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Cortisol Administration Normalizes Aberrant Functional Connectivity in Women with Depression

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Abstract

Previous resting-state functional connectivity (rsFC) research has identified aberrant connectivity in several large brain networks in depression, including the default mode (DMN), frontoparietal (FPN), and salience networks (SN). Connectivity of these networks is also related to depressive symptom severity and is affected by cortisol levels. To our knowledge, this is the first study to investigate the effects of acute cortisol administration on rsFC of DMN, FPN, and SN in individuals varying in depression history and severity. We collected resting-state fMRI scans for 74 women with and without a history of depressive disorder after administration of cortisol and placebo using a double-blind, crossover design. We conducted seed-based rsFC with seed regions from the DMN, FPN, and SN to examine the relationship between rsFC changes in these networks after cortisol, with depression history group predicting changes in rsFC after cortisol vs. placebo. To investigate rsFC changes in DMN, FPN, and SN due to the administration of cortisol as a function of depression severity we assessed the relationship between Beck Depression Inventory-II scores and rsFC changes in the networks of interest after cortisol vs. placebo administration for the entire sample. Results revealed that those with a history of depression exhibited increased connectivity between the left amygdala of the SN and left medial temporal gyrus of the DMN regardless of treatment. Further, we found that those who received cortisol had increased connectivity between the anterior insula of the SN and regions within the SN and DMN. Lastly, we found an interaction between depression symptom severity and rsFC between the PCC of the DMN and the right cerebellum of the SN, with greater depression symptoms associated with increased rsFC of the PCC and cerebellum. These findings are the first to show that

women with greater depression severity may be more likely to normalize aberrant connectivity of DMN and SN regions after acute cortisol administration. Our results could help inform clinical treatments for depression that naturally increase endogenous cortisol levels and efficiency of glucocorticoid receptors, such as long-term daily exercise. Overall, these findings contribute to the literature on the neurobiological effects of exogenous cortisol in depression.

Key words: depression, cortisol, resting-state functional connectivity, default mode network, frontoparietal network, salience network

1. Introduction

1.1. Depression Prevalence

Over 8% of adults living in the United States self-report experiencing depression symptoms in any given year (Brody et al., 2018; Ettman et al., 2020). Further, the prevalence rate of depression in recent years (e.g., 2021) is approximately three to seven times greater than that of previous years (e.g., 2019), which is thought to be due to the COVID-19 pandemic and social restrictions that followed (Bueno-Notivol et al., 2021; Ettman et al., 2020; Shah et al., 2021). Past research provides evidence that depression is two to three times more common in women than men (Brody et al., 2018; Rivera-Bonet et al., 2021) and recent research suggests that women were more adversely affected by the pandemic showing greater levels of psychiatric symptoms compared to men (Liu et al., 2020). Therefore, it is important to understand the neurobiological correlates of depression and to investigate potential treatment targets for depression as individuals are suffering from depression symptoms now more than ever.

1.2. Resting-State Functional Connectivity in Depression

Functional magnetic resonance imaging (fMRI) has been used to characterize abnormalities in cortical and subcortical brain networks in depression. For example, one fMRI method applied to resting-state fMRI data is resting-state functional connectivity (rsFC), which allows for the study of neural networks by examining the communication between brain regions to determine if anatomically distant regions reflect similar blood-oxygenated-level-dependent (BOLD) responses during a resting-state scan (Power et al., 2014). Regions that show similar BOLD time courses over the scan are considered functionally connected with one another, indicating the regions may be part of the same

neural network. On the other hand, regions exhibiting no correlation or negative

correlations with one another are typically part of different networks. Past reviews of

rsFC research provide support for the existence of large-scale brain networks in healthy

individuals and further suggest that normal connectivity of these networks may be altered

in various psychiatric disorders, including depression (Greicius, 2008; Menon, 2011).

The characteristic symptoms of depression (e.g., guilt and self-blame, deficits in

cognition, sad or depressed mood) are relevant to the functions associated with several

neural networks, including the default mode network (DMN), frontoparietal network

(FPN), and salience network (SN). For example, the DMN is typically most active and

functionally connected when turning attention inward, such as when thinking about

oneself or during negative self-focused thought (Andreasen et al., 1995; Buckner et al.,

2008; Buckner & Carroll, 2007; Gusnard et al., 2001; Philippi & Koenigs, 2014; Van

Oort et al., 2017; Yeo et al., 2011). The FPN is composed of brain regions that are most

active and functionally connected when completing cognitive tasks, such as attention or

working memory tasks, which may be more difficult for individuals with depression who

suffer from impairments in attention (Cabeza & Nyberg, 2000; Corbetta & Shulman,

2002; Fox et al., 2005; Kaiser, Andrews-Hanna, Wager, et al., 2015; Owen et al., 2005;

Vincent et al., 2008; Yaple et al., 2019). The SN has been implicated in emotional

processing, such as when processing sad stimuli or recalling sad events (Hermans et al.,

2014; Van Oort et al., 2017).

In a metanalysis of seed-based rsFC, researchers reported aberrant connectivity

within and between several neural networks in those with major depressive disorder

compared to healthy controls, including the DMN, FPN, and SN (Kaiser, Andrews-

Hanna, Wager, et al., 2015). Specifically, Kaiser and colleagues (Kaiser, Andrews-Hanna, Wager, et al., 2015) found that individuals with depression had hyperconnectivity of regions within the DMN and hypoconnectivity of regions within the FPN compared to controls. Other research has shown that connectivity within the SN in individuals with depression is mixed, with both hypo- and hyper-connectivity reported (Mulders et al., 2015; Philippi et al., 2020). Alterations of within-SN connectivity in those with a history of depression are thought to explain certain symptoms of depression, such as sad and ruminative thought patterns (Peters, Burkhouse, et al., 2016). Further, overactivity of SN has been shown to impair the anticipation of emotional outcomes in those with depressive symptomology (Rzepa & McCabe, 2016). In addition, past research posits that the SN is responsible for controlling attentional resources depending on task demands by facilitating the switch between DMN and FPN, or switching attention to internal or external information (Bernhardt et al., 2014; Peters, Van Meter, et al., 2016; Provenzano et al., 2019; Sridharan et al., 2008). In summary, hyperconnectivity of within-DMN regions, hypoconnectivity of within-FPN regions, and dysregulated within-SN connectivity relate to sad and ruminative thought patterns and cognitive impairments in individuals with a history of depression.

In terms of between network connectivity, past research in healthy adults has shown reliable negative correlations between DMN and task-active networks, such as the FPN and SN (Douw et al., 2016; Fox et al., 2005; Hellyer et al., 2014). In other words, under normal conditions, when attention is directed outward, such as during a working memory paradigm, task-active networks are most active, whereas the DMN is less active. Previous research indicates that this negative correlation between the DMN and task-

active networks is disrupted in individuals with depression or those prone to ruminative thought (Kaiser, Andrews-Hanna, Spielberg, et al., 2015; Lydon-Staley et al., 2019). Recent studies suggest that the inverse relation between DMN and FPN is diminished in those with depression, resulting in heightened connectivity between these networks (Kaiser, Andrews-Hanna, Wager, et al., 2015; Philippi et al., 2018). More specifically, past research has shown that there is hyperconnectivity between the pregenual anterior cingulate cortex (pgACC), a key node in the DMN, and the dorsolateral prefrontal cortex, a key node in the FPN, in those with depression (Philippi et al., 2018). Previous studies suggest that dysregulation of DMN-FPN connectivity in those with a history of depression may also explain the symptoms associated with depression, including rumination (Philippi et al., 2018), repetitive negative thought (Lydon-Staley et al., 2019), and impairments in working memory, attention, and emotion regulation (Hellyer et al., 2014; Kaiser, Andrews-Hanna, Spielberg, et al., 2015; Murphy et al., 2020). In terms of between-SN connectivity, Kaiser and colleagues (Kaiser, Andrews-Hanna, Spielberg, et al., 2015; Kaiser, Andrews-Hanna, Wager, et al., 2015) reported overall reduced connectivity between DMN and SN regions in those with depression. However, they also noted that results are mixed, suggesting that hypo- or hyperconnectivity between these networks may depend on whether patients with depression are directing their attention internally or externally. Said another way, the SN plays a key role in determining whether the DMN or FPN is more active and functionally connected depending on environmental situations.

