.g., amotivation, asociality, and anhedonia; $\alpha = .80$) and expression (four items; e.g., affective flattening and alogia; $\alpha = .87$). For hypothesis testing, CAINS-MAP served as the primary index of social-motivation deficits. The CAINS-MAP has been extensively validated. Elevated MAP deficits are associated with reduced desire for close relations and social engagement (e.g., Kring et al., 2013), impaired social functioning in the community (Blanchard et al., 2017; Hu et al., 2023; Kring et al., 2013), and diminished affiliative responses to laboratory social encounters (McCarthy et al., 2018). The CAINS has been successfully in a variety of clinical (Blanchard et al., 2017; Cuesta et al., 2021; Hu et al., 2023; Kring et al., 2013) and nonclinical populations (Engel & Lincoln, 2017; Xie et al., 2018).

The brief version of the Social Anhedonia Scale (SAS-B; Reise et al., 2011) is a 17-item self-report index of social anhedonia ($\alpha = .83$) derived from the Revised Social Anhedonia Scale (Eckblad et al., 1982).

The expanded Brief Psychiatric Rating Scale (BPRS; Kopelowicz et al., 2008; Ventura et al., 1993) is a 24-item interview that was used to index positive symptoms (eight items; $\alpha = .69$), depression/anxiety (four items; $\alpha = .74$), and agitation (six items; $\alpha = .53$).

Social function. The Specific Levels of Functioning (Harvey et al., 2011; Schneider & Struening, 1983) is a well-established self-report measure of real-world

Table 2. Descriptive Statistics for Symptoms and Social Function

Symptom or social factor	Mean (SD)	Range
Motivation and Pleasure (CAINS)	11.84 (7.03)	1–34
Expression (CAINS)	5.57 (3.49)	0–14
Social anhedonia (SAS-B)	5.81 (4.07)	0–17
Positive symptoms (BPRS)	12.52 (5.26)	8–31
Depression/anxiety (BPRS)	7.85 (4.10)	4–19
Agitation (BPRS)	7.63 (2.24)	6–19
Interpersonal relationships (SLOF) ^a	27.32 (6.29)	11–35
Social-network size (SNI)	11.11 (7.80)	0–36

Note: $N = 108$. BPRS = Brief Psychiatric Rating Scale; CAINS = Clinical Assessment Interview for Negative Symptoms; SAS-B = Social Anhedonia Scale–Brief; SLOF = Specific Levels of Functioning; SNI = Social Network Index.

^a $N = 107$.

interpersonal functioning. Here, the seven-item Interpersonal Relationships Scale was used to index social-interpersonal functioning ($\alpha = .89$).

The Social Network Index is a 13-item self-report index of social-network size (Cohen et al., 1997).

Descriptive statistics for symptoms and social functioning measures are provided in Table 2.

SAET

The SAET was designed to promote affiliative social interaction, positive affect, and social bonding between each participant and an opposite-sex partner (McCarthy et al., 2018). To reduce variability, the partner was always the opposite sex of the research participant. This approach is consistent with the original research validating the use of the SAET for cultivating social affiliation in the laboratory with an individual with psychosis (McCarthy et al., 2018) and aligns with previous neuroimaging studies using the handholding paradigm (Coan et al., 2017).

As shown in Figure 1a, the SAET encompasses three partnership-building tasks, conducted in a fixed order. The conversation task (3.5 min) is a semistructured task designed to create familiarity, trust, and cooperation and set the stage for the more involved tasks (Declercq et al., 2013). The conversation task was video recorded for behavioral coding (see below). The implicit-fingertip-synchrony task (8 min) consists of coordinated movements with the dyad mirroring one another's hand movements (Yun et al., 2012). The task has been shown to reduce feelings of social anxiety (Yun et al., 2012). The team-building task (10 min) is designed to foster alliance, trust, and partnership between individuals (South et al., 2005). The participant and partner were

instructed to choose a team name and build a block structure in 10 min as part of a competition with another team. The participant's team was always given feedback that they "won," and the team was given two snacks to share; the partner always offered both snacks to the participant. To maximize social rapport, trust, and affiliation, the partner expressed praise, appreciation, and positive regard for the participant's contribution to the building task.

Subjective measures. Four measures were used to determine the subjective impact of the SAET on mood and affiliation with the experimental partner. Measures were completed immediately before and after the SAET paradigm. In both cases, the participant viewed a photograph of the experimental partner while completing the assessments.

The Positive Reactions to Partner Questionnaire (PRPQ; Llerena et al., 2012) is a seven-item measure of affiliative feelings toward the partner (e.g., "I trust my partner," "My partner seemed like a warm, caring person"; $\alpha s = .81-.84$). A conceptually unrelated eighth item ("I am concerned about what my partner thinks of me") was omitted. The PRPQ served as the primary measure of subjective affiliation with the partner. The PRPQ was reverse-scored; higher scores indicate greater affiliation.

The Willingness to Interact Questionnaire (WIQ; Coyne, 1976) is a six-item measure of willingness to engage in future interactions with the partner (e.g., "How willing would you be to invite your partner to a social event?"). The WIQ was reverse-scored; higher scores indicate a greater willingness to interact ($\alpha s = .87-.89$).

The Inclusion of the Other in the Self Scale (Aron et al., 1992) is a single-item measure of perceived closeness with the partner.

The Positive and Negative Affect Scales (PANAS; Watson et al., 1988) are 10-item measures of the intensity of positive ($\alpha s = .91-.93$) and negative ($\alpha s = .86-.89$) mood.

Objective behavioral measure. Video recordings of the SAET were objectively coded using a streamlined variant of the Facial Expression Coding System (FACES; Kring & Sloan, 1991). Raters were blind to clinical status and symptom ratings. Raters manually coded the number of positive expressions emitted by participants during the SAET conversation task. Interrater agreement was acceptable (intra-class correlation coefficient = .95, 95% confidence interval = [.93, .97]), as indexed by a mean-rating, one-way random-effects model (Koo & Li, 2016). Because of technical problems with the video recorder, usable FACES data were available for 99 participants.

Handholding fMRI paradigm

Procedures. As shown in Figure 1, we used a modified version of Coan's handholding fMRI paradigm to determine whether participants with more severe appetitive MAP deficits would derive smaller neural benefits (i.e., reduced dampening of threat-elicited activation) from holding the experimental partner's hand (Coan et al., 2017). During each scan, participants used their dominant hand to hold the hand of the experimental partner (partner); an unfamiliar, unseen, and unheard opposite-sex experimenter (stranger); or no one (alone). Participants completed up to six scans in alternating quasi-random order (two scans/handholding condition; counterbalanced across participants). Participants were continuously monitored using an MRI-compatible eye tracker (Eyelink 1000; SR Research, Ottawa, Ontario, Canada) and the AFNI real-time motion plugin (Cox, 1996).

Threat-anticipation trial structure. As shown in Figure 1, scans were acquired while participants completed a randomized event-related threat-anticipation task (nine trials/condition/scan), as in prior work by Coan and colleagues. Stimulus presentation was controlled using Presentation (Version 19.0; Neurobehavioral Systems, Berkeley, CA). To elicit robust anxiety, threat trials were variable in duration ($M = 15$ s, range = 7.5–22.5 s) and culminated in the presentation of negative or neutral reinforcers with equal likelihood ($p = 0.50$). In short, the presentation of the negative reinforcers was uncertain in both timing and likelihood. Safe trials were presented for fixed duration (mean duration matched across conditions) and culminated in the presentation of neutral reinforcers ($p = 1.0$). Threat was signaled by a red "X." Safe was signaled by a blue "O." Negative reinforcers included a noxious electric shock, mildly aversive auditory clip ("error buzzer"), and a photograph of an angry or fearful face. Neutral reinforcers included a just-perceptible electrical pulse, neutral auditory stimulus (440-Hz tone), and a photograph of a neutral face. A fixation cross was presented during intertrial intervals (3.2 s).

