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Complex post-traumatic stress disorder moderates functional connectivity in people with psychosis

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ABSTRACT

Background: Altered functional connectivity in several functional networks has been found in people with psychosis, especially in the default mode (DMN), salience (SAL) and central executive (CEN) networks. Functional connectivity in people with psychosis is influenced by traumatic life experiences. Trauma histories typical of people with psychosis are associated with complex post-traumatic stress disorder (cPTSD), but no studies have explored whether post-traumatic sequelae contribute to functional dysconnectivity in people with psychosis.
Methods: Using resting-state fMRI, we compared two groups meeting diagnostic criteria for schizophrenia spectrum disorders ($N = 106$); one group additionally met ICD-11 criteria for comorbid cPTSD, whereas the other did not. We assessed between-group differences in functional connectivity between 15 pre-defined regions of the DMN, SAL and CEN. Post-hoc correlations were used to test whether intra- and/or inter-network connectivity related to cPTSD symptom severity in the comorbid cPTSD group.
Results: The comorbid cPTSD group demonstrated significantly lower functional connectivity within the DMN, SAL and CEN, as well as increased negative connectivity between the SAL and CEN. The control group showed significantly decreased connectivity of the DMN with the SAL and CEN. PTSD symptoms correlated positively with intra-SAL connectivity and DMN-SAL dysconnectivity, whereas DSOs correlated positively with intra-SAL dysconnectivity and reduced DMN-CEN connectivity.
Conclusions: Our findings broadly align with the tripartite network model explaining psychopathology in terms of DMN, SAL and CEN dysconnectivity. Intra-network dysconnectivity in subgroups of people with psychosis may relate to post-traumatic sequelae, whereas inter-network dysconnectivity may be more central in trauma-unrelated psychoses.

1. Introduction

Spontaneous fluctuations in neural activity occur at rest; these fluctuations are coordinated within groups of regions (Biswal, 2012). Regions with correlated fluctuations in activity are collectively referred to as functional networks thought to underpin essential neurocognitive

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functions (Fox et al., 2005). For instance, spontaneous thought, mentalisation and future thinking is related to connectivity in the default mode network (DMN), comprising the medial prefrontal and posterior cingulate cortices, temporoparietal junction, precuneus, angular gyrus, and superior lateral occipital cortex (Andrews-Hanna, 2012; Wang et al., 2020). The central executive network (CEN) is a competing network, composed of the dorsolateral prefrontal and posterior parietal cortices, responsible for task-oriented cognition and executive functions (Seeley et al., 2007). The salience network (SAL) – including the anterior cingulate cortex (ACC), anterior insula, rostral prefrontal cortex and supramarginal gyrus (Uddin et al., 2019) – is involved in switching from spontaneous thought (i.e., DMN) to focussed attention (i.e., CEN) via salience attribution to stimuli (Cocchi et al., 2013; Goulden et al., 2014).

The triple network theory stipulates that altered functional connectivity within and between these three pivotal networks gives rise to neurocognitive difficulties that manifest as psychopathology (Menon, 2011). Accordingly, neuroimaging studies have extensively explored functional connectivity of the DMN, SAL and CEN in people with psychosis. Meta-analytic evidence has shown reduced functional connectivity within and between these networks among people with psychosis (Brandl et al., 2019; Dong et al., 2018; Li et al., 2019; O'Neill et al., 2019). Further, functional dysconnectivity of this kind correlates with positive and negative symptoms of psychosis (Lee et al., 2018; Manoliu et al., 2013; Rotarska-Jagiela et al., 2010). These findings do not appear moderated by antipsychotic medication, strengthening their plausible involvement in underpinning psychotic experiences (Wang et al., 2017).

Childhood trauma is associated with alterations in functional connectivity (Cassiers et al., 2018) and is extremely prevalent in people with psychosis (Trauelsen et al., 2015). Emerging research suggests childhood trauma exposure moderates DMN connectivity among people with psychosis (Dauvermann et al., 2021; King et al., 2021). Research has yet to explore whether functional connectivity in people who experience psychosis may also be moderated by post-traumatic sequelae, including post-traumatic stress disorder (PTSD). Like childhood trauma, PTSD is associated with reduced connectivity within and between the DMN, SAL, and CEN (Misaki et al., 2018; Zandvakili et al., 2020), and is very common among people with psychosis (Hardy & Mueser, 2017). The complex trauma histories typical of people with psychosis suggest complex PTSD (cPTSD) – a recent classification in the latest International Classification of Disease (ICD-11 (Karatzias et al., 2017)) – may be a common comorbidity in this population (Hyland et al., 2020; Karatzias et al., 2019). cPTSD includes core PTSD symptoms alongside 'disturbances of self-organisation' (DSOs; i.e., emotional dysregulation, interpersonal difficulties and negative self-concept (Cloitre, 2020)). It seems to be more prevalent than PTSD in people with psychosis (Panayi et al., 2022). Thus, neuroimaging research exploring the effects of post-traumatic sequelae on functional connectivity in psychosis ought to consider cPTSD.

Despite a wealth of evidence surrounding the neurofunctional underpinnings of PTSD, relatively few neuroimaging studies have examined cPTSD specifically. Altered activation in the anterior cingulate, dorsomedial prefrontal and orbitofrontal cortices and hippocampus has been demonstrated among people with cPTSD compared to trauma-unexposed controls (Thomaes et al., 2009, 2013). Without the application of validated diagnostic tools to identify ICD-11 cPTSD, it remains unclear whether these findings apply to transdiagnostic post-traumatic sequelae now considered associated with, but not endemic in, cPTSD (e.g., dissociation (Ford, 2017)). Overall, there is a dearth of literature directly comparing neuroanatomical structure and function between PTSD and cPTSD, making it difficult to draw firm conclusions about neural underpinnings of the latter (Stopyra et al., 2023). Understanding these underpinnings could be used to establish mechanisms of action in trauma-focussed therapies (Charquero-Ballester et al., 2022).

This is the first study to our knowledge to examine the contribution of post-traumatic sequelae to functional connectivity in people with psychosis. Given the lack of identified functional connectivity correlates of cPTSD, we were guided by the triple network model, and aimed to identify whether cPTSD moderated functional connectivity within and between the DMN, SAL and CEN. We compared two samples of people meeting psychotic spectrum diagnostic criteria ($N = 106$); one group met ICD-11 diagnostic criteria for comorbid cPTSD ($n = 56$), whereas the other did not meet criteria for any comorbid post-traumatic stress diagnosis (psychosis controls; PCs). Region of interest (ROI) analysis was applied to assess functional connectivity differences among pre-defined DMN, SAL and CEN network seeds between groups. Post-hoc correlations were used to assess whether functional connectivity of these seeds related to cPTSD symptom severity.

2. Methods and materials

2.1. Study design

This study employed a between-subjects design, combining fMRI data collected from a subsample of participants in the Study of Trauma and Recovery (STAR trial (Peters et al., 2022)), a randomised controlled trial testing the efficacy of trauma-focused cognitive-behavioural therapy for psychosis, and a subsample from the open UCLA Consortium for Neuropsychiatric Phenomics (CNP) dataset (Poldrack et al., 2016).