In summary, within-DMN hyperconnectivity, within-FPN hypoconnectivity, and within-SN abnormal connectivity along with elevated between FPN-DMN connectivity

and dysregulated between SN-DMN connectivity relates to the previously mentioned depression symptoms, including sad and ruminative thought patterns, and deficits in working memory, attention, and emotion regulation.

1.3. Cortisol & rsFC

Activation of the hypothalamic-pituitary-adrenal (HPA) axis is responsible for the stress response, and dysfunction within the HPA-axis is consistently reported in depression (Bao et al., 2008; Holsen et al., 2013; Pariante, 2009; Parker et al., 2003; Peters et al., 2019; Peters, Van Meter, et al., 2016; Tofoli et al., 2011; Weinstein et al., 2010; Welberg & Seckl, 2001). Further, individuals with depression are known to have lower glucocorticoid receptor (GR) concentrations and may also exhibit impairments in GR-mediated negative feedback on the HPA-axis, which normally functions to inhibit further endogenous cortisol secretion (Anacker et al., 2011; Nemeroff et al., 1992; Pariante, 2009). Interestingly, the release of cortisol is known to modify connectivity of the DMN, SN, and FPN in healthy adolescents and adults, as well as those with depression symptoms (Kalafatakis et al., 2021; Peters, Burkhouse, et al., 2016; Soares et al., 2017; Taren et al., 2017; Thomason et al., 2011). For example, one study investigating endogenous levels of cortisol in individuals with a history of depression found that higher levels of endogenous cortisol were associated with greater rsFC between the DMN and FPN as well as between the SN and FPN (Peters et al., 2019). Given that endogenous cortisol has been associated with altered rsFC connectivity, it is possible that acute administration of cortisol (i.e., exogenous cortisol) may disrupt normal connectivity within and between the DMN, FPN, and SN in healthy populations. To our knowledge, only one study has examined the effects of acute cortisol administration on

rsFC in healthy male participants (Henckens et al., 2012). Henckens and colleagues (2012) reported that the administration of cortisol reduced negative correlations between the SN and DMN at rest in healthy male participants with no history of depression. A few studies using task-based fMRI suggest that exogenous cortisol can normalize connectivity of DMN regions during an emotional task in participants with a history of depression (Abercrombie et al., 2011; Rivera-Bonet et al., 2021). However, it remains unclear how acute administration of cortisol would affect rsFC in those with depression as there is limited research to date.

1.4. Conclusion of Past Literature

Several rsFC studies indicate that there is abnormal connectivity within and between the DMN, FPN, and SN in those with a history of depression compared to those with no history of depression (Hellyer et al., 2014; Kaiser, Andrews-Hanna, Spielberg, et al., 2015; Kaiser, Andrews-Hanna, Wager, et al., 2015; Lydon-Staley et al., 2019; Murphy et al., 2020; Peters et al., 2019; Philippi et al., 2018). It is plausible that an overactive HPA-axis leads to heightened levels of endogenous cortisol, which may cause the DMN to become overactive and less functionally specialized while also interfering with the between-network communication of DMN and FPN as well as DMN and SN (Peters et al., 2019). To our knowledge, no study has investigated the effect of acute cortisol administration on rsFC of these same networks in women with varying levels of depression. Acute cortisol administration in depression could have implications for the development of new treatments or interventions and understanding the mechanisms of acute cortisol administration in depression could lead to better depression treatments.

Lastly, to address a transdiagnostic perspective, we seek to understand how cortisol administration may change the connectivity of women with varying depression severities.

1.5. Aims & Hypotheses

Aim 1: The current study aims to investigate changes in rsFC of the DMN, FPN, and SN following administration of exogenous cortisol in women with different depression histories.

Hypothesis 1: Individuals with a history of depression, versus no history of depression, will have significantly decreased connectivity within DMN regions after cortisol administration compared to placebo.

Hypothesis 2: Individuals with a history of depression, versus no history of depression, will have significantly greater connectivity within FPN regions after administration of cortisol compared to placebo.

Hypothesis 3: Individuals with a history of depression, versus no history of depression, will have significantly altered connectivity within SN regions after administration of cortisol compared to placebo.

Hypothesis 4: Individuals with a history of depression, versus no history of depression, will have significantly decreased connectivity between DMN and FPN after the administration of cortisol compared to placebo.

Hypothesis 5: Individuals with a history of depression, versus no history of depression, will have significantly greater connectivity between DMN and SN after administration of cortisol compared to placebo.

Aim 2: Investigate the changes in rsFC of the DMN, FPN, and SN due to the administration of cortisol as a function of depression severity across the entire sample of women.

Hypothesis 6: Women with greater depression severity will have within FPN connectivity increases, within DMN connectivity decreases, within SN connectivity differences, and decreased connectivity between DMN-FPN and between DMN-SN after cortisol administration compared to placebo.

2. Method

2.1. Participants

Participants recruited for the current study were enrolled as part of a larger National Institutes of Health funded project examining the effects of cortisol on cognitive and neural function in depression (Abercrombie et al., 2018; Gaffey et al., 2019; Rivera-Bonet et al., 2021). Complete neuroimaging data were available for 74 participants who self-identified as 'female' for their biological sex. Participants ranged in age from 18 to 45 years old (M_{age} = 27.42, SD_{age} = 7.13). Sixty-nine percent of participant completed at least a Bachelor's degree, and 76% of participants were White (16% Asian and 5% Black). To investigate the role of depression history, participants were classified into one of two groups: (i) no history of depression (n = 28; NoDep); and (ii) any history of a Depressive Disorder (n = 46; DepHist) according to the Diagnostic and Statistical Manual of Mental Disorders-5 (American Psychiatric Association, 2013). Lastly, all participant data was collected before the start of the COVID-19 pandemic.

Participants were excluded for the following reasons: daily nicotine use; illicit drug use within four weeks of participation; current Substance Use Disorder, or within the last six months; recent pregnancy or breastfeeding (i.e., within the last six months); self-reported use of antidepressants or other psychotropic medications; hormonal contraceptive use; peri- or postmenopausal signs; highly irregular periods; claustrophobia; significant risk for suicide; lifetime history of psychosis or mania. All participants that met these criteria self-reported that they had not used antidepressants or other psychotropic medications within the half-life time frame of the particular drug. Participants were not excluded based on psychotherapeutic history. Many participants

reported taking antidepressant medications in the past and reported side effects, among other reasons, for not continuing to take medication. Psychotherapy was not provided to participants as a part of the study. Participants completed urine drug tests on three of the seven visits to the study site (diagnostic interview day and both fMRI scan days) in order to confirm no illicit drug use for the following drugs: marijuana, opiate, cocaine, amphetamine, and methamphetamine. Researchers also asked participants about illicit drug use during every session. Lastly, due to the repeated-measure nature of the research, five participants were excluded because they did not complete one of the two required scans (e.g., placebo or cortisol).