Procedures. Before scanning, staff explained the threat-anticipation task and confirmed full understanding. Benign and aversive electrical stimulation levels were individually titrated.

Benign stimulation. Participants were asked whether they could "reliably detect" a 16-V stimulus and whether it was "at all unpleasant." If the participant could not detect the stimulus, the voltage was increased by 2 V, and the process was repeated. If the participant indicated that the stimulus was unpleasant, the voltage was reduced by 2 V, and the process was repeated. The final level chosen served as the benign electrical reinforcer during the neuroimaging assessment ($M = 22.8$ V, $SD = 0.8$).

Aversive stimulation. Participants received a 75-V stimulus and were asked whether it was "as unpleasant as you are willing to tolerate." If the participant indicated that they were willing to tolerate more intense stimulation, the voltage was increased by 5 V, and the process was repeated. If the participant indicated that the stimulus was too intense, the voltage was reduced by 5 V, and the process was repeated. The final level chosen served as the negative electrical reinforcer during the neuroimaging assessment ($M = 85.4$ V, $SD = 27.9$).

Electrical reinforcers. Electrical reinforcers (100 ms; 2-ms pulses every 10 ms) were generated using an MRI-compatible, constant-voltage stimulator system (STMEPM-MRI; Biopac Systems, Inc., Goleta, CA) and delivered using MRI-compatible, disposable carbon electrodes (Biopac) attached to the final joint on the fourth and fifth digits of the nondominant hand.

Visual reinforcers. Trial-unique face stimuli (1.8 s) were adapted from prior work and consisted of photographs of unfamiliar male (50%) and female adults expressing unambiguous negative (fearful/angry) or neutral expressions (Hur et al., 2022). Color images were converted to gray scale, brightness was normalized, and images were masked to occlude nonfacial features (e.g., hair). Visual stimuli were digitally back-projected (Powerlite Pro G5550; Epson America, Inc., Long Beach, CA) onto a semi-opaque screen mounted at the head end of the scanner bore and viewed using a mirror mounted on the head coil.

Auditory reinforcers. Auditory reinforcers (1.8 s) were adapted from open-access online sources and delivered using an amplifier (PA-1 Whirlwind) with an in-line noise-reducing filter to ear buds (S14; Sensimetrics, Gloucester, MA) fitted with noise-reducing ear plugs (Hearing Components, Inc., St. Paul, MN).

Skin-conductance data acquisition

To confirm the validity of the threat manipulation, skin conductance was continuously acquired during each scan using a Biopac system (MP-150; Biopac Systems, Inc., Goleta, CA). Skin conductance (250 Hz; 0.05-Hz high-pass) was measured using MRI-compatible disposable electrodes (EL507) attached to the second and third digits of the nondominant hand.

MRI data acquisition

MRI data were acquired using a Siemens Magnetom TIM Trio 3 Tesla scanner (32-channel head-coil). Foam inserts were used to mitigate potential motion artifact. To further mitigate motion artifact, for the final 12

participants, a strip of medical tape was positioned just above the forehead, providing tactile feedback (Krause et al., 2019). Sagittal T1-weighted anatomical images were acquired using a magnetization prepared rapid acquisition gradient echo sequence (TR = 2,400 ms; TE = 2.01 ms; inversion = 1,060 ms; flip = 8°; slice thickness = 0.8 mm; in-plane = 0.8 mm²; matrix = 300 × 320; field of view = 240 × 256). A T2-weighted image was collected coplanar to the T1-weighted image (TR = 3,200 ms; TE = 564 ms; flip = 120°). To enhance resolution, a multiband sequence was used to collect oblique-axial echo planar imaging (EPI) volumes (acceleration = 6; TR = 1,250 ms; TE = 39.4 ms; flip = 36.4°; slice thickness = 2.2 mm, number of slices = 66; in-plane = 2.1875 mm²; matrix = 96 × 96; 301 volumes × 6 scans). Images were collected in the oblique axial plane (approximately -20° relative to the anterior commissure-posterior commissure [AC-PC] plane) to minimize potential susceptibility artifacts. The scanner automatically discarded seven volumes before the first recorded volume. To enable field-map correction, two oblique-axial spin echo (SE) images were collected in each of two opposing phase-encoding directions (rostral to caudal/caudal to rostral) coplanar to the functional volumes (TR = 7,220 ms; TE = 73 ms). Respiration and pulse were continuously measured during scanning using a respiration belt and photo-plethysmograph affixed to the first digit of the nondominant hand.

Skin-conductance data-processing pipeline

Skin-conductance data were processed using PsPM (Version 4.0.2) and in-house MATLAB (Version 9.9.0.1467703) code (Bach et al., 2018; Bach & Friston, 2013). Data were de-spiked using *filloutliers* (150-sample moving-median widow; modified Akima cubic Hermite interpolation). Each scan was then band-pass filtered (0.009–0.333 Hz), median centered, and down-sampled (4 Hz). Subject-specific skin-conductance response functions (SCRFs) were estimated by fitting the four parameters of the canonical SCRf (Bach et al., 2010) to the grand-average reinforcer response using *fmincon* and a cost function that maximized variance explained and penalized negative coefficients.

MRI data-processing pipeline

Methods were optimized to minimize spatial-normalization error and other potential noise sources. Methods were similar to those described in other recent reports by our group (e.g., Hur et al., 2022). Data were visually inspected before and after processing for quality assurance.

Anatomical data processing. T1-weighted images were inhomogeneity corrected using N4 (Tustison et al., 2010) and filtered using ANTS DenoiseImage (Avants et al., 2011). Brains were extracted using BEaST (Eskildsen et al., 2012) with brain-extracted and normalized reference brains from IXI (BIAC, 2022). Brain-extracted T1 images were normalized to a version of the brain-extracted 1-mm T1-weighted MNI152 (Version 6) template (Grabner et al., 2006) modified to remove extracerebral tissue. Normalization was performed using the diffeomorphic approach implemented in SyN (Version 2.3.4; Avants et al., 2011). T2-weighted images were rigidly coregistered with the corresponding T1 before normalization. The brain-extraction mask from the T1 was applied. Tissue priors were unwrapped to the native space of each T1 using the inverse of the diffeomorphic transformation (Lorio et al., 2016). Brain-extracted T1 and T2 images were segmented using native-space priors generated in FAST (Version 6.0.4; Jenkinson et al., 2012) for subsequent use in T1-EPI coregistration (see below).

Field-map data. SE images and topup were used to create field maps. Field maps were converted to radians, median-filtered, and smoothed (2 mm). The average of the motion- and distortion-corrected SE images was inhomogeneity corrected using N4 and masked to remove extracerebral voxels using 3dSkullStrip (Version 20.2.14).

Functional data processing. EPI files were de-spiked using 3dDespike, slice-time corrected to the TR center using 3dTshift, and motion corrected to the first volume and inhomogeneity corrected using ANTS (12-parameter affine). Transformations were saved in ITK-compatible format for subsequent use (McCormick et al., 2014). The first volume was extracted for EPI-T1 coregistration. The reference EPI volume was simultaneously coregistered with the corresponding T1-weighted image in native space and corrected for geometric distortions using boundary-based registration (Jenkinson et al., 2012). This step incorporated the previously created field map, undistorted SE, T1, white-matter image, and masks. To further minimize potential normalization error, the reference EPI volumes were spatially normalized to the MNI template using the transforms from the anatomical images, intensity standardized, and averaged to create a study-specific EPI template in MNI space (Dohmatob et al., 2018; Grabner et al., 2014; Huang et al., 2010). Normalized EPI reference volumes were then warped to the study-specific EPI template, providing a final degree of spatial tuning. The spatial transformations necessary to transform each EPI volume from native space to the reference EPI, from the reference EPI to the T1, from the T1 to the MNI template, and from the MNI template to the study-specific EPI template were concatenated and

applied to the processed EPI data in a single step to minimize incidental spatial blurring. Normalized EPI data were resampled (2 mm^3) using fifth-order b-splines and spatially smoothed (6-mm) using 3DblurInMask.