2.2. Participants

STAR trial participants completing the fMRI study at baseline ($N = 70$) who met ICD-11 diagnostic criteria for cPTSD ($n = 57$) were invited to take part in the study. One participant declined to complete the resting-state functional scan and as such $n = 56$ were included in the comorbid-cPTSD group. These data were combined with resting-state fMRI data from UCLA CNP participants meeting DSM-IV criteria for schizophrenia but no post-traumatic stress diagnosis ($n = 50$), leading to a combined $N = 106$. The comorbid cPTSD group was predominantly female (57.9 %) whereas the UCLA sample was predominantly male (76 %). The groups did not significantly differ on age ($t(101.15)= 1.14$; $p = .26$) or rates of antipsychotic prescription ($\chi^2(1)= .91$; $p = .34$). Scores on psychotic symptom severity (described in Supplementary Material 1) were transformed into standardised Z-scores which indicated the groups did not differ on severity of hallucinations ($t(86)= 0.02$; $p = .98$) or delusions ($t(87)= -0.02$; $p = .98$).

31 % of the comorbid cPTSD group were recruited from Early Intervention for Psychosis services in England, where best practice guidance advises against the use of potentially stigmatizing labels (e.g. schizophrenia, schizoaffective disorder) among those experiencing first-episode psychosis. Instead, ICD-10 F28 (other nonorganic psychotic disorder) or F29 (unspecified psychotic disorder) categories are routinely applied. Clinical characteristics of each group are presented in Tables 1 and 2, respectively.

Inclusion criteria of parent studies are documented in full elsewhere (Peters et al., 2022; Poldrack et al., 2016). These broadly included adults registered with mental health services who had a diagnosis of schizophrenia-spectrum disorder (or those who satisfied diagnostic criteria) with capacity to consent at the time of recruitment. STAR trial exclusion criteria included primarily-organic aetiology of psychosis or PTSD, primary diagnosis of substance misuse, requirement of an interpreter and receipt of trauma-focussed therapies within the three months preceding referral. Participants were excluded from the UCLA CNP schizophrenia subgroup if they had a lifetime diagnosis of substance misuse, bipolar, depression, anxiety disorders (including PTSD) or attention-deficit and hyperactivity disorder (though participants met criteria for additional diagnoses on the SCID-I, listed in Table 1). Both studies excluded participants with clinical contraindications for an MRI scan (e.g., metal in the body, possibility of pregnancy).

Table 1
. Clinical characteristics of the sample (N = 106).

Group	Characteristic		%
Comorbid cPTSD (n = 56)	ICD-10 Psychotic Spectrum Diagnosis	Schizophrenia	19.30
		Schizoaffective disorder	3.51
		Persistent delusional disorder	12.28
		Other nonorganic psychotic disorder	24.56
		Unspecified nonorganic psychosis	40.36
	Other diagnoses	Anxiety disorders (Generalized anxiety, OCD and other anxiety disorders)	22.81
		Autism	8.77
		Bipolar	14.04
		Depression (with or without psychotic features)	73.68
		Personality disorders (including borderline and other personality disorders)	43.86
		Substance-related disorders	8.77
		Other (e.g., ADHD, eating disorders, severe stress and adjustment disorder)	14.04
	Hears voices		75.44
Psychosis controls (n = 50)	DSM-IV Psychotic Spectrum Diagnosis	Paranoid Schizophrenia	42.00
		Disorganised Schizophrenia	2.00
		Residual Schizophrenia	12.00
		Schizoaffective disorder	22.00
		Undifferentiated Schizophrenia	22.00
	Other DSM-IV diagnoses	Depression	26.00
		Bipolar	4.00
		Attention Deficit and Hyperactivity Disorder	18.00
		Any substance misuse or dependence	60.00
			M(SD)
Comorbid cPTSD (n = 56)	ITQ-PTSD		17.93 (3.64)
	ITQ-DSO		18.95 (3.37)
	PSYRATS-Delusions		17.63 (3.01)
	PSYRATS-Voices		31.00 (5.05)
Psychosis controls (n = 50)	SAPS-Hallucinations		2.30 (1.75)
	SAPS-Delusions		2.54 (1.47)

Note: M = Mean; SD = Standard Deviation; PTSD = Post-traumatic Stress Disorder; DSO = Disturbances of Self-Organisation; ITQ = International Trauma Questionnaire (Cloitre et al., 2018); PSYRATS = Psychotic Symptom Rating Scales (Drake et al., 2007) SAPS = Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms

2.3. Clinical assessment measure

The *International Trauma Questionnaire* (ITQ (Cloitre et al., 2018)) is a 12-item self-report scale assessing the presence and severity of PTSD and DSOs within the past month. Each subscale comprises 3 symptom clusters, themselves composed of 2 items each, and 3 items capturing the functional impact of the cluster. All items are scored on a 5-point Likert scale from 0 ('Not at all') to 4 ('Extremely'). The ITQ diagnostic algorithm was used here to identify participants meeting criteria for ICD-11 cPTSD. The algorithm identifies a probable diagnosis of PTSD when a participant scores $\geq$2 on at least one item in each PTSD cluster, plus $\geq$2 on at least one functional impairment item associated with these symptoms. The cPTSD threshold includes that of PTSD plus a score of $\geq$2 on at least one item in each DSO cluster and of $\geq$2 on at least one functional impairment item associated with these symptoms. PTSD and DSO items were totalled to derive continuous severity scores, with higher scores indicating higher severity. Both subscales demonstrate high internal consistency (all α's = ≥ .79 (Cloitre et al., 2018)).

Table 2
Test statistics of significant differences in functional connectivity between specific ROIs of each cluster.

Connection	*T*	*p-FDR*
Cluster 1: DMN-SAL		
PCC-ACC	4.47	<.001
PCC-Anterior Insula (R)	4.19	<.001
LP (R)-ACC	4.14	.001
mPFC-Anterior Insula (R)	3.63	.001
mPFC-ACC	3.59	.001
LP (L)- Anterior Insula (L)	3.82	.002
Cluster 2: DMN-CEN		
PCC-lPFC (L)	6.23	<.001
mPFC-lPFC (R)	6.08	<.001
PCC-lPFC(R)	4.39	<.001
mPFC-lPFC (L)	4.51	<.001
Cluster 3: Intra-DMN		
PCC-LP (L)	4.49	<.001
mPFC-LP (R)	3.97	.001
mPFC-PCC	3.85	.001
mPFC-LP (L)	3.66	.001
Cluster 4: Intra-SAL		
ACC-Anterior Insula (R)	4.82	<.001
ACC-Anterior Insula (L)	4.34	<.001
rPFC (R)-Anterior Insula (R)	4.28	.001
Anterior Insula (R)-SMG (L)	3.47	.002
Anterior Insula (R)-SMG (R)	3.28	.003
Cluster 5: SAL-CEN		
lPFC(R)-ACC	4.78	<.001
lPFC(L)-ACC	4.03	.001
pPC (L)-Anterior Insula (L)	4.12	.001
lPFC(R)-Anterior Insula (R)	3.73	.001
Cluster 6: Intra-CEN		
PPC (L)-lPFC (L)	2.94	.004
PPC (L)-lPFC (R)	2.91	.004

Note: DMN = Default Mode Network; SAL = Salience Network; CEN = Central Executive Network; L = Left; R = Right; ACC = Anterior Cingulate Cortex; PCC = Posterior Cingulate Cortex; mPFC = Medial Prefrontal Cortex; rPFC = Rostral PFC; lPFC = Lateral PFC; LP = Lateral Parietal Cortex; SMG = Supramarginal gyrus

2.4. Resting-state paradigm

The STAR fMRI study involved an 8-minute structural scan, followed by a pre-task 5-minute resting-state scan, a 10-minute fMRI task, post-task resting-state scan, and another 10-minute fMRI task. This study analysed pre-task resting-state functional scan data. Participants were fitted with a respiration belt and were asked to keep as still as possible as they lay supine in the MRI scanner. The scanner was fitted with a mirror reflecting a screen onto which the tasks were projected, enabling participants to view the screen for the duration of the scan. A white fixation cross was presented on a plain black background for 5 minutes, with participants instructed to relax and keep their eyes open and fixed on the cross.