2.2. Procedures

Participants completed two fMRI scans separated by about one week. One hour before each scan, participants received either the placebo or the 20mg hydrocortisone pill for oral administration. The pills were identical in appearance and prepared by the University of Wisconsin Pharmaceutical Research Center. Past work using oral hydrocortisone administration showed peak cortisol levels 90 minutes after administration (Abercrombie et al., 2018). Administration of cortisol was double-blinded and randomized for each participant across both scan days. Importantly, previous researchers who used double-blinding in cortisol administration reported that participants were not able to perform above chance-level at guessing which condition cortisol was administered (Frost et al., 2018; Henckens et al., 2012). Finally, all participants went through a mock scan, which was completed before either scan day, to acclimate to the MRI scanning environment.

All participants were recruited from Madison, Wisconsin (WI), or the surrounding area, via paper and digital flyers posted online and in community areas, and through advertisements sent to counseling centers and clinics in the local area. All participants provided written informed consent and were paid for their participation in accordance with the local IRB.

2.3. Measures

2.3.1. Beck Depression Inventory (BDI-II)

Participant depression severity was assessed using the Beck Depression Inventory-II (BDI-II) at each visit (Beck et al., 1996). The BDI-II is composed of 21 self-report items used to measure depression-related symptom severity within the past two weeks. An example item from the BDI-II would be, *"How often have you found that you could not cope with all the things you had to do?"* Items on the BDI-II are ranked on a Likert scale from 0, indicating a "never" response, to 4, indicating a "very often" response. Some BDI-II items are reverse scored before a final BDI-II score is computed. A recent review examining the reliability of the BDI-II reported an average Cronbach Alpha of 0.90 (Eser & Asku, 2021), and test-retest reliability of the BDI-II, after one-week, is also high at 0.93 (Beck et al., 1996; Eser & Asku, 2021). The test-retest reliability of BDI-II scores for the current study was high at 0.98. Therefore, the average of BDI-II scores from the two fMRI scan visits (i.e., placebo and cortisol) was used for all analyses.

2.3.2. Structured Clinical Interview for DSM-IV-TR Axis I Disorders-Patient Edition (SCID)

The Structured Clinical Interview for the DSM-IV (SCID-I/P for DSM-IV TR; First, 1997) modified to assess DSM-5 criteria, was used for the psychopathology screening for all participants. The SCID is a structured interview used to assess Axis I disorders, which include depression, anxiety, posttraumatic stress disorder, and phobias, among other disorders. Only one participant in the NoDep group was found to have a diagnosis of a psychiatric condition in remission, Social Phobia.

2.4. MRI Data Acquisition

As part of the dissertation, I used previously collected MRI data (Abercrombie et al., 2018; Gaffey et al., 2019; Rivera-Bonet et al., 2021). The two MRI scans (i.e., placebo and cortisol) were collected using a 3T GE MRI scanner (Discovery MRI 750; GE Medical Systems, Waukesha, WI) equipped with an 8-channel radiofrequency coil array (GE Healthcare, Waukesha, WI). As mentioned above, the participants were scanned in a randomized and double-blinded manner, meaning roughly half of the participants received placebo during the first scan day. The resting-state fMRI data were collected using T2*-weighted Echo Planar Imaging (EPI) sequence (TR/TE/FA: 2150 ms/22ms/79°, matrix: 64 x 64, FOV: 22.4 cm, slice thickness: 3.5 mm, voxel size: 3.5 mm x 3.5 mm x 3.5 mm, slices: 40 sagittal, 280 total volumes) using thin slices and short echo time in order to minimize signal dropout in the ventromedial prefrontal cortex. Each participant was instructed during each resting-state scan (~10 min) to remain "calm, still, and awake" with their eyes open fixating on a cross back-projected onto a screen via an LCD projector (Avotec, Stuart, FL). To enable image registration and group comparison

of the functional data, high-resolution T1-weighted structural imaging data were acquired

using a weighted BRAVO pulse sequence (TI: 450ms, TR/TE/flip angle (FA): 8.16

ms/3.2 ms/12°, matrix: 256 x 256 x 160, field of view (FOV): 215.6 mm, slice thickness:

1 mm, voxel size: 1 mm x 1 mm x 1 mm, slices: 156).

2.5. Preprocessing and Motion Analysis

As part of the dissertation, I completed the following steps using previously

collected MRI data. The two resting-state fMRI scans were preprocessed using AFNI

(Cox, 1996) and FSL (FMRIB Software Library;). A rigid-body volume registration was

done first to compensate for participant motion during scanning (3dvolreg, fourth volume

as the base image volume). Second, field map correction was done using sagittal field

maps for all participants (collected via a 3D SPGR sequence; TR/TE/FA: 5ms/1.8ms/7°,

matrix: 192 x 128 x 44, FOV: 230mm, slice thickness: 3.5mm) to geometrically unwarp

EPIs to reduce distortion caused by magnetic field inhomogeneities (IDEAL sequence;

Reeder et al., 2005) and FMRIB Software Library (Woolrich et al., 2009). Next, the

following preprocessing steps were performed for all participant data for each of the

scans: (1) slice-time correct EPI slices (3dTshift, using first slice as a reference), (2)

omitted first three volumes (3dcalc), (3) aligned EPI data to respective T1-weighted

anatomical images (align_epi_anat.py) and transformed images to MNI-152 atlas space

(LPI) in a single interpolation to 3 x 3 x 3mm^3 voxels, (4) the 3D + time series were

despiked (3dDespike), and (5) data were temporally filtered (band-pass: .01 Hz $< f <$ .08

Hz) and spatially smoothed with a 6-mm full-width half-maximum (FWHM) Gaussian

kernel (3dBandPass). Normalized T1 anatomical images were segmented into gray

matter, white matter, and cerebrospinal fluid (CSF) using FAST in FSL (Zhang et al.,

2001). White matter and CSF segments were used as masks to extract a representative

time series from each tissue type for nuisance regression. Then, a voxelwise multiple

linear regression was performed (3dDeconvolve) to remove signal associated with motion

and other typical nuisance variables (Ciric et al., 2017) including: six motion parameters

(three translations, three rotations) which were obtained from the rigid body alignment of

EPI volumes and their six derivatives, white matter time series, ventricular CSF time

series, and finally a second-order polynomial to model baseline signal and slow drift. In

order to further control for participant motion, volumes used in the GLM were censored

for excessive motion, as described in the paragraph below. This final preprocessed file

for each participant was used in the rsFC analyses.

We also examined motion for each participant, as individual differences in

participant motion can contribute to resting-state correlations, and clinical populations

have been found to move more during scan time compared to controls (Power et al.,

2015). Participants were excluded based on the following criteria: mean framewise

motion displacement >3mm (i.e., volume to volume movement across the time series),

and/or total scan time <4 min after censoring all time points with framewise motion

displacement >.2mm and extreme timeseries displacement (i.e., time points were >10%

of voxels were outliers; Power et al., 2015). These thresholds were selected to provide the

most conservative criteria for motion correction (Power et al., 2012; Yan et al., 2013).

Average root-mean-squared (RMS) displacement was used as a summary of participant

motion, as has been done in previous work (Ciric et al., 2017; Philippi et al., 2020, 2021).

We investigated associations between average RMS and depression group, depression

severity, and treatment order (placebo versus cortisol).

2.6. Functional Connectivity Analysis

We performed seed-based voxelwise rsFC analyses (Biswal et al., 1995) using six

seed regions of interest (ROIs) from the DMN, FPN, and SN. Specifically, we used two

seed ROIs from the DMN, the mPFC and the posterior cingulate cortex (PCC; Buckner et

al., 2008; Sheline et al., 2009). Coordinates for the mPFC and PCC seeds were selected

from a network-perspective, coming from a seminal paper investigating self-referential

thought in depression (Sheline et al., 2009). In addition, the dorsolateral prefrontal cortex,

a key node in the FPN was used as a seed ROI (Peters, Burkhouse, et al., 2016; Van Oort

et al., 2017) and the coordinates for this seed were based on previous research (Peters,

Burkhouse, et al., 2016). Finally, we used three ROIs from the SN, the bilateral amygdala

and anterior insula, which are considered key nodes in the network (Kaiser, Andrews-

Hanna, Wager, et al., 2015; Peters et al., 2019; Seeley et al., 2007; Vaisvaser et al., 2013;

Wang et al., 2007). The bilateral amygdala coordinates for this study were created using

the Harvard-Oxford subcortical atlas and the coordinates for the anterior insula were

based on previous research using a network-perspective (Seeley et al., 2007).