Skin-conductance modeling

Robust general linear models (GLMs) were used to separate electrodermal signals associated with the anticipation epochs from those evoked by other aspects of the threat-anticipation task (e.g., reinforcer delivery). Modeling was performed separately for each participant and scan using *robustfit*. Subject-specific SCRFs were convolved with rectangular regressors time-locked to the presentation of the reinforcers (separately for each trial type), visual masks, and rating prompts. To quantify skin-conductance level during the anticipation epochs, first-level residuals were averaged separately for each subject and condition.

fMRI modeling

Single-participant (“first-level”) GLMs were used to separate hemodynamic signals associated with the anticipatory periods of the threat-anticipation paradigm from those evoked by other aspects of the task. GLMs were implemented in SPM12 (Version 7771) using the default autoregressive model and the temporal band-pass filter set to the hemodynamic response function (HRF) and 128 s (Wellcome Centre for Human Neuroimaging, 2022). Threat signals were modeled using variable-duration rectangular (“box-car”) regressors time-locked to the anticipation epochs of threat trials and convolved with a canonical HRF and its temporal derivative. Periods corresponding to reinforcer presentation were simultaneously modeled using the same approach, separately for each combination of cue (threat/safe) and outcome (aversive/benign). Consistent with prior work (e.g., Hur et al., 2022), nuisance variates included estimates of volume-to-volume displacement, motion (6 parameters \times 3 lags), cerebrospinal fluid (CSF) signal, instantaneous pulse and respiration rates, and ICA-derived nuisance signals (e.g., brain edge, CSF edge, global motion, white matter; Pruim et al., 2015). Volumes with excessive volume-to-volume displacement ($> 0.5\text{ mm}$) and those during and immediately following aversive reinforcer delivery were censored.

Analytic strategy

Overview. The overarching goal of this study was to test the hypothesis that individuals with more severe MAP symptoms would derive reduced benefits from affiliation

under controlled laboratory conditions both outside and inside of the MRI scanner. Analyses were implemented in IBM SPSS (Version 27.0.1.0) and SPM12 (Version 6678; Wellcome Centre for Human Neuroimaging, 2022). Some figures were created using MRICron and MRICroGL (Rorden, 2019, 2021). Clusters and local maxima were labeled using standard atlases (Desikan et al., 2006; Frazier et al., 2005; Mai et al., 2015), supplemented by relevant neuro-anatomical descriptions (Bedini & Baldauf, 2021).

SAET confirmatory testing. Paired Student’s *t* tests were used to confirm that on average, the SAET enhanced mood and feelings of affiliation toward the experimental partner.

SAET hypothesis testing and exploratory analyses. Regressions were used to test the central hypothesis that clinician-rated MAP deficits (CAINS-MAP) would be associated with diminished affiliation with the experimental partner following the SAET. To test the impact of MAP deficits on anticipatory responses, parallel analyses were conducted using measures collected immediately before the SAET. To clarify specificity, a series of multiple regressions was used to determine whether MAP deficits explain unique variance in SAET reactivity over and above variation in clinician-rated positive symptoms, depression/anxiety, and agitation. As detailed in the Supplemental Material available online, regression analyses also enabled us to explore (a) the possibility that MAP deficits explain variance in SAET reactivity while controlling for categorical diagnostic status (mean-centered binary variable) and (b) relations with social-network size and daily interpersonal functioning.

Handholding paradigm confirmatory testing. A paired Student’s *t* test was used to confirm that the handholding paradigm elicited heightened psychophysiological arousal, indexed by skin conductance during the anticipatory epoch of threat and safe trials. A whole-brain voxelwise (“second-level”) repeated measures (“random effects”) GLM was used to confirm that threat (relative to safe) activated key regions of the canonical threat-anticipation network (Hur et al., 2022; Shackman & Fox, 2021). Significance was assessed using $p < .05$, whole-brain familywise error (FWE) corrected for cluster extent and cluster-defining threshold of $p < .001$ (Eklund et al., 2016).

Handholding paradigm hypothesis testing and exploratory analyses. We anticipated that individuals with more severe MAP deficits would derive diminished neural benefits—that is, reduced dampening of threat-elicited activation—from holding the partner’s hand compared with holding no hand at all (Coan et al., 2017). To test this hypothesis, we first computed voxelwise threat-potential contrasts (threat relative to unmodeled safe

Table 3. Response to the Social-Affiliation-Enhancement Task

Variable	Before SAET Mean (SD)	After SAET Mean (SD)	<i>t</i>	<i>p</i>	Cohen's <i>d</i>
Affiliation (PRPQ) ^a	28.85 (4.93)	31.87 (3.43)	7.85	< .001	0.76
Willingness to Interact (WIQ) ^a	20.56 (5.89)	24.93 (4.81)	10.49	< .001	1.01
Closeness (IOSS)	2.48 (1.78)	5.06 (1.70)	15.92	< .001	1.53
Positive affect (PANAS-PA)	34.57 (9.33)	37.16 (9.07)	4.74	< .001	0.46
Negative affect (PANAS-NA)	13.17 (4.40)	12.25 (4.39)	-3.39	< .001	-0.33

Note: *N* = 108. IOSS = Inclusion of the Other in the Self Scale; NA = negative affect; PA = positive affect; PANAS = Positive and Negative Affect Scales; PRPQ = Positive Reactions to Partner Questionnaire; SAET = social-affiliation-enhancement task; WIQ = Willingness to Interact Questionnaire.

^a*N* = 107 because of missing pre-SAET data for one participant.

anticipation) separately for the partner and alone conditions. We then computed the difference between the two contrasts (partner minus alone), equivalent to a single-*df* interaction contrast (Valence [Threat, Safe] × Handholding [Partner, Alone]). This contrast provides an overall neural index of handholding benefit; low values indicate increased benefits of holding the partner's hand (i.e., dampened threat potentiation relative to the alone condition). With this key contrast as the outcome, we used a whole-brain voxelwise regression to identify regions where the degree of handholding benefit covaried with clinician-rated MAP deficits (CAINS-MAP) while controlling for potential nuisance variation in mean-centered age and biological sex ($p < .05$, whole-brain FWE corrected). Robust regression (Tukey's bi-weight) was used to confirm that results were not unduly influenced by outlying observations (Wager et al., 2005). In addition, to clarify specificity of the CAINS-MAP analysis, we explored the possibility of parallel associations for clinician-rated affective flattening/alogia (CAINS-Expression) and for the stranger condition of the handholding paradigm (Fig. 1).

Paralleling the SAET behavioral analyses summarized above, a series of voxelwise multiple regressions was used to confirm that MAP deficits continued to explain significant variance in the neural index of handholding benefits (see above) over and above variation in clinician-rated positive symptoms, depression/anxiety, and agitation and to explore the possibility that MAP deficits continued to explain significant variance in neural reactivity while controlling for categorical diagnostic status (mean-centered binary variable). These follow-up specificity tests were performed separately for each of the four relevant clinical variables within the subset of voxels showing whole-brain significant associations with CAINS-MAP ($p < .05$, FWE corrected for the number of voxels tested).