This study involves data collected from a subsample of STAR trial participants who provided fully-informed consent to the use of their data for future research. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008 (NHS Research Ethics committee ref: 20/LO/0853).

2.5. Image acquisition

Scans were collected across three sites: the University of Manchester (3T Intera, Philips, Best, Netherlands), King's College London (3T Discovery MR750, General Electric Medical Systems, Milwaukee, WI, USA), and the University of Newcastle (3T Achieva dStream, Philips, Best, Netherlands). T2-weighted MR images of the blood oxygen level-dependent (BOLD) signal were acquired using a 2D echo planar sequence (TR = 2s, TE = 30 ms, flip angle = 75°, slice thickness = 3 mm, interslice gap = 3.3 mm). Details of the UCLA CNP scanning paradigm and image acquisition protocol are documented fully elsewhere (Poldrack et al., 2016).

3. Preprocessing

Images were loaded into Matlab R2018a (The Mathworks Inc, 2018) for analysis using Statistical Parametric Mapping (SPM12 v7771 (The Wellcome Centre for Neuroimaging, 2020)). Functional scans were first spatially realigned to correct for motion during the scan and unwarped to correct for field inhomogeneities. A slice timing correction was then used to account for the delay between slices in each volume. The mean of unwarped functional images was then co-registered with skull-stripped bias-corrected T1-weighted images before being normalised to MNI space. Normalised images were then spatially smoothed with a 12mm Full Width at Half Maximum (FWHM) Gaussian kernel.

3.1. Functional connectivity analysis

Due to complexities involved in statistically modelling network connectivity, there are no agreed-upon gold-standard power calculations developed for functional connectivity research (Helwegen et al., 2023). We note our sample size was comparable to or larger than other clinical samples in prior network connectivity studies (Cancel et al., 2017; Dauvermann et al., 2021; Patton et al., 2025).

The CONN functional connectivity toolbox (v22) was used to complete ROI-based functional connectivity analyses (Whitfield-Gabrieli & Nieto-Castanon, 2012). ROIs included 15 pre-defined seeds of intrinsic functional networks determined by the CONN toolbox according to the Harvard-Oxford Cortical and Subcortical Atlas. DMN seeds included the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), and bilateral lateral parietal cortices. SAL seeds included the anterior cingulate cortex (ACC), bilateral anterior insula, rostral PFC (rPFC) and supramarginal gyri (SMG). CEN seeds included the bilateral lateral PFC (lPFC) and posterior parietal cortices. MNI coordinates of each network seed are presented in Supplementary Table 1. ROI-to-ROI connectivity matrices were estimated characterizing the functional connectivity between each pair of ROIs. Functional connectivity strength was represented by Fisher-transformed bivariate correlation coefficients from a general linear model (Nieto-Castanon, 2020), estimated separately for each pair of ROIs, characterizing the association between their BOLD signal timeseries. Group-level analyses were then performed using a General Linear Model for each individual connection, with first-level connectivity measures at this connection as dependent variables (one independent sample per subject), and group membership (i.e., comorbid cPTSD or no-cPTSD) as the independent variable. Age, sex and antipsychotic prescription were entered as covariates of no interest. Since site uniquely varied in the comorbid cPTSD group, inclusion as a covariate would have resulted in non-estimable contrasts with PCs. Sensitivity analyses in the comorbid group did not demonstrate significant differences in functional connectivity among the DMN, SAL and CEN between scanning sites (see Supplementary Table 2). Findings were considered significant at a conservative combined threshold of *p*-uncorrected < 0.001 at the connection level and *p*-FDR < 0.005 at the cluster level to mitigate Type I error (Woo et al., 2014; Eklund et al., 2016). FDR corrections were applied using the Benjamini-Hochberg (1995) method.

4. Results

4.1. ROI-to-ROI analysis

ROI analysis was conducted for 15 seeds comprising the DMN, SAL and CEN, revealing six differing clusters between groups. Three reflected reduced functional connectivity within the DMN (F [3,99] = 8.83, *p-FDR* < .001), SAL (F [3,99] = 7.63, *p-FDR* < .001) and CEN (F [3,99] = 2.85, *p-FDR* = .041) in the comorbid cPTSD group. The three remaining clusters demonstrated negative hyperconnectivity between the SAL and CEN in the cPTSD group (F [3,99] = 4.48, *p-FDR* = .007), as well as decreased negative connectivity of the DMN with the SAL (F [3,99] = 15.75, *p-FDR* = <.001) and CEN in PCs (F [3,99] = 13.74, *p-FDR* = <.001). The specific ROIs comprising each cluster presented alongside test statistics in Table 2.

4.2. Post-hoc correlations

In the comorbid cPTSD group, Fisher-transformed connectivity coefficients between all 15 ROIs were extracted and entered into Pearson correlations with cPTSD symptom subscales. No relationships survived correction for multiple comparisons (corrected $p < .002$). We therefore identified trends that survived adjustment for age, sex and antipsychotic prescription at a more liberal threshold ($p < .01$). These suggested intra-SAL connectivity and DMN-SAL dysconnectivity positively related to PTSD symptoms, whereas DSOs positively related to intra-SAL dysconnectivity and reduced negative DMN-CEN connectivity. Test statistics are presented in Table 3 and correlations presented graphically in Fig. 1.

5. Discussion

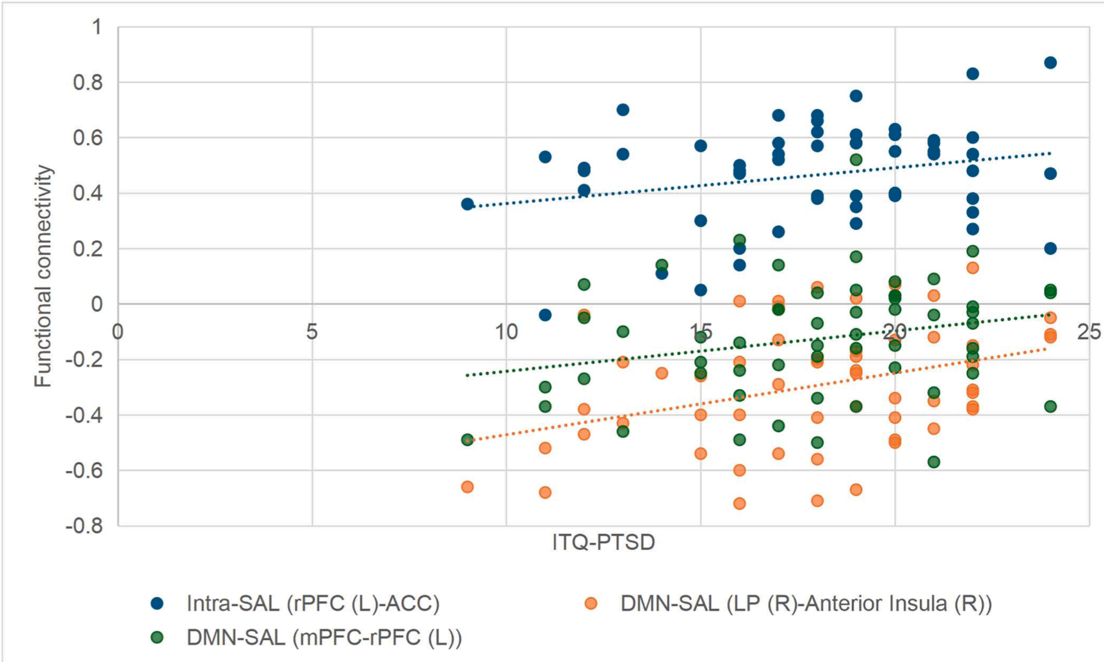
In the first functional neuroimaging study to consider post-traumatic sequelae among people with psychosis, we found differences in resting-state functional connectivity in people with psychosis who did and did not meet ICD-11 diagnostic criteria for cPTSD. The comorbid cPTSD group demonstrated reduced functional connectivity within the DMN, SAL and CEN, as well as negative SAL-CEN hyperconnectivity. The psychosis group displayed decreased DMN-SAL and DMN-CEN connectivity. Post-hoc correlation analyses suggested intra-SAL connectivity and DMN-SAL dysconnectivity may correlate positively with PTSD symptoms, whereas DSOs may positively correlate with intra-SAL dysconnectivity and reduced DMN-CEN connectivity.