To create the seed ROIs for the rsFC analysis, we first used the coordinates for

these ROIs to create 6-mm radius seed masks in MNI space. Next, the transformation

matrix from the registration procedure was used to align the seed ROIs masks to MNI

template space.

To compute rsFC for each participant for each treatment, the mean resting-state

BOLD time series from each seed ROI was included in a GLM (3dDeconvolve) to

calculate the correlation between each seed ROIs time series and all other voxels in the

brain. To create correlation maps for each ROI, the following steps were performed: (1)

used GLM output to convert R^2 values to correlation coefficient values (r) and (2) used

Fisher's r-to-z transformation to convert r to z-scores. The resulting z- scores were

entered into the second-level statistical analyses to determine support for or evidence

against the current hypotheses.

2.7. rsFC Statistical Analyses

2.7.1 Aim 1

To examine the relationship between rsFC changes of DMN, FPN, and SN due to

acute cortisol administration in women with different depression histories ($N = 74$) we

performed a mixed-model analysis of variance (ANOVA) with depression history group

predicting connectivity changes after cortisol administration for each network seed

region. Furthermore, for Aim 1, a sensitivity analysis in G*Power (Faul et al., 2007,

2009) using 'ANOVA: Repeated measures, within-between interaction' indicated that

with sample sizes of 28 (NoDep) and 46 (DepHist) and an alpha of 5% (two-sided), we

would have 80% power to detect a moderate effect size of $f = 0.17$ (small $= .10$; medium

$= .25$). The same sensitivity analysis with a Bonferonni corrected alpha value of .008

revealed a medium effect of $f = 0.24$.

To correct for multiple comparisons, we used a family-wise error (FWE)

correction approach at the cluster level using a whole-brain mask in AFNI (3dClustSim;

Carp, 2012; Forman et al., 1995) and applied cluster-extent thresholding. To address the

non-Gaussian nature of fMRI data (Eklund et al., 2016), the auto-correlation function in

AFNI (-acf) was used to calculate FWHM for each subject (3dFWHMx). The cluster-

extent threshold corresponds to the statistical probability of $\alpha = .05$ of identifying a

random noise cluster at a predefined voxelwise threshold of $p < .001$ (uncorrected). Using

this whole-brain FWE cluster correction, a cluster-corrected size was identified and

clusters larger than 52 voxels were identified as statistically significant in the analyses

(p_{FWE} < .008 Bonferroni corrected for number of seed ROIs; 32 voxels whole-brain

cluster-corrected without Bonferroni correction, p <.05).

2.7.2 Aim 2

Aim 2 investigated the rsFC changes in DMN, FPN, and SN due to the

administration of cortisol as a function of depression severity. We performed repeated-

measures ANOVAs using the entire smaple (N = 74) to assess the relationship between

the average BDI-II scores from the two fMRI visits, a continuous predictor, and the

average rsFC changes in the networks of interest as a result of cortisol administration. For

Aim 2, a sensitivity analysis in G*Power (Faul et al., 2007, 2009) using 'ANOVA:

Repeated measures, within-between interaction' indicated that with a total sample of 74

participants and an alpha of 5% (two-sided), we would have 80% power to detect a

moderate effect of f = 0.15. The same sensitivity analysis with a Bonferonni corrected

alpha value of .008 revealed a medium effect of f = 0.21. Lastly, the same multiple

comparisons correction method described in Aim 1 was applied in Aim 2.

2.8. Statistical Assumptions Checks

For each of the significant results we examined whether statistical assumptions were

met for the mixed-design ANOVAs for aim one and the repeated measures ANOVAs for

aim 2.

2.8.1 Aim 1 Assumptions

For aim 1, the assumption of normality was met as Box's M = 4.37, F = 1.41, p =

0.24. We also met the assumption of sphericity for aim 1, as Mauchley's W = 1.00. The

assumption of independence was also met as rsFC of one participant did not influence the

rsFC data of a second participant. Outlier checks for aim one identified one potential

outlier. The 5% trim mean and mean values for aim one were not significantly different,

therefore no data were removed as outliers for aim one.

2.8.2 Aim 2 Assumptions

For aim 2, the assumption of sphericity was met, as Mauchley's $W = 1.00$. The

assumption of independence was also met as the rsFC data of one participant did not

influence the rsFC data of other participants. Potential outliers were identified during an

outlier check for the significant findings for aim 2. However, the 5% trimmed values did

not significantly differ from the mean values of the results for aim 2, thus no values were

removed as outliers for the analyses included under aim 2.

Results

3.1. Demographic Variable Results

We first examined whether there were any differences between the two

depression groups (NoDep and DepHist) in age, education, or race. Specifically, we

performed an independent-samples t-test for age and two Pearson's chi-square tests for

education and race. We found no significant differences in age, $t(72) = -0.53$, $p = .44$,

education, $\chi^2 (5) = 2.41$, $p = .79$, or race, $\chi^2 (2) = 2.32$, $p = .31$, between the participants

in the NoDep and DepHist groups (Table 1). Given that there were no differences

between the depression history groups, we did not include these demographic variables as

covariates in the analyses for Aim 1 and Aim 2 described below.

3.2. Aim 1 Results

3.2.1 rsFC After Cortisol Administration in Women with Different Depression

Histories

To address aim 1, we performed 2 (treatment) x 2 (group) mixed-design

ANOVAs using 3dMVM in Afni to determine whether there were any differences in

rsFC for the DMN, FPN, and SN seed ROIs between the two treatments (placebo and

cortisol) and the two depression history groups (NoDep and DepHist). We found a

significant main effect of depression group for connectivity between the left amygdala

seed of the SN and a significant cluster in the left middle temporal gyrus (MTG) of the

DMN, $F(1,72) = 19.47$, $p < 0.001$, $\eta_p^2 = .213$ (Figure 1). This effect was driven by the

rsFC between the SN and DMN regions being lower in the depression history compared

to the no depression history group (Table 2). There was no significant main effect of

treatment, $F(1,72) = .83$, $p = .366$, and no interaction between treatment and depression

group, $F(1,72) = .78$, $p = .38$, for the left amygdala seed of the SN. For Aim 1, all other

mixed-model ANOVAs conducted in Afni for the remaining DMN, FPN, and SN seed

ROIs were not significant ($p_{FWE} > .05$). Although the significant main effect of group for

the left amygdala was significant after correction for multiple comparisons ($p_{FWE} < .05$),

it did not remain significant after a Bonferroni correction for the six network seed ROIs

used in the present study ($p_{FWE} > .008$). This finding does not provide support for the

hypotheses in aim 1.