Prior work focused on spouses and other naturally occurring social partnerships in psychiatrically healthy samples suggests that affiliative handholding dampens threat reactivity relative to the alone control condition (Coan et al., 2017). Given the hypothesized impact of MAP deficits in our transdiagnostic sample (where

77.5% of fMRI participants were diagnosed with psychotic disorders) and the potentially weakened effect of using an experimenter partner (compared with longer-term romantic partners and friends in Coan et al., 2017), we did not expect to observe this sort of simple mean difference in the present study. Nevertheless, we report exploratory whole-brain voxelwise analyses of the average between-conditions differences in threat potentiation (e.g., partner vs. alone; $p < .05$, whole-brain FWE corrected).

Results

The SAET robustly enhances affiliation with the experimental partner

In the first phase of the laboratory session, participants completed the SAET (Fig. 1). As a precursor to hypothesis testing, we used a series of Student's *t* tests to confirm that the SAET (Fig. 1) enhanced affiliative feelings, willingness to interact, perceived closeness, and positive affect while decreasing negative affect ($ps < .05$; Table 3). Across measures, effects were substantial, underscoring the validity of the task (mean Cohen's $|d| = 0.82$).

Negative symptoms undermine the emotional benefits of positive social interaction

A series of regressions was used to test whether individuals with more severe MAP symptoms (CAINS-MAP) show diminished perceptions and signs of affiliation with the de novo experimental partner in the laboratory (assessed both before and immediately following the SAET). As shown in Table 4, individuals with more severe negative symptoms (CAINS-MAP and CAINS-Expression) reported significantly lower feelings of affiliation and positive affect both in anticipation of and immediately following the social interaction ($ps < .05$). Relations with the other post-SAET measures (e.g.,

Table 4. Symptom Correlates of Responses to the Social-Affiliation-Enhancement Task

Symptom	Affiliation (PRPQ)		Willingness to interact (WIQ)		Closeness (IOSS)		PANAS-PA		PANAS-NA		FACES positive ^b
	Before SAET ^a	After SAET	Before SAET ^a	After SAET	Before SAET	After SAET	Before SAET	After SAET	Before SAET	After SAET	During SAET
Motivation and pleasure (CAINS)	-0.22*	-0.33***	-0.01	-0.14	-0.03	-0.10	-0.15	-0.22*	0.19	.13	-0.27**
Expression (CAINS)	-0.24*	-0.19*	-0.11	-0.04	0.01	-0.02	-0.22*	-0.21*	0.24*	.16	-0.31***
Social anhedonia (SAS-B)	-0.18	-0.25*	0.07	-0.02	-0.08	-0.02	-0.09	-0.10	0.27**	0.29**	-0.23*
Positive symptoms (BPRS)	-0.05	0.08	-0.01	0.09	0.02	0.08	0.05	0.06	0.23*	0.20*	-0.03
Depression/anxiety (BPRS)	-0.04	0.03	-0.10	-0.03	0.02	-0.02	-0.02	0.01	0.28**	0.19*	-0.05
Agitation (BPRS)	-0.12	-0.03	0.00	-0.08	0.12	-0.09	-0.01	-0.09	0.21*	.17	-0.06

Note: $N = 108$. Statistically significant correlates are shown in bold. BPRS = Brief Psychiatric Rating Scale; CAINS = Clinical Assessment Interview for Negative Symptoms; FACES = Facial Expression Coding System; NA = negative affect; PA = positive affect; PANAS = Positive and Negative Affect Scales; PRPQ = Positive Reactions to Partner Questionnaire; SAET = social-affiliation-enhancement task; SAS-B = Social Anhedonia Scale-Brief; WIQ = Willingness to Interact Questionnaire; IOSS = Inclusion of the Other in the Self Scale.

^a $N = 107$ because of missing pre-SAET data for one participant.

^b $N = 99$.

* $p < .05$. ** $p < .01$. *** $p < .005$.

willingness to interact) were in the expected direction but did not reach significance.

Participants were unobtrusively videotaped during the SAET, which enabled us to quantify the number of positive facial expressions—an objective behavioral index of affiliation and positive mood—emitted while conversing with the partner. Regression analyses revealed that participants with more severe social MAP deficits (CAINS-MAP) emitted fewer positive expressions during the SAET (Table 4; $p < .05$). A broadly similar pattern of associations was evident for clinician-rated expressivity symptoms (CAINS-Expression) and self-reported social anhedonia (SAS-B), indicating sensible convergence across informants and scales (Table 4). However, variation in clinician-rated positive symptoms, depression/anxiety, and agitation (BPRS) were unrelated to partner affiliation, suggesting a degree of specificity. Consistent with this general pattern, in a series of simultaneous regression models, CAINS-MAP remained associated with post-SAET perceptions—including reduced affiliation (PRPQ: partial correlation [pr] = -0.35 , $p < .001$), diminished positive affect (PANAS-Positive Affect: $pr = -0.20$, $p = .04$), and fewer positive facial expressions ($pr = -0.26$, $p = .01$) during the interaction—while controlling for the three BPRS scales. Similar results were evident for CAINS-Expression (PRPQ: $pr = -0.21$, $p = .04$; PANAS-Positive Affect: $pr = -0.22$, $p = .03$; facial expressions: $pr = -0.31$, $p = .002$).

Collectively, these observations demonstrate that negative symptoms are associated with diminished socio-emotional benefits under controlled conditions in the laboratory, as indexed by both subjective perceptions and objective behavioral signs. All of the key postinteraction associations remained significant while controlling for categorical diagnostic status. The one exception was that CAINS-Expression was no longer associated with self-reported postinteraction affiliation while controlling for diagnostic status. Overall, these results underscore the added predictive value of dimensional variation in negative symptoms (see Supplementary Results in the Supplemental Material). Moreover, exploratory analyses indicated that individuals who experienced lower levels of affiliation and positive affect during the SAET tended to have smaller social networks and report reduced interpersonal functioning in their daily lives, reinforcing both the validity and the real-world relevance of our laboratory assessments of affiliation (see Table S1 in the Supplemental Material).

Threat had the intended consequences on physiological arousal and brain function

As a precursor to hypothesis testing, we confirmed that the threat-anticipation component of the handholding

fMRI paradigm had the intended impact on physiological arousal (skin conductance) and brain function (fMRI activation). As expected, threat anticipation was associated with significantly elevated signs of arousal, $t(68) = 4.07$, $p < .001$. Likewise, a whole-brain voxelwise GLM confirmed that threat anticipation was associated with significant activation across a widely distributed set of cortical regions previously implicated in the expression and regulation of human fear and anxiety (Shackman & Fox, 2021), including the midcingulate cortex, anterior insula, and frontal operculum ($p < .05$, whole-brain FWE corrected; Fig. 2a; Tables S2–S3 in the Supplemental Material). Taken together, these observations reinforce the validity of our experimental threat manipulation. In contrast to prior work focused on naturally occurring social partners (e.g., spouses) in psychiatrically healthy samples (Coan et al., 2006, 2017), whole-brain voxelwise analyses did not uncover significant mean differences between any of the three handholding conditions.