Meta-analyses of resting-state fMRI among people with psychosis have demonstrated reduced functional connectivity within and between the DMN, SAL and CEN (Brandl et al., 2019; Dong et al., 2018; Li et al., 2019; O'Neill et al., 2019). Given connectivity within these networks was lower in the comorbid cPTSD group compared to PCs, we extend prior findings by suggesting cPTSD may contribute to functional dysconnectivity in people with psychosis. Concordantly, functional dysconnectivity of the DMN and CEN are consistently implicated in PTSD (Akiki et al., 2017; Fenster et al., 2018). That said, our findings are somewhat surprising in that intra-SAL hyperconnectivity is typically implicated in PTSD, especially post-traumatic hyperarousal (Breukelaar et al., 2021; Patel et al., 2012). We partially replicated this previous finding, in that SAL connectivity related to PTSD symptom severity at

Table 3
. Pearson correlation coefficients between functional connectivity and symptom severity.

Networks	ROIs	*r*	
		PTSD	DSO
Intra-SAL	rPFC (L)-ACC	.364	-
	rPFC (L)-Anterior Insula (R)	-	-.370
DMN-SAL	LP (R)-Anterior Insula (R)	.360	-
	mPFC-rPFC (L)	.371	-
DMN-CEN	LP (R)-lPFC (R)	-	.413
	mPFC-lPFC (R)	-	.393

Note: DMN = Default Mode Network; SAL = Salience Network; CEN = Central Executive Network; L = Left; R = Right; ACC = Anterior Cingulate Cortex; mPFC = Medial Prefrontal Cortex; rPFC = Rostral PFC; lPFC = Lateral PFC; LP = Lateral Parietal Cortex; PTSD = Post-traumatic Stress Disorder; DSO = Disturbances of Self-Organisation
All p's < .01



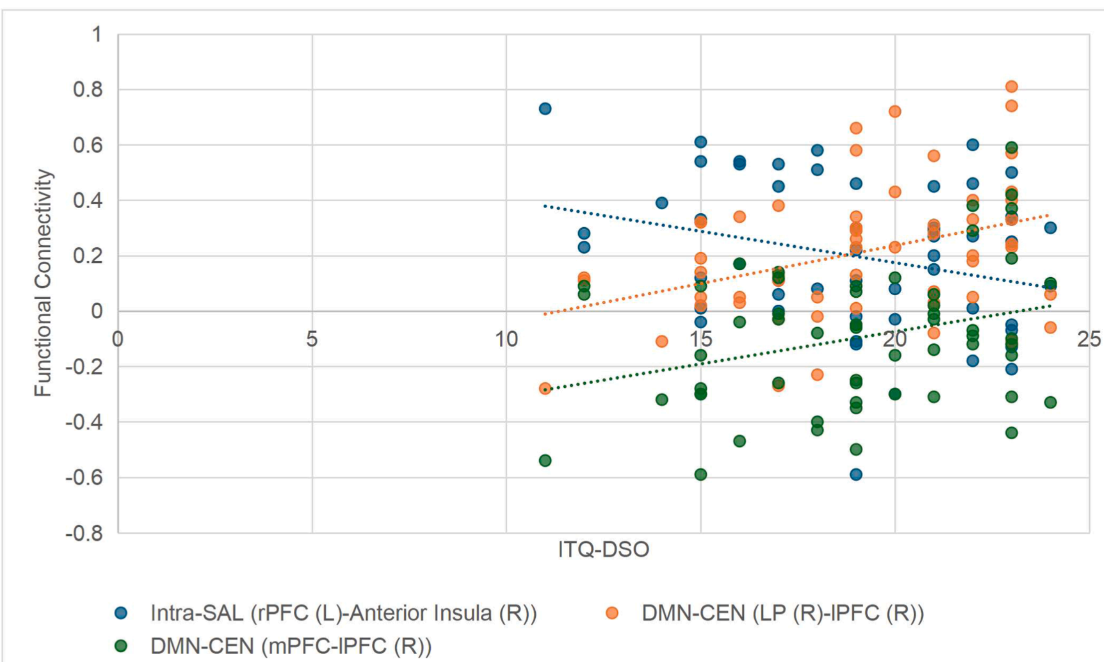


Fig. 1. Trends between functional connectivity and cPTSD symptom severity in the comorbid group. **A.** Core PTSD severity relates to SAL hyperconnectivity and DMN-SAL dysconnectivity. **B.** DSO severity relates to SAL dysconnectivity and reduced negative DMN-CEN connectivity.

trend-level. Yet, intra-SAL connectivity was lower overall in the comorbid cPTSD group compared to controls. SAL dys/connectivity may differentiate between PTSD/cPTSD, as hyperarousal is less central to complex post-traumatic presentations that are characterised instead by emotional numbness and dissociation (Frewen & Lanius, 2006; Levin et al., 2021; McElroy et al., 2019). Psychological experiences of this kind are related to anterior insula deactivation (Fenster et al., 2018; Lanius et al., 2010), which contributed to all SAL dysconnectivity in the comorbid cPTSD group. Further neuroimaging research comparing PTSD and cPTSD is required to understand whether insula-related SAL dysconnectivity is a distinguishing feature of cPTSD.

Negative SAL-DMN connectivity and positive SAL-CEN connectivity is associated with 'dynamic switching' from self-referential, spontaneous thought (i.e., DMN activation) to focussed attention on external stimuli (i.e., CEN activation; Goulden et al., 2014). Similarly, the DMN and CEN are negatively connected in healthy controls, owing to their competing functions (Sherman et al., 2014). Disintegration of these networks is associated with cognitive difficulties in psychosis as well as alterations in socio-emotional processing (Nekovarova et al., 2014). In turn, our results broadly align with prior research supporting the triple network model of psychopathology, in that PCs demonstrated SAL-DMN and SAL-CEN dysconnectivity as well as reduced negative DMN-CEN connectivity (Menon, 2011). The comorbid cPTSD group, on the other hand, displayed negative SAL-CEN hyperconnectivity. Given PCs did not meet criteria for post-traumatic stress diagnosis, our findings may therefore hint at disparate neural underpinnings of pathways to psychosis differentiated by their trauma-relatedness (Howes & Murray, 2014). Indeed, connectivity biotypes have been identified in people with psychosis, one characterised by hypoconnectivity and another by hyperconnectivity (Fernández-Linsenbarth et al., 2021; Liang et al., 2021). The characterisation of trauma-related and -unrelated psychoses by resting-state functional connectivity guided by the triple network model is a potential avenue for future replication studies, as this could provide neurobiological evidence for differential psychosis pathways that indicate targeted treatments (e.g., trauma-informed or -focussed interventions *versus* cognitive remediation).

