Default Mode Network (DMN) Signature of Depression: A Systematic Review of Resting-state fMRI Studies

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INTRO

The recent ACBS task force report indicated that CBS research should take multilevel and multimodal approaches. Biophysiological CBS research was identified as an important dimension. Historically, neurobiological correlates of ACBS constructs have been limited. We aimed to address this gap by presenting data from a systematic review to examine the Default Mode Network (DMN) signatures of depression. Alterations in DMN are well-known in Major depressive disorder (MDD), often reflected as abnormalities in resting state functional connectivity (rsFC). However, there have been inconsistencies in prior findings. The current study aimed to synthesize consistent patterns across studies and highlight key areas of divergence.

METHODS

This study is a pilot synthesis from the larger study. We synthesized findings from 10 resting-state fMRI studies published in 2015-2022, examining DMN functional connectivity among individuals with MDD. The papers were selected based on predetermined inclusion and exclusion criteria by two independent reviewers. Inclusion criteria were original peer-reviewed studies using fMRI with human participants divided into at least two depression group(s) and healthy control group(s). Exclusion criteria were any studies opposite to those described above and complex comorbidities. Five independent coders extracted data from papers, and the synthesis was done by the first author.

DISCUSSION

The current review highlighted consistent findings regarding the relationship between MDD and disrupted functional connectivity within the Default Mode Network (DMN)- the posterior cingulate cortex (PCC)–medial prefrontal cortex (mPFC) axis. Altered DMN activity was also associated with depressive symptom severity, rumination, and relapse vulnerability, indicating the DMN's relevance as a dynamic and clinically sensitive biomarker of MDD.

However, there were also inconsistencies among findings. Participants with adolescent-onset and recurrent phases showed greater DMN disruption. A few studies revealed subtypes with hyper-connectivity. One subtype of depression was also identified, characterized by hyper-connectivity in DMN.

Future research could prioritize precision mapping of DMN subtypes and integrate multi-modal designs to improve clinical knowledge.

RESULTS

STUDY	COUNTRY	AVG AGE (EXP/CON)	SEX % MALE (EXP/CON)	MEASURES	FMRI MACHINE	REGIONS SCANNED
BARTOVA ET AL. (2015)	Austria	26.8 / 25.3	43.5 / 40	The German version of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I)	Not stated	amPFC, PCC, PHG, mFG, dlPFC, vlPFC, IPL, PCu, Temporal lobe, Insula, Cingulate cortex
CUI ET AL. (2021)	China	27.5 / 26.16	30.56 / 36.07	The Mini International Neuropsychiatric Interview (MINI) 5.0, based on the DSM-IV criteria The 16-Item Quick Inventory of Depressive Symptomatology and Self-Report (QIDS-SR16) The Hamilton Depression Rating Scale (HAMD17)	3.0 T Siemens MAGNETOM Prisma MRI scanner (Siemens Medical Solutions, Erlangen, Germany) with a 64-channel phased-array head coil	amPFC, PCC, PFC, PFd, PFCv, PFCm, IPL, dmPFC, PHC, PCu, Temporal lobe
GUO ET AL. (2018)	China	28.63 / 26.92	39.77 / 49.09	The Structural Clinical Interview for DSM-IV (SCID), patient version The Hamilton Depression Rating Scale (HAMD17)	Siemens (Trio) 3T scanners	PCC, Cuneus, Frontal cortex, Temporal gyrus, Parietal lobule, Occipital cortex
JU ET AL. (2022)	China	36.5 / 36.3	44.55 / 47.79	The Hamilton Rating Scale for Depression (HAMD24)	GE MRI system (Signa HDxT 3.0-tesla scanner)	Default Mode Network (DMN) Cingulo-Opercular Network (CON) Salience Network (SN) Ventral Attention Network (VAN)
LIANG ET AL. (2020)	China	32.45 / 30.43	30.58 / 59.55	The Hamilton Depression Rating Scale (HAMD)	Not stated	sFC, vmPFC, PCC, PrC, IPL, MTG, mPFC, PCC, LTC, dmPFC, PCu Angular Gyrus
SENDI ET AL. (2021)	China	32.91 / 31.05	38.17 / 36.46	The structured clinical interview for diagnostic (SCID-P) and statistical manual of mental disorders confirmed depression in individuals with MDD	3T Philips scanner (Achieva, Netherlands) with an 8-channel phased-array head coil	ACC, pACC, sgACC, PCC, PCu
TANG ET AL. (2022)	China	37.43 / 36.88	35.43 / 40.8	The ICD-10 or DSM-IV criteria The Hamilton Depression Rating Scale (HAMD17)	Siemens 3.0T	mPFC, PCC, IPL, LTC, RSC, aMPFC, dmPFC, vmPFC, TPJ
XIAO ET AL. (2022)	China	26.93 / 29.42	30 / 37.21	Mini Neuropsychiatric International Interview (MINI) following the criteria of DSM-IV The Hamilton Rating Scale for Depression (HAMD24)	3.0T GE scanner (General Electric, Waukesha, WI, USA)	mPFC, PCC, dPFC, IPL, LTC, lPFC, vPFC
YAN ET AL. (2019)	China	Not stated, range 18-65 / Not stated, range 18-65	36.46 / Not stated	The Hamilton rating scale for depression (HAMD)	Not stated	Visual Network (VN) sensory-motor network (SMN) Dorsal Attention Network (DAN) Ventral Attention Network (VAN) Subcortical Network Frontoparietal Network (FPN) Default Mode Network (DMN)
ZAMOSCIK ET AL. (2018)	Germany	41.61 / 44.53	33.74 / 30	The Structured Clinical Interview for DSM-IV axis I (SCID) The self-rated Beck Depression Inventory II-RevisedThe Montgomery and Asberg Depression Rating Scale (MADRS)	Tim Trio 3.0 T MRI Scanner, Siemens, 12-channel head coil	PCC, Insula, Hippocampus, Right Parahippocampal Gyrus, Left Middle/Superior Temporal Gyrus

Consistencies in findings:

- Functional connectivity of DMN decreased in individuals with MDD, in which the posterior cingulate cortex (PCC) and the medial prefrontal cortex (mPFC) axis were well-reported (Bartova et al., 2015; Guo et al., 2018; Sendi et al., 2021; Yan et al., 2019).

- Decreased DMN connectivity association with greater depression severity (Bartova et al., 2015), rumination, and recurrence risk (Guo et al., 2018; Yan et al., 2019) was frequently reported (Ju et al., 2022).

- Treatments including antidepressants demonstrated a normalization effect on the DMN (Cui et al., 2021; Ju et al., 2022).

Inconsistencies in findings:

- Despite the dominant hypo-connectivity pattern, another DMN-based subtypes of depression was reported with hyper-connectivity (with greater DMN coherence than healthy controls), challenging the common assumption of DMN suppression in MDD (Liang et al., 2020).

- Individuals with adolescent-onset MDD showed stronger DMN disruptions than those with adult-onset (Bartova et al., 2015), and recurrent MDD patients showed greater PCC–mPFC disconnection compared to first-episode individuals (Yan et al., 2019).

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