MAP deficits undermine the neuroregulatory benefits of handholding

We anticipated that individuals with more severe MAP deficits would derive diminished neural benefits—that is, reduced dampening of threat-elicited activation—from holding the partner's hand compared with the alone control condition. To test this, we first computed voxelwise threat-potential contrasts (threat minus safety) separately for the partner and alone conditions. We then computed the difference between the two contrasts (partner minus alone). This “double-difference” contrast provides an overall neural index of handholding benefit; high values indicate decreased benefits of holding the partner's hand (i.e., dampened threat potentiation relative to the alone condition). We then used a whole-brain voxelwise regression to identify regions where the degree of handholding benefit covaried with clinician-rated MAP deficits. As shown in Figures 2b and 2c, results revealed two dorsal frontoparietal clusters: one in the region of the frontal eye field (FEF), at the posterior margin of the superior frontal sulcus (pSFS), and the other in the intraparietal sulcus (IPS). A third cluster was situated more ventrally, in the rostral portion of the supramarginal gyrus (SMG), where it abuts the postcentral sulcus (PCS). In each of these regions, individuals with more severe MAP symptoms derived smaller benefits from holding the partner's hand ($p < .05$, whole-brain FWE corrected; Figs. 2d–2f; Table S4 in the Supplemental Material). Nearly identical associations were evident using a robust regression approach, which attenuates the influence of unduly influential observations (Figs. 2d–2f). Significant associations were not evident for either clinician-rated

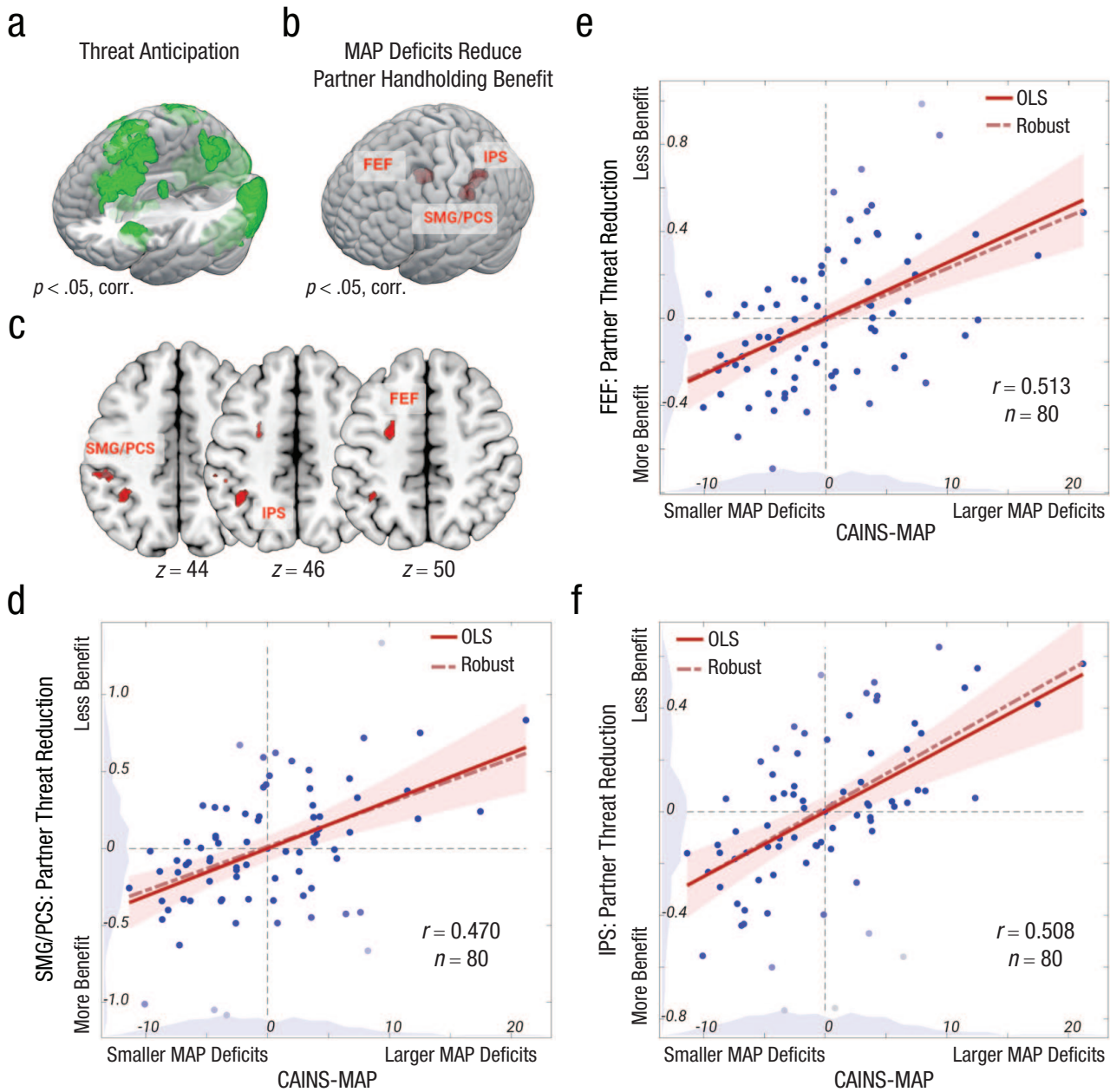


Fig. 2. Motivation and pleasure deficits undermine the neural benefits of social affiliation. (a) Threat anticipation. A whole-brain voxelwise general linear model confirmed that threat (relative to safe) anticipation was associated with significant activation in regions previously implicated in the expression and regulation of fear and anxiety ($p < .05$, whole-brain corrected for cluster extent). (b, c) Motivation and pleasure (MAP) deficits reduce partner handholding benefit. A whole-brain voxelwise regression was used to identify regions where the degree of handholding benefit covaried with clinician-rated MAP symptoms. Results revealed significant clusters in the left putative human frontal eye field (FEF) region, intraparietal sulcus (IPS), and supramarginal gyrus (SMG) where it abuts the postcentral sulcus (PCS; $p < .05$, whole-brain corrected; Table S4 in the Supplemental Material available online). (d) SMG/PCS. (e) FEF. (f) IPS. Blue circles represent cases. Solid red line indicates the ordinary least squares (OLS) regression slope. Broken orange line indicates the robust regression slope. Purple humps along the axes depict the smoothed density distributions for each variable. CAINS = Clinical Assessment Interview for Negative Symptoms.

affective flattening/alogia (CAINS-Expression) or the stranger condition, suggesting a degree of specificity. Follow-up analyses confirmed that the association between FEF, IPS, and SMG/PCS activation and clinician-related MAP deficits remained evident when controlling

for variation in clinician-rated positive symptoms, depression/anxiety, or agitation (BPRS; $p < .05$, FWE corrected for the number of voxels tested; Tables S5–S7 in the Supplemental Material). Paralleling the SAET behavioral results (see above), these associations also

remained significant when controlling for diagnostic status (Table S8 in the Supplemental Material). In short, MAP deficits appear to undermine the stress-buffering neural benefits of affiliation.

FEF and IPS are often conceptualized as hubs within a larger functional circuit, the dorsal attention network (DAN) or “dorsal frontoparietal network” (Uddin et al., 2019). Consistent with this possibility, supplementary analyses confirmed that the frontoparietal peaks identified by our analyses (Table S4 in the Supplemental Material) show robust coupling in the absence of an explicit task (intrinsic functional connectivity) and are consistently coactivated across a range of experimental challenges (Yarkoni et al., 2011; Supplementary Results in the Supplemental Material).

Discussion

Among individuals living with psychosis-spectrum disorders, social amotivation and anhedonia are common, can be debilitating, and are often challenging to treat, underscoring the importance of understanding the factors that promote affiliative deficits (Blanchard et al., 2017; Kalin et al., 2015; Kirkpatrick et al., 2006; Kring et al., 2013; Moe et al., 2021; Rocca et al., 2014). Here, we leveraged a comprehensive multimethod approach to test the overarching hypothesis that MAP deficits—assessed using “gold-standard” clinician ratings—undermine the stress-buffering neural benefits of affiliative touch (Fig. 1). Outside of the scanner, participants completed the SAET, a set of procedures for cultivating affiliation with an experimental partner. On average, the SAET produced robust increases in perceived affiliation, willingness to interact with the partner, perceived closeness, and positive mood (Table 3), replicating and extending prior work by our group (Blanchard et al., 2015; McCarthy et al., 2018) and consistent with more naturalistic observations (Clark & Watson, 1988; Shackman et al., 2018; Watson, 1988; Watson et al., 1992). Yet individuals with more severe clinician-rated negative symptoms derived smaller emotional benefits from the partner, as indexed by subjective report and objective facial behavior (Table 4). Following the conclusion of the SAET, we used the handholding fMRI paradigm—which combines a well-established threat-anticipation manipulation with varying degrees of affiliative touch—to determine whether MAP deficits also undermine the social regulation of threat-evoked neural activity. On average, the anticipation of aversive stimulation amplified psychophysiological skin-conductance arousal and recruited a variety of cortical regions previously implicated in the expression and regulation of fear and anxiety (e.g., anterior insula; Fig. 2a). Paralleling the SAET results, individuals with more severe MAP

deficits (but not expressive symptoms) showed diminished neural benefits—reduced dampening of threat-elicited activation—from holding the partner’s hand in several frontoparietal regions, including the FEF and IPS (Figs. 2d–2f; Table S4 in the Supplemental Material). In short, MAP symptoms disrupt the acute emotional and neuroregulatory benefits of affiliation.