The findings of our post-hoc correlations are consistent with the triple network model: disintegration of the DMN-SAL related positively to PTSD severity, and reduced DMN-CEN modulation related to DSO severity. The tripartite model may therefore provide a neural basis of cPTSD in people with psychosis. Notably, however, DMN-SAL dysconnectivity and DMN-CEN connectivity was significantly more pronounced in PCs. Given the absence of post-traumatic sequelae sufficiently severe to warrant a PTSD diagnosis in PCs, triple network dysconnectivity likely incurs wider, transdiagnostic, cognitive consequences. Consistently, Menon's model argues that DMN-SAL-CEN dysconnectivity underpins a variety of psychopathological difficulties via various processes (e.g., aberrant salience detection and engagement of adaptive, goal-directed cognition (Menon, 2011)). Future research exploring psychophysiological interactions will be helpful in this respect to uncover the mechanism by which functional connectivity may give rise to symptoms of cPTSD in people with psychosis. Conversely, within-network dysconnectivity was evident in the comorbid cPTSD group but did not correlate with symptom severity. This may be due to the use of composite core PTSD and DSO scores, rather than symptom subscale scores, given differential cPTSD symptoms are associated with reduced connectivity in disparate networks (Tursich et al., 2015). Thus, another important avenue for future research is the understanding of symptom-specific underpinnings of cPTSD in psychosis.

Discrepancies between parent datasets of this study pose significant limitations, as disparities in data acquisition (e.g., scanners; scanning protocol) may underlie group differences. For one, we cannot rule out differences due to scanner site in these analyses. We performed scanner harmonisation, acquiring the same sequences at each site, and confirmed via sensitivity analysis that functional connectivity did not differ systematically by site. Yet, group differences should be interpreted tentatively as they may be influenced by 'batch' shifts (location/scale) in imaging features. Controlling for site differences should be prioritised in future multisite MRI studies to evaluate the validity of our results. Another important limitation is that, whilst PTSD was ruled out, trauma exposure was not measured in the control group. Though reduced functional connectivity within the DMN has been consistently implicated in PTSD, DMN dysconnectivity is also evident among trauma-exposed controls (Bao et al., 2021; DiGangi et al., 2016). Likewise, childhood trauma has been shown to moderate DMN connectivity in people with psychosis (Dauvermann et al., 2021). As such, differences in DMN connectivity in our study may reflect increased trauma exposure in the cPTSD group as opposed to cPTSD caseness, consistent with the elevated risk of developing cPTSD following prolonged and/or repeated trauma (Karatzias et al., 2017). Concordantly, we did not uncover significant relationships between DMN connectivity and cPTSD symptom severity. Controlling for trauma exposure is therefore of paramount importance for replication studies to isolate the neural underpinnings of post-traumatic sequelae rather than trauma exposure itself.

Despite no agreed-upon method, statistical innovations allow for power calculations in functional connectivity studies, such as simulation-based power estimation (Bi et al., 2024). Empirical estimation based on reliability studies may also be used to guide sample size (Helwegen et al., 2023). Future studies may apply such techniques to ensure acceptable levels of statistical power are achieved. Further, though we opted for commonly-used metrics to allow comparability to other studies, the application of Pearson correlations to address this research question may have posed another limitation, given recent advances in statistical modelling of functional connectivity which uncover more robust neurocognitive biomarkers (e.g., tangent analysis; Abbas et al., 2023). The application of static functional connectivity analysis may have further restricted our findings, given dynamic connectivity analysis has demonstrated robustness against statistically noisy data like that used in our study (Chow et al., 2025). Future studies characterising the resting-state functional underpinnings of cPTSD in people with psychosis may find novel statistical approaches reveal more nuanced findings that harmonise those presented here.

An alternative explanation for the differences uncovered in this study is the disparity of sexes between groups: the cPTSD group primarily female and PCs primarily male. Though prior studies have uncovered sex differences in functional connectivity within the DMN, SAL and CEN, the directions of these differences are opposite to those uncovered here (i.e., typically increased intra-network connectivity in females and inter-network connectivity in males (Allen et al., 2011; Tunç et al., 2016)). Combined with the inclusion of sex as a covariate in analyses, it is therefore unlikely our findings represent sex differences between groups.

The dearth of research characterising resting-state functional connectivity in cPTSD led us to identify ROIs using a transdiagnostic model. Restricting our analyses to the DMN, SAL and CEN may have overlooked important differences in additional functional networks. For instance, altered affective network connectivity among the amygdala, orbitofrontal cortex and temporal poles may give rise to emotional dysregulation in cPTSD (Lanius et al., 2011), and altered functional connectivity in somatosensory networks (e.g., auditory, motor, language networks) may play a role in hallucinatory experiences in psychosis (Li et al., 2019). Thus, future research characterising functional connectivity differences in psychosis subgroups may explore the relative contributions of intrinsic networks aside from the DMN, SAL and CEN, especially since other networks may be associated with more specific functions and, by extension, symptomatology.

In the first functional neuroimaging study to consider cPTSD, we uncovered complex differences in resting-state connectivity among subgroups of people with psychosis; subgroups that did and did not meet ICD-11 criteria for comorbid cPTSD. Our findings suggest that cPTSD may contribute to intra-network functional dysconnectivity in psychosis, but not inter-network dysconnectivity. Further multimodal research is required to contextualise these differences and their neurocognitive consequences to truly elucidate the neural underpinnings of cPTSD in psychosis.

CRediT authorship contribution statement

Peter Panayi: Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Filippo Varese:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Emmanuelle Peters:** Writing – review & editing, Funding acquisition, Conceptualization. **Liam Mason:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Richard Bentall:** Writing – review & editing, Funding acquisition, Conceptualization. **Amy Hardy:** Writing – review & editing, Funding acquisition, Conceptualization. **Katherine Berry:** Writing – review & editing, Supervision, Conceptualization. **William Sellwood:** Writing – review & editing, Supervision, Conceptualization. **Robert Dudley:** Writing – review & editing, Funding acquisition. **Raphael Underwood:** Writing – review & editing, Supervision, Data curation. **Craig Steel:** Writing – review & editing, Funding acquisition. **Hassan Jafari:** Writing – review & editing, Data curation. **Rebecca Elliott:** Writing – review & editing, Supervision, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

None.

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Supplementary materials

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References

Abbas, K., Liu, M., Wang, M., Duong-Tran, D., Tipnis, U., Amico, E., Kaplan, A.D., Dzemidzic, M., Kareken, D., Ances, B.M., Harezlak, J., Goñi, J., 2023. Tangent functional connectomes uncover more unique phenotypic traits. iScience 26 (9), 107624. https://doi.org/10.1016/j.isci.2023.107624.

Akiki, T.J., Averill, C.L., Abdallah, C.G., 2017. A network-based neurobiological model of PTSD: evidence from structural and functional neuroimaging studies. Curr. Psychiatry Rep. 19 (11). https://doi.org/10.1007/s11920-017-0840-4.

Allen, E.A., Erhardt, E.B., Damaraju, E., Gruner, W., Segall, J.M., Silva, R.F., Havlicek, M., Rachakonda, S., Fries, J., Kalyanam, R., Michael, A.M., Caprihan, A., Turner, J.A., Eichele, T., Adelsheim, S., Bryan, A.D., Bustillo, J., Clark, V.P., Ewing, S.W.F., Calhoun, V.D., 2011. A baseline for the multivariate comparison of resting-state networks. Front. Syst. Neurosci. 5. https://doi.org/10.3389/FNSYS.2011.00002.