3.3. Aim 2 Results

3.3.1. rsFC After Cortisol Administration as a Function of Depression Severity

To address aim 2, we performed repeated measures ANOVAs using 3dMVM in

Afni to investigate the interaction between depression severity (BDI) and treatment

(placebo vs. cortisol) across women with different depression symptom severities. There

was a significant main effect of treatment for rsFC between the right anterior insula of the

SN and the left inferior frontal gyrus of the ventral attention network, $p_{FWE} < .05$, $F(1,72)$

$= 14.38$, $p < .001$, $\eta_p^2 = 0.166$. Specifically, there was greater rsFC between the right

anterior insula of the SN and left inferior frontal gyrus of the ventral attention network

after acute cortisol administration as compared with placebo scans (Figure 3a). We also

found a significant main effect of treatment for rsFC between the right anterior insula

seed of the SN and the left superior temporal gyrus (STG) of the DMN, $p_{FWE} < .05$,

$F(1,72) = 16.25$, $p < .001$, $\eta_p^2 = 0.184$. Specifically, there was greater rsFC between the

right anterior insula of the SN and the left STG of the DMN after acute cortisol

administration compared with placebo scans (Figure 3b; Table 2). There was no

interaction between depression severity and treatment for the right anterior insula seed

($p_{FWE} >.05$)

        We found a significant interaction between depression severity and treatment for

rsFC between the posterior cingulate cortex (PCC) seed of the DMN and lobule VIIIa of

the right cerebellum, part of the ventral attention network, $p_{FWE} < .05$, $F(1,72) = 22.58$, p

$< .001$, $\eta_p^2 = 0.239$ (Figure 2b). Figure 3c shows that greater depression severity was

associated with increased rsFC connectivity between the PCC of the DMN and right

cerebellum (VIIIa) of the ventral attention network after cortisol administration compared

to placebo (Table 2). Although this interaction was significant after correction for

multiple comparisons ($p_{FWE} < .05$), this result did not remain significant after Bonferroni

correction for the six seed ROIs ($p_{FWE} > .008$). There were no significant main effects of

depression severity or treatment for the PCC seed ($p_{FWE} > .05$). All other repeated

measure ANOVAs for the other DMN, FPN, and SN seed ROIs did not meet the

threshold for statistical significance ($p_{FWE} >.05$).

4. **Discussion**

To our knowledge, this is the first study to investigate the effects of acute cortisol administration on rsFC of large-scale neural networks in women with different depression histories and severities. The present study examined the relationship between rsFC changes of DMN, FPN, and SN due to acute cortisol administration in women with different depression histories. Additionally, we investigated the interaction between depression severity and treatment type across women with different depression symptom severities.

4.1. Aim 1 Discussion

4.1.1. Main Effect of Depression Group

Overall, there was little support for aim 1 of the current study. Hypothesis 5 predicted that cortisol would increase SN-DMN connectivity in depression and decrease in no depression. Although the results do not support the interaction predicted in hypothesis 5, there was a main effect of depression history group. Specifically, the history of depressive disorders group had reduced rsFC between the left amygdala of the SN and the left MTG of the DMN compared to the no depression group, regardless of cortisol. These findings are consistent with previous research showing reduced rsFC between SN-DMN in depression (Kaiser, Andrews-Hanna, Spielberg, et al., 2015). The SN is thought to control, at least in part, the activity and connectivity of the DMN depending on situations and task demands (Peters et al., 2019; Peters, Van Meter, et al., 2016; Provenzano et al., 2019). Additionally, decreased SN-DMN connectivity in individuals with depression may also explain the role of the SN in hyperactivity in the DMN (Sridharan et al., 2008). All other models assessing main effects of treatment

(cortisol or placebo) and group (no history of depression and history of depression) did not reach statistical significance, nor did interactions between the two factors for the remainder of DMN, FPN, and SN seed ROIs. The lack of results supporting Aim 1 hint at depression severity, not depression group, being a key factor in understanding how cortisol may be able to normalize rsFC of individuals with a history of depression. In other words, grouping individuals into one of two groups (e.g., no history of depression group and history of depressive disorders group) may not be the best way to investigate cortisol's effect on brain connectivity in individuals with depression.

4.2. Aim 2 Discussion

Aim 2 investigated the interaction between depression severity (BDI-II scores) and treatment type (placebo vs. cortisol) related to connectivity of the DMN, FPN, and SN across women with different depression symptom severities. First, we found a main effect of treatment for rsFC of the anterior insula, part of the SN, and two separate clusters, the left inferior frontal gyrus (IFG) of the ventral attention network and the left superior temporal gyrus (STG) of the DMN. There was also an interaction between treatment and depression severity for the rsFC of the PCC of the DMN and the right Lobule VIIIa of the cerebellum, part of the ventral attention network. The functions and networks of each significant cluster for aim 2 are discussed below.

4.2.1. Main Effects of Treatment

The IFG is thought to be part of the ventral attention network (Vossel et al., 2014; Yeo et al., 2011) which overlaps with regions in the salience network (SN; Seeley et al., 2007). Thus, the SN and ventral attention network are functionally similar such that both networks show increased activity and rsFC during emotional processing or when

orienting attention toward the internal or external environment for further processing
(Hermans et al., 2014; Seeley et al., 2007; Van Oort et al., 2017; Vossel et al., 2014; Yeo
et al., 2011). Due to the function of these networks, the connectivity patterns of the IFG
likely change given the specifics of mental states and task demands (Baer et al., 2019;
Sezer et al., 2022). The finding of increased rsFC between the right anterior insula of the
SN and the left IFG of the ventral attention network/SN during the cortisol scan
compared to the placebo scan provides partial support for Aim 2. Said another way, the
administration of cortisol increased within-SN connectivity regardless of depression
severity.

The STG is thought to be a main component of the DMN (Bilevicius et al., 2018;
Yeo et al., 2011). The finding of increased rsFC of the right anterior insula of the SN and
the left STG of the DMN during the cortisol treatment compared to placebo provides
partial support to aim 2. We predicted increased rsFC between DMN-SN after cortisol
administration in those with the highest depression severity. We found a main effect of
treatment showing that, regardless of depression severity, connectivity between DMN-SN
(e.g., STG-anterior insula) increased. In other words, the administration of cortisol
reduced the normal negative correlation between the DMN and SN. Although no
interaction was present, the increased DMN-SN connectivity regardless of depression
severity is interpreted that there are natural negative DMN-SN correlations in those with
depression (Kaiser, Andrews-Hanna, Spielberg, et al., 2015; Kaiser, Andrews-Hanna,
Wager, et al., 2015) and that cortisol eliminates these correlations. This finding is also
consistent with previous research which reported that cortisol administration reduced
negative correlations between DMN-SN in male participants with no history of

depression (Henckens et al., 2012). Currently, we believe that the administration of

cortisol may allow for individuals, regardless of depression severity, to more easily

switch between task-active and task-inactive networks (Bernhardt et al., 2014;

Holtzheimer & Mayberg, 2011; Peters et al., 2019; Provenzano et al., 2019; Sridharan et

al., 2008). In other words, increasing exogenous, and potentially endogenous, cortisol

may prevent individuals from getting stuck in one network (Holtzheimer & Mayberg,

2011).

4.2.2. Interaction of Treatment and Depression Symptom Severity

The only significant interaction between treatment and depression severity for aim

2 occurred for the rsFC between the PCC seed of the DMN and Lobule VIIIa of the right

cerebellum, thought to be part of the ventral attention network (Buckner et al., 2011;

Stoodley & Schmahmann, 2009). Figure 3C shows that those with heightened depression

severity had increased rsFC between the PCC of the DMN and Lobule VIIIa of the

cerebellum of the ventral attention network after cortisol administration compared to

placebo. Given that the ventral attention network and SN are part of the same functional

network (Seeley et al., 2007), our findings indicate that greater depression severity was

associated with increased DMN-SN connectivity after cortisol treatment versus placebo.

Previous research findings of reduced DMN-SN connectivity in those with a history of

depression (Kaiser, Andrews-Hanna, Spielberg, et al., 2015; Kaiser, Andrews-Hanna,

Wager, et al., 2015), coupled with the current results, suggest that cortisol may be

normalizing rsFC between DMN-SN in individuals with greater depression severity.