Negative symptoms undermine the acute emotional benefits of affiliation

Individuals with psychosis-spectrum disorders often have impoverished social networks, and even when available, social relationships are often lower in quality (Cloutier et al., 2021; Green et al., 2018; Izon et al., 2018; Koutra et al., 2014, 2016). Indeed, most of the participants in the present study were either divorced or had never married by midlife (Table 1), consistent with other work (e.g., Olsson et al., 2016). The SAET provides a useful tool for rigorously quantifying individual differences in affiliative capacity under well-controlled laboratory conditions (McCarthy et al., 2018). The present results show that participants with more severe negative symptoms experienced diminished feelings of partner affiliation and lower levels of positive affect both in anticipation of and in response to the SAET. These subjective reports are complemented by objective measures of facial affect, which showed that individuals with more severe negative symptoms also emitted fewer positive expressions while interacting with the partner. Negative symptoms continued to show significant associations with SAET reactivity after controlling for other clinician-rated symptoms or diagnostic status based on the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association, 2013). Taken together, these observations reinforce the hypothesis that MAP deficits can undermine the emotional responses typically experienced from positive social contact (Hur et al., 2020; Shackman et al., 2018). The findings also indicate that expressive negative symptoms were related to diminished affiliative responses. The results of our exploratory analyses, which show that individuals who experienced lower levels of affiliation and positive affect during the SAET have smaller social networks and diminished levels of interpersonal functioning in the community, reinforce the real-world relevance of SAET reactivity. A key challenge for the future will be determining whether SAET reactivity is prognostic of longer-term social and clinical outcomes.

The behavioral findings from the SAET are relevant to considering the role of anticipatory pleasure deficits in negative symptoms and impairments in affiliation (Engel et al., 2016; Gard et al., 2007). Our results

indicated that negative symptoms are associated with diminished positive appraisals of an affiliative partner and lower self-reported positive affect, and this was evident both in anticipation of and immediately following the semistructured social interaction. These associations remained significant when controlling for nonnegative symptoms, suggesting a degree of specificity, and when controlling for diagnostic status, reinforcing the added value of our transdiagnostic dimensional approach. These observations extend prior work focused on postinteraction correlates in schizophrenia using the SAET (McCarthy et al., 2018) and a video-based affiliation task (Blanchard et al., 2015). Examination of daily experiences using ecological momentary assessment have found that more severe MAP symptoms are associated with less time spent with others and diminished positive affect in unstructured social contexts, similar to our laboratory findings (Kasanova et al., 2018). Thus, deficits in both anticipatory and consummatory pleasure may contribute to aberrant affiliative interactions in individuals with psychosis-spectrum disorders.

MAP symptoms undermine the acute neuroregulatory benefits of affiliation

Humans routinely seek the company of friends and family in response to stressors (Cottrell & Epley, 1977), and there is ample evidence that intimate social partners play a critical role in buffering stress and regulating negative affect (Bolger & Eckenrode, 1991; Buote et al., 2007; Coan & Sbarra, 2015; Marroquin, 2011; Myers, 1999; Zaki & Williams, 2013). Work in psychiatrically healthy samples demonstrates that affiliation buffers the neural impact of stressors; participants reporting higher levels of social support derive greater neural benefits (dampened threat reactivity) from holding the hand of their spouse or other well-established social partners (Coan et al., 2017). Such a “main effect” of affiliative touch was not evident in the present sample. This may reflect the use of an experimental affiliative partner rather than long-term romantic partners or friends (Coan et al., 2017). It seems likely that this nil effect also reflects a consequence of the substantial MAP deficits that characterize our sample, which largely comprised individuals with psychotic disorders. Consistent with this hypothesis, results demonstrated that individuals with more severe MAP deficits showed reduced benefits—manifesting as diminished dampening of threat-elicited activation—from holding the partner’s hand in several regions, including the FEF and IPS, key nodes in the DAN (Fig. 2). Parallel associations were not evident when holding the stranger’s hand, consistent with work by Coan and colleagues (2017). Key brain-behavior associations were not evident for

expressivity symptoms, and they remained significant when controlling for clinician-rated agitation, depression/anxiety, and positive symptoms. Consistent with our transdiagnostic conceptual framework, they also remained significant when controlling for diagnostic status. Collectively, these observations indicate that MAP symptoms undermine the acute neuroregulatory benefits of affiliation in psychosis. Interpersonal emotion regulation is widely conceptualized as a key motivation for affiliation (Coan & Sbarra, 2015; Cohen, 2004; Cottrell & Epley, 1977; Williams et al., 2018), and it will be useful to determine whether individuals who derive smaller neural benefits from affiliative touch are also less likely to seek out social experiences in their daily lives (Kasanova et al., 2018).

Prior work suggests that the regulatory impact of affiliation on distress is likely to be complex and multifaceted (Pontari, 2009). Like other fMRI studies of the handholding paradigm, our results do not directly address the psychological processes influenced by affiliative touch. Nevertheless, converging lines of neuroimaging and mechanistic evidence indicate that the DAN plays a crucial role in the goal-directed allocation of attention to stimuli and responses (Armstrong & Moore, 2007; Buschman & Kastner, 2015; Corbetta & Shulman, 2002; Moore & Armstrong, 2003; Schafer & Moore, 2011; Vernet et al., 2014). The DAN has been implicated in a wide variety of attentionally demanding tasks, including sustained states of vigilant attention (Esterman et al., 2012) and the deliberate regulation of negative mood (Buhle et al., 2014; Morawetz et al., 2020). As Coan and colleagues (2017) previously hypothesized, these observations raise two possibilities. One possibility is that affiliative touch directly dampens threat reactivity. The anticipation of uncertain threat—a central feature of the handholding paradigm (Fig. 1)—elicits a sustained state of heightened vigilance for potentially threat-relevant information (Shackman et al., 2011). The reduction in DAN activity that we observed among individuals with less severe MAP deficits (Fig. 2) is consistent with a reduction in vigilance. A second possibility is that the interpersonal regulation of stress reduces the need to self-regulate and deploy attention-demanding reappraisal strategies. Both hypotheses are consistent with the ecologically grounded social-baseline theory, which posits that the presence of social resources reduces the need to scan the environment for potential danger and, in turn, lessens the need to self-regulate distress (Beckes & Coan, 2011; Coan & Maresh, 2014; Coan & Sbarra, 2015). Adjudicating between these alternatives remains an important avenue for future research, with implications for understanding the nature of the social-regulatory deficits we identified in individuals with more severe MAP deficits.