Andrews-Hanna, J.R., 2012. The brain's default network and its adaptive role in internal mentation. Neuroscientist 18 (3), 251–270. https://doi.org/10.1177/1073858411403316.

Bao, W., Gao, Y., Cao, L., Li, H., Liu, J., Liang, K., Hu, X., Zhang, L., Hu, X., Gong, Q., Huang, X., 2021. Alterations in large-scale functional networks in adult posttraumatic stress disorder: a systematic review and meta-analysis of resting-state functional connectivity studies. Neurosci. Biobehav. Rev. 131, 1027–1036. https://doi.org/10.1016/j.neubiorev.2021.10.017.

Bi, C., Nichols, T., Lee, H., Yang, Y., Ye, Z., Pan, Y., Hong, E., Kochunov, P., Chen, S., 2024. BNPower: a power calculation tool for data-driven network analysis for whole-brain connectome data. Imaging Neurosci 2, imag–2–00099. https://doi.org/10.1162/imag_a_00099.

Biswal, B., 2012. Resting state fMRI: a personal history. NeuroImage 62 (2), 938–944. https://doi.org/10.1016/j.neuroimage.2012.01.090.

Brandl, F., Avram, M., Weise, B., Shang, J., Simões, B., Bertram, T., Hoffmann Ayala, D., Penzel, N., Gürsel, D.A., Bäuml, J., Wohlschläger, A.M., Vukadinovic, Z., Koutsouleris, N., Leucht, S., Sorg, C., 2019. Specific substantial dysconnectivity in schizophrenia: a transdiagnostic multimodal meta-analysis of resting-State functional and structural Magnetic resonance imaging studies. Biol. Psychiatry 85 (7), 573–583. https://doi.org/10.1016/J.BIOPSYCH.2018.12.003.

Breukelaar, I.A., Bryant, R.A., Korgaonkar, M.S., 2021. The functional connectome in posttraumatic stress disorder. Neurobiol. Stress 14, 100321. https://doi.org/10.1016/j.ynstr.2021.100321.

Cancel, A., Comte, M., Boutet, C., Schneider, F.C., Rousseau, P.-F., Boukezzi, S., Gay, A., Sigaud, T., Massoubre, C., Berna, F., Zendjidjian, X.Y., Azorin, J.-M., Blin, O., Fakra, E., 2017. Childhood trauma and emotional processing circuits in schizophrenia: A functional connectivity study. Schizophrenia Res. 184, 69–72. https://doi.org/10.1016/j.schres.2016.12.003.

Cassiers, L.L.M.M., Sabbe, B.G.C.C., Schmaal, L., Veltman, D.J., Penninx, B.W.J.H.J.H., Eede, F.Van Den, Van Den Eede, F., 2018. Structural and functional brain abnormalities associated with exposure to different childhood trauma subtypes: a systematic review of neuroimaging findings. Front. Psychiatry 9 (AUG). https://doi.org/10.3389/fpsyt.2018.00329.

Charquero-Ballester, M., Kleim, B., Vidaurre, D., Ruff, C., Stark, E., Tuulari, J.J., McManners, H., Bar-Haim, Y., Bouquillon, L., Moseley, A., Williams, S.C.R., Woolrich, M.W., Kringelbach, M.L., Ehlers, A., 2022. Effective psychological therapy for PTSD changes the dynamics of specific large-scale brain networks. Hum. Brain Mapp. 43 (10), 3207–3220. https://doi.org/10.1002/hbm.25846.

Chow, W.W., Seghouane, A.K., Seghier, M.L., 2025. A Statistical Characterization of Dynamic Brain Functional Connectivity. Human brain mapp. 46 (2), e70145. https://doi.org/10.1002/hbm.70145.

Cloitre, M., 2020. ICD-11 complex post-traumatic stress disorder: simplifying diagnosis in trauma populations. Br. J. Psychiatry 216 (3), 129–131. https://doi.org/10.1192/bjp.2020.43.

Cloitre, M., Shevlin, M., Brewin, C.R., Bisson, J.I., Roberts, N.P., Maercker, A., Karatzias, T., Hyland, P., 2018. The International Trauma Questionnaire: development of a self-report measure of ICD-11 PTSD and complex PTSD. Acta Psychiatr. Scand. 138 (6), 536–546. https://doi.org/10.1111/acps.12956.

Cocchi, L., Zalesky, A., Fornito, A., Mattingley, J.B., 2013. Dynamic cooperation and competition between brain systems during cognitive control. Trends Cogn. Sci. 17 (10), 493–501. https://doi.org/10.1016/J.TICS.2013.08.006.

Dauvermann, M.R., Mothersill, D., Rokita, K.I., King, S., Holleran, L., Kane, R., McKernan, D.P., Kelly, J.P., Morris, D.W., Corvin, A., Hallahan, B., McDonald, C., Donohoe, G., 2021. Changes in default-mode network associated with childhood trauma in schizophrenia. Schizophr. Bull. 47 (5), 1482–1494. https://doi.org/10.1093/schbul/sbab025.

DiGangi, J.A., Tadayyon, A., Fitzgerald, D.A., Rabinak, C.A., Kennedy, A., Klumpp, H., Rauch, S.A.M., Phan, K.L., 2016. Reduced default mode network connectivity following combat trauma. Neurosci. Lett. 615, 37–43. https://doi.org/10.1016/j.neulet.2016.01.010.

Dong, D., Wang, Y., Chang, X., Luo, C., Yao, D., 2018. Dysfunction of large-scale brain networks in schizophrenia: a meta-analysis of resting-State functional connectivity. Schizophr. Bull. 44 (1), 168–181. https://doi.org/10.1093/schbul/sbx034.

Drake, R., Haddock, G., Tarrier, N., Bentall, R., Lewis, S., 2007. The psychotic symptom rating scales (PSYRATS): their usefulness and properties in first episode psychosis. Schizophr. Res. 89 (1–3), 119–122. https://doi.org/10.1016/j.schres.2006.04.024.

Eklund, A., Nichols, T.E., Knutsson, H., 2016. Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. Proceedings of the National Acad. Sci. United States America 113 (28), 7900–7905. https://doi.org/10.1073/pnas.1602413113.

Fenster, R.J., Lebois, L.A.M., Ressler, K.J., Suh, J., 2018. Brain circuit dysfunction in post-traumatic stress disorder: from mouse to man. Nat. Rev. Neurosci. 19 (9), 535–551. https://doi.org/10.1038/s41583-018-0039-7.

Fernández-Linsenbarth, I., Planchuelo-Gómez, Á., Beño-Ruiz-de-la-Sierra, R.M., Díez, A., Arjona, A., Pérez, A., Rodríguez-Lorenzana, A., del Valle, P., de Luis-García, R., Mascialino, G., Holgado-Madera, P., Segarra-Echevarría, R., Gomez-Pilar, J., Núñez, P., Bote-Boneaechea, B., Zambrana-Gómez, A., Roig-Herrero, A., Molina, V., 2021. Search for schizophrenia and bipolar biotypes using functional network properties. Brain Behav. (12), 11. https://doi.org/10.1002/BRB3.2415.

Ford, J.D., 2017. Complex trauma and complex posttraumatic stress disorder. In: Gold, S. N., Cook, J.M., Dalenberg, C.J. (Eds.), Complex trauma and complex posttraumatic stress disorder. APA Handb. Trauma Psychol.: Found. Knowl. (Vol. 1) 1, 281–305. https://doi.org/10.1037/0000019-015.