Simlar to the current study, previous task-dependent rsFC findings revealed that

abnormal task-dependent rsFC of a DMN seed was normalized after cortisol

administration in women with depression (Rivera-Bonet et al., 2021). In summary, the

present findings provide support to a neurocognitive model in which alterations in neural

networks are closely linked with psychiatric conditions such as depression (Kaiser,

Andrews-Hanna, Wager, et al., 2015).

4.3. Clinical Implications and Future Directions

Given that greater depression severity was associated with normalization of

between network connectivity in response to acute cortisol administration, the findings

from the current study have several clinical implications. First, practicing mindfulness

may be one way to strengthen aberrant connectivity between DMN and SN (Sezer et al.,

2022) which may result in more effective modulation of endogenous cortisol during acute

social stressors that negatively impact those with depression (Peters, Burkhouse, et al.,

2016; Peters, Van Meter, et al., 2016; Sezer et al., 2022). In other words, strengthening

abnormal connectivity between these networks during task-active states, such as during

mindfulness or during specific therapies, may be one way to normalize the connectivity

between these networks during rest and result in remediation of depression symptoms.

Further, another viable option for treating depression is improving the efficiency or

function of glucocorticoid receptors (GR) in humans (Anacker et al., 2011). For example,

research investigating the efficacy of exercise to ameliorate depressive symptoms found

that it does not differ from antidepressant medications (Cooney et al., 2013), which have

their molecular effects on GR function (Anacker et al., 2011). Said another way, exercise

is thought to be a viable alternative treatment for depression, specifically for those who

may have tried multiple antidepressant regimens or for those who view side effects of

antidepressant to outweigh the benefits of the medication (Cooney et al., 2013; Gomes de

Assis & Cieszczyk, 2020). It is also possible that daily physical exercise, whether being

resistance, strength, or anaerobic exercise, can ameliorate depressive symptoms by

improving GR function. Lastly, researchers believe that exercise could be used as a

treatment option for those with depression, though exercise in conjunction with

pharmacological (e.g., antidepressants) and/or psychological treatments (e.g.,

psychotherapy) may be the best form of treatment for those with greater than mild or

moderate depression (Beesley & Mutrie, 1997; Cooney et al., 2013; Gomes de Assis &

Cieszczyk, 2020).

4.4 Limitations

The current study had several limitations that are important to mention. First,

there are obvious sex differences that appear in the cortisol literature (Abercrombie et al.,

2011; Kirschbaum et al., 1992; Stroud et al., 2002) and these should be considered when

conceptualizing future aims and hypotheses involving samples with men and women, and

generalizing results across all biological sexes is cautioned.

Second, the number of participants in each group was uneven, including twenty-

eight women ($n = 28$) with no history of depression (NoDep), and forty-six women ($n =$

46) who had differing depression histories (DepHist). Thus, future work using larger

sample sizes are needed to replicate the current results and to potentially find a greater

effect of cortisol on rsFC of large-scale neural networks.

Additionally, factors other than the impaired functionality of the HPA axis and

GR functionality should be discussed when trying to understand the effects of cortisol on

rsFC in those with depression. For example, past research found factors such as

childhood trauma and childhood emotional abuse often have a moderating effect on

cognitive and neurobiological outcome variables when studying samples with varying

levels of depression (Abercrombie et al., 2011, 2018; Heim et al., 2008). This is

consistent with animal models of early life trauma which reveal that rats who experience

early life trauma show enhanced learning under high-stress whereas animals with no

history of early life trauma show enchanced learning under reduced stress (Champagne et

al., 2008). Future research investigating the role of cortisol on rsFC in depression should

include childhood truma and emotional abuse measures in their models to determine if

they, in addition to depression severity, impact rsFC in depression after cortisol

administration.

Further, the depression history group (DepHist, $n = 46$) included individuals who

have current depressive disorders as well as individuals who have remitted depression.

This large depression history group may be considered a hetereogeneous group to some,

which may also be viewed as a limitation of the current analyses. Also, due to the clinical

nature of the research participants were recruited through convience sampling via flyers

and ads and were included in the study if they met all inclusion criteria (see participants

section).

Lastly, the administration of cortisol as a potential treatment mechanism for

depression needs to be discussed. The acute and chronic effects of excess cortisol are

well-known, and we do not believe that the administration of cortisol should serve as a

primary treatment for persons with any level of depression (Pariante & Lightman, 2008).

4.5 Conclusion

In summary, this study is the first to demonstrate that the administration of

cortisol normalizes rsFC between DMN and SN regions in women with greater

depression severity. Although this study increased exogenous cortisol through

pharmacological manipulation, researchers suggest that those with severe depression

symptomology will benefit more from psychotherapeutic treatment in conjunction with

other interventions such as daily physical exercise.

Figures

Figure 1. Bar Graph Showing the Main Effect of Group for rsFC Between the Left Amygdala, a SN Seed, and the Left Middle Temporal Gyrus, a FPN Cluster, by Depression History Group for Aim 1.
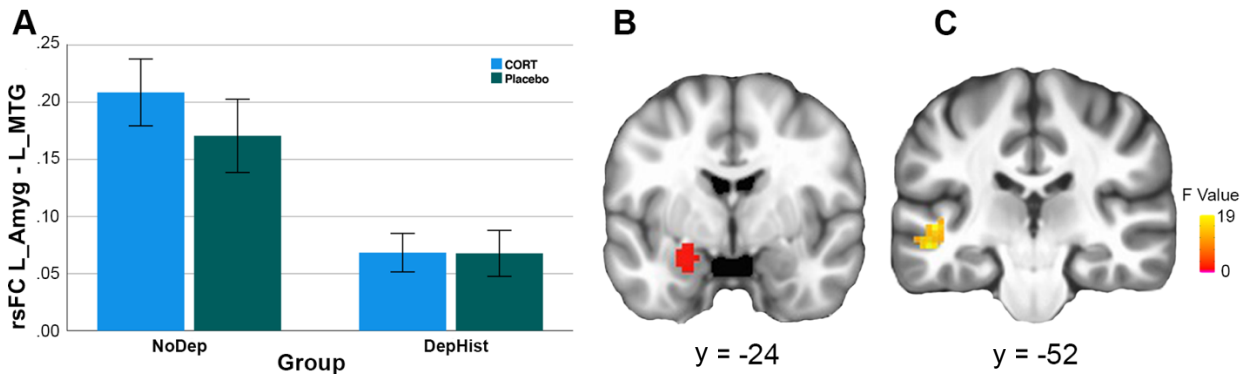
Note. A. For Aim 1, there was a main effect of depression history group for rsFC between the left amygdala of the SN (B.) and the left middle temporal gyrus extending to the superior temporal gyrus (C.), of the DMN, $F(1,71) = 21.45$, $p < 0.001$, $\eta_p^2 = 0.232$. The effect appears to be driven by the no depression history group (NoDep) such that there is significantly increased connectivity between the left amygdala of the SN and the left middle temporal gyrus of FPN in the no depression group compared to the depression history group. The error bars on each bar graph depict +/- 1 standard error, and all results survived whole-brain cluster correction $p_{FWE} < .05$, $p < .001$ uncorrected. Acronyms: SN = Salience Network; FPN = Frontoparietal Network; L_Amyg = Left amygdala; L_MTG = Left middle temporal gyrus; CORT = cortisol; NoDep = no depression group; DepHist = depression history group. (B) Picture of the left amygdala seed in red. (C) Picture of left middle temporal gyrus cluster.

Figure 2. Pictures of the Anterior Insula and PCC Seeds with significant clusters for

Aim 2.