Limitations

There are several limitations to the present study. First, although our focus on an opposite-sex experimental partner has a number of inferential advantages, it will be important to extend the present approach to naturally occurring relationships with both sexes. Second, we lacked the power to investigate fine-grained differences across diagnoses (e.g., schizophrenia vs. borderline personality disorder) or between clinical and community participants. Future research is needed to extend the present approach to other disorders marked by prominent affiliative deficits (e.g., social anxiety disorder). Third, clinical participants were receiving a range of medications, with uncertain impacts on the variables under study (although some studies suggest that deficits in psychotic disorders are present across medication status; e.g., Moran et al., 2022). Because medication types and dosages were clinically determined and we lack information on adherence, we are not able to determine what impact, if any, medication may have (Blanchard & Neale, 1992). Fourth, selection criteria (e.g., ability to tolerate fMRI procedures, no current substance use disorder, ability to meet weight and size limits of the MRI) may covary with clinical characteristics of psychosis and possibly contribute to underrepresentation of some characteristics. Psychotic disorders are characterized by high comorbidity with anxiety disorders (Braga et al., 2013), and there is some evidence that participants of fMRI studies may be biased toward lower levels of trait anxiety compared with behavior-only studies (Charpentier et al., 2021). People with psychotic disorders also have high rates of substance use disorders (Brunette et al., 2018; Sara et al., 2014) and obesity (Bak et al., 2014; Foley & Morley, 2011; Wirshing, 2004). Fifth, although our primary measure of MAP deficits (CAINS-MAP) is both psychometrically sound and well validated, it is a multidimensional instrument encompassing several facets of social and nonsocial reward, including appetitive motivation and hedonic pleasure. Unpacking this conceptual complexity is an important avenue for future research on psychosis and other mental illnesses. Finally, we acknowledge that we did not preregister our approach, outcomes, or predictions (e.g., see Gonzales & Cunningham, 2015). We encourage future studies to do so as a guard against biases and questionable research practices (Fox et al., 2018; Krypotos et al., 2019).

Conclusions

The present results indicate that negative symptoms—both MAP and expressive symptoms—are associated with diminished feelings and signs of affiliation with an experimental social partner. Our neuroimaging results

show that individuals with more severe MAP deficits also derive diminished neural benefits, that is, reduced dampening of threat-related activation, from affiliative touch. These findings provide fresh insights into the diminished social motivation that often marks individuals with psychosis-spectrum disorders. Further research is needed to examine the factors that may contribute to experiential affiliative deficits in psychosis-spectrum disorders. From a clinical perspective, difficulties experiencing the emotion-regulatory effects of social contact could exacerbate the stress sensitivity that characterizes psychosis-spectrum disorders (Myin-Germeys & van Os, 2007; Reininghaus et al., 2016). Our findings also suggest potential clinical benefits of treatments that specifically target these experiential deficits. Psychosocial treatments have been developed that could hold promise to enhance affiliative experience, including compassion training (e.g., Braehler et al., 2013; Johnson et al., 2011; Martins et al., 2018) and treatments intended to improve positive affect (and thus possibly motivation and affiliation) in schizophrenia (Favrod, Nguyen, Chaix, et al., 2019; Favrod, Nguyen, Tronche, et al., 2019) and other disorders (e.g., Craske et al., 2019).

Transparency

Action Editor: Vina Goghari

Editor: Jennifer L. Tackett

Author Contributions

Jack J. Blanchard and Jason F. Smith contributed equally.

Jack J. Blanchard: Conceptualization; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Writing – original draft; Writing – review & editing.

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Declaration of Conflicting Interests

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

Funding

This research was supported by National Institute of Mental Health R01-MH110462 (to J. J. Blanchard) and additional

support by other grants from the National Institutes of Health (AA030042, DA050808, MH102870, MH121409, MH131264).

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Acknowledgments

We acknowledge assistance and critical feedback from members of the Laboratory of Emotion and Psychopathology and the staff of the Maryland Neuroimaging Center.

Supplemental Material

Additional supporting information can be found at <http://journals.sagepub.com/doi/suppl/10.1177/21677026241227886>

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Supplementary Results:

Motivation and Pleasure Deficits Undermine the Benefits of Social Affiliation in Psychosis

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Dimensional Variation in Negative Symptoms Explain Variance in Social Affiliation not Captured by Diagnostic Status

The results detailed in **Table 4** in the main report show that individuals characterized by more severe negative symptoms (CAINS-MAP and CAINS-Expression) show diminished social affiliation in the laboratory, as indexed by subjective perceptions and objective behavioral signs. To clarify the predictive value of dimensional variation in negative symptoms, we performed a series of exploratory regression analyses that controlled for binary variation in diagnostic status (i.e., cases vs. controls). Results demonstrated that individuals with more severe social motivation and pleasure deficits (CAINS-MAP) experienced diminished feelings of affiliation, both before ($pr=-0.25$, $p<0.005$) and following the semi-structured interaction ($pr=-0.32$, $p<0.005$); reported lower levels of positive affect following the interaction ($pr=-0.20$, $p<0.04$); and emitted fewer positive facial expressions during the interaction ($pr=-.23$, $p<.05$). When controlling for diagnostic status, more severe CAINS-Expression symptoms remained significantly associated with diminished feelings of affiliation before the interaction ($pr=-0.28$, $p<0.005$) but not after the interaction ($pr = -0.17$, ns); lower levels of positive affect, both before ($pr=-0.26$, $p<0.01$) and following the interaction ($pr = -0.19$, $p<0.05$); and displayed fewer positive facial expressions during the SAET ($pr=-0.27$, $p<0.01$). These findings demonstrate that dimensional variation in clinician-rated negative symptoms capture unique variance in social affiliative deficits, over-and-above that explained by traditional DSM-5 diagnoses.

Table S1. Real-World Correlates of the SAET (N=108)

<u>Real-World Social Function</u>	<u>Affiliation (PRPQ)</u>	<u>Willingness to Interact (WIQ)</u>	<u>Closeness (IOSS)</u>	<u>PANAS-PA</u>	<u>PANAS-NA</u>	<u>FACES Positive Expressions^a</u>
Social Network Size (SNI)	0.27***	0.11	0.10	0.22*	-0.03	0.14
Interpersonal Functioning (SLOF)	0.39***	0.28***	0.23*	0.36***	0.24***	0.09

^aN=99. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$. Abbreviations—FACES, Facial Expression Coding System; IOSS, Inclusion of the Other in the Self Scale; NA, negative affect; PA, positive affect; PANAS, Positive and Negative Affect Scales; PRPQ, Positive Reactions to Partner Questionnaire; SAET, Social Affiliation Enhancement Task; SLOF, Specific Levels of Functioning; SNI, Social Network Index; WIQ, Willingness to Interact Questionnaire.

Supplementary Table S2. Descriptive statistics for clusters and local extrema showing greater activation during the anticipation of Threat compared to Safe ($p < 0.05$, whole-brain FWE for cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
37,672	R Lateral Occipital Cortex, inferior	12.39	34	-90	-6
	R Occipital Pole	12.71	34	-92	-10
	L Temporal Occipital Fusiform Cortex	5.33	-42	-60	-16
	L Lateral Occipital Cortex, inferior	11.54	-32	-88	0
37,416	L Occipital Pole	10.77	-28	-92	-6
23,128	L Paracingulate Gyrus (<i>midcingulate cortex</i>)	4.60	-10	30	30
	Paracingulate Gyrus (<i>midcingulate cortex</i>)	5.33	0	28	34
	Cingulate Gyrus, anterior (<i>midcingulate cortex</i>)	6.54	0	18	34
	L Juxtapositional Lobule Cortex	4.57	-2	6	54
	R Juxtapositional Lobule Cortex	5.32	2	6	60
	L Superior Frontal Gyrus	5.42	-16	-2	68
	R Superior Frontal Gyrus	6.23	18	-6	72
5,264	R Postcentral Gyrus	3.39	36	-38	68
	R Superior Parietal Lobule	6.30	22	-46	70
	R Lateral Occipital Cortex, superior division/ Superior Parietal Lobule	4.71	26	-56	68
4,520	R Frontal Operculum Cortex	5.48	36	24	6
	R Temporal Pole	5.21	58	14	-4
	R Central Opercular Cortex	4.58	54	6	2
3,824	L Superior Parietal Lobule	4.40	-32	-52	54
	L Lateral Occipital Cortex, superior	4.39	-28	-62	58
3,096	R Right Putamen	5.62	22	6	-8
	R Right Pallidum	4.68	16	4	0
2,176	L Frontal Orbital Cortex	5.05	-30	28	-2
	L Frontal Operculum Cortex	5.59	-32	22	8
1,488	R Precentral Gyrus	4.91	50	0	50
728	L Left Caudate	4.23	-16	16	-4
	L Left Putamen	4.10	-28	4	-6
696	L Precentral Gyrus	4.39	-40	-4	48