Fox, M.D., Snyder, A.Z., Vincent, J.L., Corbetta, M., Van Essen, D.C., Raichle, M.E., 2005. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proc. Natl. Acad. Sci. 102 (27), 9673–9678. https://doi.org/10.1073/pnas.0504136102.

Frewen, P., Lanius, R.A., 2006. Toward a psychobiology of posttraumatic self-dysregulation: reexperiencing, hyperarousal, dissociation, and emotional numbing. In: Yehuda, R. (Ed.), Psychobiology of Posttraumatic Stress Disorders: A Decade of Progress. Blackwell Publishing, pp. 110–124.

Goulden, N., Khusnulina, A., Davis, N.J., Bracewell, R.M., Bokde, A.L., McNulty, J.P., Mullins, P.G., 2014. The salience network is responsible for switching between the default mode network and the central executive network: replication from DCM. NeuroImage 99, 180–190. https://doi.org/10.1016/J.NEUROIMAGE.2014.05.052.

Hardy, K.V., Mueser, K.T., 2017. Editorial: trauma, psychosis and posttraumatic stress disorder. Front. Psychiatry 8 (220). https://doi.org/10.3389/fpsyt.2017.00220.

Helwegen, K., Libedinsky, I., van den Heuvel, M.P., 2023. Statistical power in network neuroscience. Trends cogni. sci. 27 (3), 282–301. https://doi.org/10.1016/j.tics.2022.12.011.

Howes, O.D., Murray, R.M., 2014. Schizophrenia: an integrated sociodevelopmental-cognitive model. Lancet 383 (9929), 1677–1687. https://doi.org/10.1016/S0140-6736(13)62036-X.

Hyland, P., Shevlin, M., Fyvie, C., Cloitre, M., Karatzias, T., 2020. The relationship between ICD-11 PTSD, complex PTSD and dissociative experiences. J. Trauma Dissociation: Off. J. Int. Soc. Study Dissociation (ISSD) 21 (1), 62–72. https://doi.org/10.1080/15299732.2019.1675113.

Karatzias, T., Cloitre, M., Maercker, A., Kazlauskas, E., Shevlin, M., Hyland, P., Bisson, J. I., Roberts, N.P., Brewin, C.R., 2017. PTSD and complex PTSD: ICD-11 updates on concept and measurement in the UK, USA, Germany and Lithuania. Eur. J. Psychotraumatol. 8 (sup7), 1418103. https://doi.org/10.1080/20008198.2017.1418103.

Karatzias, T., Hyland, P., Bradley, A., Cloitre, M., Roberts, N.P., Bisson, J.I., Shevlin, M., 2019. Risk factors and comorbidity of ICD-11 PTSD and complex PTSD: findings from a trauma-exposed population based sample of adults in the United Kingdom. Depress. Anxiety 36 (9), 887–894. https://doi.org/10.1002/da.22934.

King, S., Holleran, L., Mothersill, D., Patlola, S., Rokita, K., McManus, R., Kenyon, M., McDonald, C., Hallahan, B., Corvin, A., Morris, D., Kelly, J., McKernan, D., Donohoe, G., 2021. Early life adversity, functional connectivity and cognitive performance in Schizophrenia: the mediating role of IL-6. Brain Behav. Immun. 98, 388–396. https://doi.org/10.1016/J.BBI.2021.06.016.

Lanius, R.A., Bluhm, R.L., Frewen, P.A., 2011. How understanding the neurobiology of complex post-traumatic stress disorder can inform clinical practice: a social cognitive and affective neuroscience approach. Acta Psychiatr. Scand. 124 (5), 331–348. https://doi.org/10.1111/j.1600-0447.2011.01755.x.

Lanius, R.A., Vermetten, E., Loewenstein, R.J., Brand, B., Schmahl, C., Bremner, J.D., Spiegel, D., 2010. Emotion modulation in PTSD: clinical and neurobiological evidence for a dissociative subtype. Am. J. Psychiatry 167 (6), 640–647. https://doi.org/10.1176/appi.ajp.2009.09081168.

Lee, W.H., Doucet, G.E., Leibu, E., Frangou, S., 2018. Resting-state network connectivity and metastability predict clinical symptoms in schizophrenia. Schizophr. Res. 201, 208–216. https://doi.org/10.1016/j.schres.2018.04.029.

Levin, Y., Hyland, P., Karatzias, T., Shevlin, M., Bachem, R., Maercker, A., Ben-Ezra, M., 2021. Comparing the network structure of ICD-11 PTSD and complex PTSD in three African countries. J. Psychiatr. Res. 136, 80–86. https://doi.org/10.1016/J.JPSYCHIRES.2021.01.041.

Li, S., Hu, N., Zhang, W., Tao, B., Dai, J., Gong, Y., Tan, Y., Cai, D., Lui, S., 2019. Dysconnectivity of multiple brain networks in schizophrenia: a meta-analysis of resting-state functional connectivity. In: Frontiers in Psychiatry, 10. https://doi.org/10.3389/fpsyt.2019.00482.

Liang, S., Wang, Q., Greenshaw, A.J., Li, X., Deng, W., Ren, H., Zhang, C., Yu, H., Wei, W., Zhang, Y., Li, M., Zhao, L., Du, X., Meng, Y., Ma, X., Yan, C.G., Li, T., 2021.

Aberrant triple-network connectivity patterns discriminate biotypes of first-episode medication-naive schizophrenia in two large independent cohorts. Neuropsychopharmacol. 2020 46 (8), 1502–1509. https://doi.org/10.1038/s41386-020-00926-y. *468*.

Manoliu, A., Riedl, V., Doll, A., Bäuml, J.G., Mühlau, M., Schwerthöffer, D., Scherr, M., Zimmer, C., Förstl, H., Bäuml, J., Wohlschläger, A.M., Koch, K., Sorg, C., 2013. Insular dysfunction reflects altered between-network connectivity and severity of negative symptoms in schizophrenia during psychotic remission. Front. Hum. Neurosci. 7, 48023. https://doi.org/10.3389/FNHUM.2013.00216.

McElroy, E., Shevlin, M., Murphy, S., Roberts, B., Makhashvili, N., Javakhishvili, J., Bisson, J., Ben-Ezra, M., Hyland, P., 2019. ICD-11 PTSD and complex PTSD: structural validation using network analysis. World Psychiatry 18 (2), 236. https://doi.org/10.1002/WPS.20638.

Menon, V., 2011. Large-scale brain networks and psychopathology: a unifying triple network model. Trends Cogn. Sci. 15 (10), 483–506. https://doi.org/10.1016/j.tics.2011.08.003.

Misaki, M., Phillips, R., Zotev, V., Wong, C.K., Wurfel, B.E., Krueger, F., Feldner, M., Bodurka, J., 2018. Connectome-wide investigation of altered resting-state functional connectivity in war veterans with and without posttraumatic stress disorder. NeuroImage: Clin. 17, 285–296. https://doi.org/10.1016/j.nicl.2017.10.032.

Nekovarova, T., Fajnerova, I., Horacek, J., Spaniel, F., 2014. Bridging disparate symptoms of schizophrenia: a triple network dysfunction theory. Front. Behav. Neurosci. 8. https://doi.org/10.3389/fnbeh.2014.00171.

Nieto-Castanon, A., 2020. Functional connectivity measures. Handbook of Functional Connectivity Magnetic Resonance Imaging Methods in CONN. Hilbert Press, pp. 26–62.

O'Neill, A., Mechelli, A., Bhattacharyya, S., 2019. Dysconnectivity of large-scale functional networks in early psychosis: a meta-analysis. Schizophr. Bull. 45 (3), 579–590. https://doi.org/10.1093/SCHBUL/SBY094.