A

x = 37   y = -43   x = -55

B

x = -6   y = 9
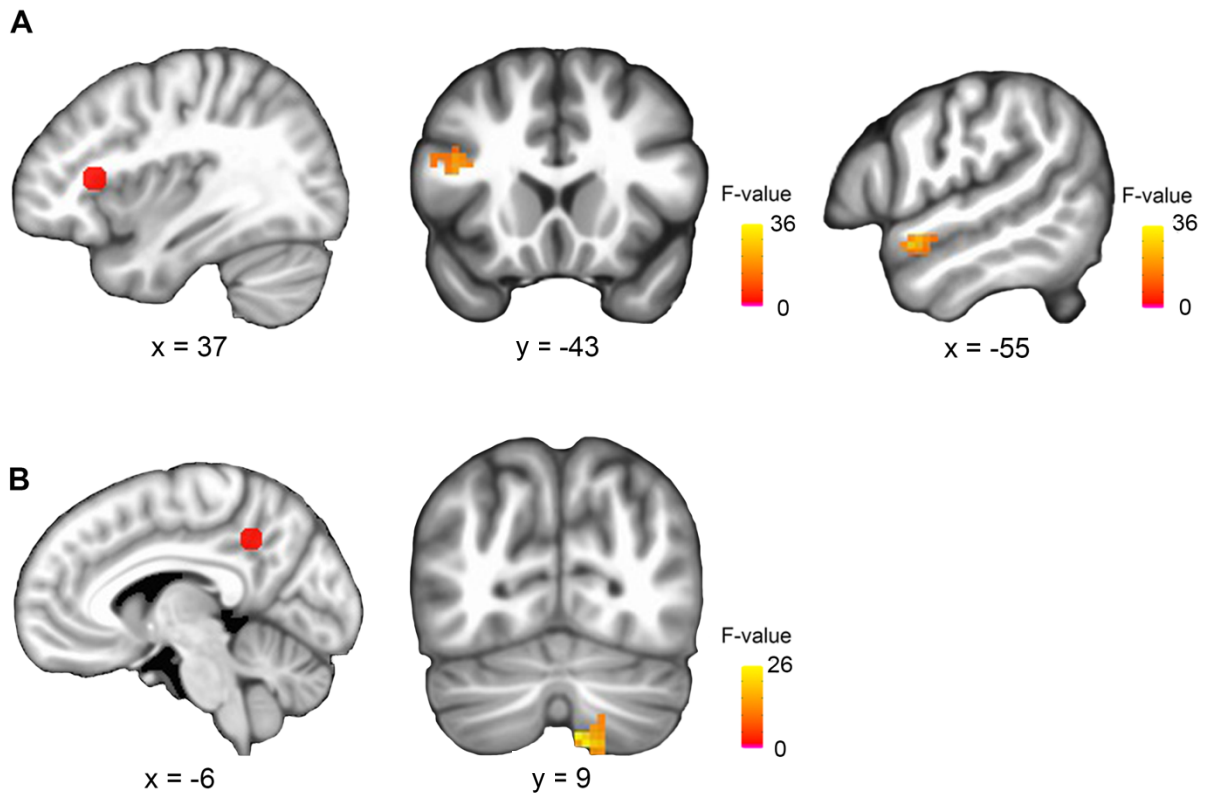
Note. A. Depicts the right anterior insula seed (red) and the two significant clusters

(orange) at the left inferior frontal gyrus (middle), $p_{FWE} < .05$, $F(1,72) = 14.38$, $p < .001$,

$\eta_p^2 = 0.166$ (Figure 3A), and the left superior frontal lobe (right), $p_{FWE} < .05$, $F(1,72) =$

16.25, $p < .001$, $\eta_p^2 = 0.184$ (Figure 3B). The right anterior insula is a SN seed, the left

inferior frontal gyrus cluster (x = -43) is a ventral attention network region, and the left

superior temporal gyrus cluster (x = -55) is a DMN region. F-values for the clusters range

from 0 (red) to 36 (yellow). B. Depicts the significant interaction of treatment and

depression symptoms for rsFC between the left posterior cingulate cortex (PCC) seed of

the DMN in red and a cluster at the right lobule VIIIa of the cerebellum, part of the

ventral attention entwork, in yellow/orange, $F(1,72) = 9.43$, $p = .003$, $\eta_p^2 = 0.116$ (Figure

3c). The F-values for this cluster range from 0 (red) to 26 (yellow).

Figure 3. Bar Graphs of Main Effects of Treatment for rsFC Between Ant_Ins Seed and L_IFG and L_STG Clusters and Scatterplot of Interaction between Treatment and Depression Severity for rsFC of PCC Seed with R_Cb Cluster for Aim2.
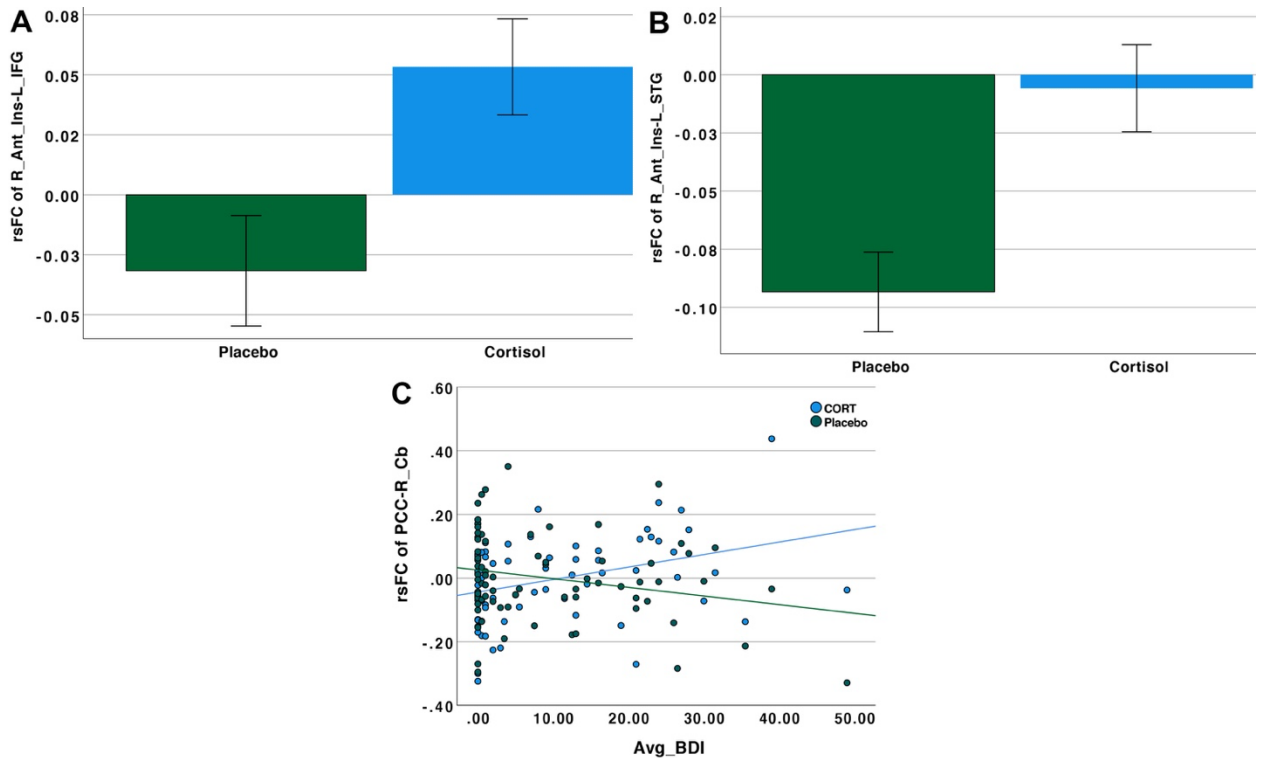
Note. A. Depicts the bar graph showing the significant main effect of treatment for the rsFC between the right anterior insula (Ant_Ins) seed and the left inferior frontal gyrus (L_IFG) cluster, $p_{FWE} < .05$, $F(1,72) = 14.38$, $p < .001$, $\eta_p^2 = 0.166$.