Abbreviations—L, left; R, right,

Supplementary Table S3. Descriptive statistics for clusters and local extrema showing greater activation during the anticipation of Safe compared to Threat ($p < 0.05$, whole-brain FWE corrected for cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
53,984	R Cingulate Gyrus, posterior	3.73	16	-44	0
	R Angular Gyrus	3.82	60	-60	16
	L Lingual Gyrus	7.74	-8	-66	2
	R Lateral Occipital Cortex, superior	4.99	48	-70	24
	R Lingual Gyrus	7.64	6	-72	4
	L Cuneal Cortex	4.69	-16	-80	28
	R Intracalcarine Cortex	8.92	14	-80	10
	R Cuneal Cortex	6.94	12	-86	22
53,984	L Occipital Pole	6.44	-6	-92	18
5,040	L Supramarginal Gyrus, posterior	4.02	-60	-44	10
	L Middle Temporal Gyrus, temporooccipital	5.01	-54	-52	6
	L Angular Gyrus	4.10	-46	-54	16
	L Lateral Occipital Cortex, inferior	4.84	-40	-66	14
	L Lateral Occipital Cortex, superior	4.74	-32	-72	44
1,152	L Middle Frontal Gyrus	4.95	-50	32	22
1,136	R Middle Frontal Gyrus	4.34	36	20	58
824	L Middle Temporal Gyrus, temporooccipital	4.50	-64	-52	-10

Abbreviations—L, left; R, right,

Supplementary Table S4. Descriptive statistics for clusters and local extrema where the neural 'benefit' of holding the Partner's hand covaries with CAINS-MAP symptoms ($p < 0.05$, whole-brain FWE corrected for cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
1,176	L Putative Frontal Eye Field (<i>Posterior Superior Frontal Sulcus, Posterior Superior Frontal Gyrus, Dorsal Precentral Sulcus</i>)	5.12	-26	-6	50
1,008	L Anterior Supramarginal Gyrus (<i>Ventral Bank of the Postcentral Sulcus</i>)	4.57	-46	-34	42
1,000	L Intraparietal Sulcus (<i>Superior Parietal Lobule</i>)	4.52	-36	-46	46

Note: See the main report for a detailed description of the analytic strategy. Positive values indicate decreased benefits of holding the Partner's hand (i.e., dampened threat potentiation relative to the Alone condition). Abbreviations—L, left.

Supplementary Table S5. Descriptive statistics for clusters and local extrema where the neural ‘benefit’ of holding the Partner’s hand covaries with CAINS-MAP symptoms, while controlling for clinician-rated positive symptoms (BPRS; $p < 0.05$, FWE corrected for the number of voxels tested and cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
488	L Putative Frontal Eye Field	4.59	-26	-6	52
504	L Anterior Supramarginal Gyrus	4.55	-44	-32	40
416	L Intraparietal Sulcus	4.30	-36	-46	46

Note: See the main report for a detailed description of the analytic strategy. Positive values indicate *decreased* benefits of holding the Partner’s hand (i.e., dampened threat potentiation relative to the Alone condition). Abbreviations—L, left.

Supplementary Table S6. Descriptive statistics for clusters and local extrema where the neural ‘benefit’ of holding the Partner’s hand covaries with CAINS-MAP symptoms, while controlling for clinician-rated depression/anxiety symptoms (BPRS; $p < 0.05$, FWE corrected for the number of voxels tested and cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
408	L Putative Frontal Eye Field	4.49	-26	-6	50
488	L Anterior Supramarginal Gyrus	4.48	-44	-34	42
464	L Intraparietal Sulcus	4.40	-36	-46	44

Note: See the main report for a detailed description of the analytic strategy. Positive values indicate *decreased* benefits of holding the Partner’s hand (i.e., dampened threat potentiation relative to the Alone condition). Abbreviations—L, left.

Supplementary Table S7. Descriptive statistics for clusters and local extrema where the neural ‘benefit’ of holding the Partner’s hand covaries with CAINS-MAP symptoms, while controlling for clinician-rated agitation symptoms (BPRS; $p < 0.05$, FWE corrected for the number of voxels tested and cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
352	L Putative Frontal Eye Field	4.80	-26	-6	52
432	L Anterior Supramarginal Gyrus	4.52	-44	-32	38
520	L Intraparietal Sulcus	4.51	-36	-46	46
80	L Supramarginal Gyrus	4.00	-54	-34	44
8	L Putative Frontal Eye Field (Posterior Superior Frontal Sulcus, Posterior Superior Frontal Gyrus)	3.52	-22	2	54

Note: See the main report for a detailed description of the analytic strategy. Positive values indicate *decreased* benefits of holding the Partner’s hand (i.e., dampened threat potentiation relative to the Alone condition). Abbreviations—L, left.

Supplementary Table S8. Descriptive statistics for clusters and local extrema where the neural ‘benefit’ of holding the Partner’s hand covaries with CAINS-MAP symptoms, while controlling for mean-centered diagnostic status ($p < 0.05$, FWE corrected for the number of voxels tested and cluster extent).

mm ³	Region	<i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>
224	L Putative Frontal Eye Field	4.15	-26	-6	52
768	L Anterior Supramarginal Gyrus	5.22	-44	-32	40
376	L Intraparietal Sulcus	4.26	-36	-46	46

Note: See the main report for a detailed description of the analytic strategy. Positive values indicate *decreased* benefits of holding the Partner’s hand (i.e., dampened threat potentiation relative to the Alone condition). Abbreviations—L, left.

Supplementary Analyses of the Frontoparietal Regions

FEF and IPS are often conceptualized as hubs within a larger functional circuit—the Dorsal Attention Network (DAN) (Uddin et al., 2019)—which suggests that they represent a coherent functional circuit. If so, then we would expect them to show robust intrinsic functional connectivity and a consistent pattern of co-activation across experimental challenges (Laird et al., 2013; Yeo et al., 2011). We used Neurosynth—a cloud-based suite of semi-automated neuroinformatics tools and databases—to confirm these two expectations (Yarkoni et al., 2011).

We began by assessing the intrinsic functional connectivity of the FEF and IPS in the Yeo-Buckner database—which incorporates ‘resting-state’ fMRI data from 1,000 participants (Yeo et al., 2011)—using the peak locations identified by our individual differences analyses as seeds (**Supplementary Table S4**). As expected, results revealed robust functional connectivity between the FEF and IPS peaks (Yarkoni, 2023a, 2023b).

We used a conceptually similar seed-based approach to probe FEF-IPS co-activation. This semi-automated analysis leveraged a computer-generated database of 507,891 stereotactic coordinates derived from 14,371 published neuroimaging studies. This allowed us to perform a series of automated meta-analyses, each quantifying the likelihood that activation in one of the seed locations is associated with significant coactivation in the other (FDR $q < 0.01$, whole-brain corrected). Mirroring the functional connectivity results, this revealed robust FEF-IPS co-activation (Yarkoni, 2023a, 2023b).

Collectively, these observations provide clear evidence that the FEF and IPS regions identified in our primary analyses (**Supplementary Table S4**) are part of a coherent functional circuit, often termed the DAN.

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