Panayi, P., Berry, K., Sellwood, W., Campodonico, C., Bentall, R.P., Varese, F., 2022. The role and clinical correlates of complex post-traumatic stress disorder in people with psychosis. Front. Psychol. 13, 700. https://doi.org/10.3389/fpsyg.2022.791996.

Patel, R., Spreng, R.N., Shin, L.M., Girard, T.A., 2012. Neurocircuitry models of posttraumatic stress disorder and beyond: a meta-analysis of functional neuroimaging studies. Neurosci. Biobehav. Rev. 36 (9), 2130–2142. https://doi.org/10.1016/j.neubiorev.2012.06.003.

Patton, H.N., Maximo, J.O., Bryant, J.E., Lahti, A.C., 2025. Early life stress and functional connectivity in antipsychotic-naïve first episode psychosis patients. Schizophrenia 11 (1). https://doi.org/10.1038/s41537-024-00552-3.

Peters, E., Hardy, A., Dudley, R., Varese, F., Greenwood, K., Steel, C., Emsley, R., Keen, N., Bowe, S., Swan, S., Underwood, R., Longden, E., Byford, S., Potts, L., Heslin, M., Grey, N., Turkington, D., Fowler, D., Kuipers, E., Morrison, A., 2022. Multisite randomised controlled trial of trauma-focused cognitive behaviour therapy for psychosis to reduce post-traumatic stress symptoms in people with co-morbid post-traumatic stress disorder and psychosis, compared to treatment as usual: study protocol for the STAR (Study of Trauma And Recovery) trial. Trials 23 (1), 1–26. https://doi.org/10.1186/S13063-022-06215-X/FIGURES/3.

Poldrack, R.A., Congdon, E., Triplett, W., Gorgolewski, K.J., Karlsgodt, K.H., Mumford, J. A., Sabb, F.W., Freimer, N.B., London, E.D., Cannon, T.D., Bilder, R.M., 2016. A phenome-wide examination of neural and cognitive function. Sci. Data 3 (1), 160110. https://doi.org/10.1038/sdata.2016.110.

Rotarska-Jagiela, A., van de Ven, V., Oertel-Knöchel, V., Uhlhaas, P.J., Vogeley, K., Linden, D.E.J., 2010. Resting-state functional network correlates of psychotic symptoms in schizophrenia. Schizophr. Res. 117 (1), 21–30. https://doi.org/10.1016/J.SCHRES.2010.01.001.

Seeley, W.W., Menon, V., Schatzberg, A.F., Keller, J., Glover, G.H., Kenna, H., Reiss, A.L., Greicius, M.D., 2007. Dissociable intrinsic connectivity networks for salience processing and executive control. J. Neurosci. 27 (9), 2349–2356. https://doi.org/10.1523/JNEUROSCI.5587-06.2007.

Sherman, L.E., Rudie, J.D., Pfeifer, J.H., Masten, C.L., McNealy, K., Dapretto, M., 2014. Development of the default mode and Central executive networks across early adolescence: a longitudinal study. Dev. Cogn. Neurosci. 10, 148–159. https://doi.org/10.1016/j.dcn.2014.08.002.

Stopyra, M.A., Simon, J.J., Rheude, C., Nikendei, C., 2023. Pathophysiological aspects of complex PTSD – a neurobiological account in comparison to classic posttraumatic stress disorder and borderline personality disorder. Rev. Neurosci. 34 (1), 103–128. https://doi.org/10.1515/revneuro-2022-0014.

The Mathworks Inc. (2018). *MATLAB* (9.4.0 (R2018a)). The Mathworks Inc.

The Wellcome Centre for Neuroimaging, 2020. *SPM* (No. 7771). The Wellcome Centre for Neuroimaging. http://www.fil.ion.ucl.ac.uk/spm/software/spm12/.

Thomaes, K., Dorrepaal, E., Draijer, N., de Ruiter, M.B., Elzinga, B.M., Sjoerds, Z., van Balkom, A.J., Smit, J.H., Veltman, D.J., 2013. Increased anterior cingulate cortex and hippocampus activation in Complex PTSD during encoding of negative words. Soc. Cogn. Affect. Neurosci. 8 (2), 190–200. https://doi.org/10.1093/scan/nsr084.

Thomaes, K., Dorrepaal, E., Draijer, N.P.J., de Ruiter, M.B., Elzinga, B.M., van Balkom, A. J., Smoor, P.L.M., Smit, J., Veltman, D.J., 2009. Increased activation of the left hippocampus region in Complex PTSD during encoding and recognition of emotional words: a pilot study. Psychiatry Res.: Neuroimaging 171 (1), 44–53. https://doi.org/10.1016/j.pscychresns.2008.03.003.

Trauelsen, A.M., Bendall, S., Jansen, J.E., Nielsen, H.G.L., Pedersen, M.B., Trier, C.H., Haahr, U.H., Simonsen, E., 2015. Severity and persistence versus type of childhood adversity in non-affective first-episode psychosis. Schizophr. Res. 168 (1–2), 573–574. https://doi.org/10.1016/j.schres.2015.06.020.

Tunç, B., Solmaz, B., Parker, D., Satterthwaite, T.D., Elliott, M.A., Calkins, M.E., Ruparel, K., Gur, R.E., Gur, R.C., Verma, R., 2016. Establishing a link between sex-related differences in the structural connectome and behaviour. Philos. Trans. R. Soc. B: Biol. Sci. 371 (1688). https://doi.org/10.1098/RSTB.2015.0111.

Tursich, M., Ros, T., Frewen, P.A., Kluetsch, R.C., Calhoun, V.D., Lanius, R.A., 2015. Distinct intrinsic network connectivity patterns of post-traumatic stress disorder symptom clusters. Acta Psychiatr. Scand. 132 (1), 29–38. https://doi.org/10.1111/acps.12387.

Uddin, L.Q., Yeo, B.T.T., Spreng, R.N., 2019. Towards a universal taxonomy of macro-scale functional Human brain networks. Brain Topogr. 32 (6), 926–942. https://doi.org/10.1007/s10548-019-00744-6.

Wang, S., Tepfer, L.J., Taren, A.A., Smith, D.V., 2020. Functional parcellation of the default mode network: a large-scale meta-analysis. Sci. Rep. 10 (1), 16096. https://doi.org/10.1038/s41598-020-72317-8.

Wang, S., Zhan, Y., Zhang, Y., Lv, L., Wu, R., Zhao, J., Guo, W., 2017. Abnormal functional connectivity strength in patients with adolescent-onset schizophrenia: a resting-state fMRI study. Eur. Child Adolesc. Psychiatry 26 (7), 839–845. https://doi.org/10.1007/s00787-017-0958-2.

Whitfield-Gabrieli, S., Nieto-Castanon, A., 2012. CONN: a functional connectivity toolbox for correlated and anticorrelated brain networks. Brain Connect. 2 (3), 125–141.

Woo, C.W., Krishnan, A., Wager, T.D., 2014. Cluster-extent based thresholding in fMRI analyses: pitfalls and recommendations. NeuroImage 91, 412–419. https://doi.org/10.1016/j.neuroimage.2013.12.058.

Zandvakili, A., Barredo, J., Swearingen, H.R., Aiken, E.M., Berlow, Y.A., Greenberg, B.D., Carpenter, L.L., Philip, N.S., 2020. Mapping PTSD symptoms to brain networks: a machine learning study. Transl. Psychiatry 10 (195). https://doi.org/10.1038/s41398-020-00879-2.