B. Depicts the bar graph showing the significant main effect of treatment for mean rsFC between the right Ant_Ins seed and the left superior temporal gyrus (L_STG) cluster, $p_{FWE} < .05$, $F(1,72) = 16.25$, $p < .001$, $\eta_p^2 = 0.184$.

C. Depicts the scatterplot showing the significant interaction between treatment and depression severity for rsFC of the posterior cingulate cortex seed and lobule VIIIa of the right cerebellum, $F(1,72) = 9.43$, $p = .003$, $\eta_p^2 = 0.116$. Regression lines are plotted separately for cortisol (light blue lines and dots) and placebo (dark green lines and dots) scans showing the relationship between rsFC and average BDI.

Acronyms: PCC = posterior cingulate cortex; DMN = Default Mode Network; R_Cb = lobule VIII of the right cerebellum; CORT = cortisol; Avg_BDI = average BDI-II scores from both scan days.

Tables

Table 1

Demographic variables by depression group

	NoDep (*n* = 28)	DepHist (*n* = 46)
Age[a]	26.9 (7.7)	27.8 (6.8)
Education Level[a]		
High school diploma/equivalent	0	1
Some college, no degree	12	14
Associate's degree	1	1
Bachelor's degree	7	15
Master's degree	6	13
Doctoral degree	2	2
Race[a]		
White	21	35
Asian	4	8
Black	3	1
Unknown	0	2
Avg. BDI-II[b]	0.9 (1.4)	14.3 (12.2)

Notes. BDI-II = Beck Depression Inventory-II; NoDep = no history of depression group;

DepHist = depression history group

[a] There were no significant differences between depression groups in age, $t(72) = -0.53$, *p*

= .44, education, $X^2 (74, 5) = 2.41$, $p = .79$, or race, $X^2 (74, 2) = 2.32$, $p = .31$, between the

participants in the NoDep and DepHist groups.

[b] BDI-II scores ranged from 0 to 47; as expected, we found significant differences

between the two groups in depression severity, $t(72) = -5.79$, $p < .001$.

Table 2

Group Resting-State Functional Connectivity Results for Networks of Interest

Seed ROI	Cluster location	MNI coordinates (x, y, z)	Cluster size (voxels)	F-value	[a]Average connectivity NoDep	[a]Average connectivity DepHist
PCC	Right Cerebellum Lobule VIIIa	9, -72, -51	44	22.58	Cortisol: -0.06 (0.13) Placebo: -0.00 (0.15)	Cortisol: 0.02 (0.13) Placebo: 0.00 (0.13)
Anterior Insula	Left inferior frontal gyrus	-43, 19, 25	40	5.86	Cortisol: 0.04 (0.16) Placebo -0.00 (0.21)	Cortisol: 0.06 (0.18) Placebo: -0.05 (0.19)
Anterior Insula	Left superior temporal gyrus	-55, 4, -12	33	16.25	Cortisol: -0.03 (0.19) Placebo: -.10 (0.16)	Cortisol: 0.01 (0.14) Placebo: -0.09 (0.14)
Left Amyg	Left middle temporal gyrus extend to superior temporal gyrus	-52, -24, -9	32	18.87	Cortisol: 0.22 (0.15) Placebo: 0.17 (0.17)	Cortisol: 0.07 (0.11) Placebo: .08 (0.14)

Note. Regression results from resting-state analysis were not significant at $p_{FWE} = 0.05$, $p = 0.001$ voxelwise uncorrected threshold. ROI = region of interest; PCC = posterior cingulate cortex; Amyg = amygdala.

[a]Average raw connectivity scores correspond to z-scores; means and standard deviations are reported for each group.

References

Abercrombie, H. C., Frost, C. P., Walsh, E. C., Hoks, R. M., Cornejo, M. D., Sampe, M.

      C., Gaffey, A. E., Plante, D. T., Ladd, C. O., & Birn, R. M. (2018). Neural

      Signaling of Cortisol, Childhood Emotional Abuse, and Depression-Related

      Memory Bias. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*,

      3(3), 274–284. https://doi.org/10.1016/j.bpsc.2017.11.005

Abercrombie, H. C., Jahn, A. L., Davidson, R. J., Kern, S., Kirschbaum, C., & Halverson,

      J. (2011). Cortisol's effects on hippocampal activation in depressed patients are

      related to alterations in memory formation. *Journal of Psychiatric Research*,

      45(1), 15–23. https://doi.org/10.1016/j.jpsychires.2010.10.005

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental*

      Health Disorders-5.

Anacker, C., Zunszain, P. A., Carvalho, L. A., & Pariante, C. M. (2011). The

      glucocorticoid receptor: Pivot of depression and of antidepressant treatment? *In*

      Search Of The Biological Basis Of Mood Disorders: Exploring Out Of The

      Mainstream, *36*(3), 415–425. https://doi.org/10.1016/j.psyneuen.2010.03.007

Andreasen, N. C., O'Leary, D. S., Cizadlo, T., Arndt, S., Rezai, K., Watkins, G. L.,

      Ponto, L. L. B., & Hichwa, R. D. (1995). Remembering the past: Two facets of

      episodic memory explored with positron emission tomography. *The American*

      Journal of Psychiatry, *152*(11), 1576–1585.

      https://doi.org/10.1176/ajp.152.11.1576

Baer, R., Gu, J., Cavanagh, K., & Strauss, C. (2019). Differential sensitivity of

      mindfulness questionnaires to change with treatment: A systematic review and

meta-analysis. *Psychological Assessment*, *31*(10), 1247–1263.

https://doi.org/10.1037/pas0000744

Bao, A.-M., Meynen, G., & Swaab, D. F. (2008). The stress system in depression and

neurodegeneration: Focus on the human hypothalamus. *The Endocrine Nervous*

System: Source and Target for Neuroactive Steroids, *57*(2), 531–553.

https://doi.org/10.1016/j.brainresrev.2007.04.005

Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. F. (1996). Comparison of Beck

Depression Inventories-IA and-II in Psychiatric Outpatients. *Journal of*

Personality Assessment, *67*(3), 588–597.

https://doi.org/10.1207/s15327752jpa6703_13

Beesley, S., & Mutrie, N. (1997). Exercise is beneficial adjunctive treatment in

depression. *BMJ (Clinical Research Ed.)*, *315*(7121), 1542–1543. PubMed.

https://doi.org/10.1136/bmj.315.7121.1542a

Bernhardt, B. C., Smallwood, J., Tusche, A., Ruby, F. J. M., Engen, H. G., Steinbeis, N.,

& Singer, T. (2014). Medial prefrontal and anterior cingulate cortical thickness

predicts shared individual differences in self-generated thought and temporal

discounting. *NeuroImage*, *90*, 290–297.

https://doi.org/10.1016/j.neuroimage.2013.12.040

Bilevicius, E., Smith, S. D., & Kornelsen, J. (2018). Resting-state network functional

connectivity patterns associated with the mindful attention awareness scale. *Brain*

Connectivity, *8*(1), 40–48. https://doi.org/10.1089/brain.2017.0520

Biswal, B., Zerrin Yetkin, F., Haughton, V. M., & Hyde, J. S. (1995). Functional

connectivity in the motor cortex of resting human brain using echo-planar mri.

Magnetic Resonance in Medicine, *34*(4), 537–541.

https://doi.org/10.1002/mrm.1910340409

Brody, D., Pratt, L., & Hughes, J. (2018). *Prevalence of Depression Among Adults Aged*

20 and Over: United States, 2013–2016. Center for Disease Control and

Prevention. https://www.cdc.gov/nchs/products/databriefs/db303.htm

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default

network. *Annals of the New York Academy of Sciences*, *1124*(1), 1–38.

https://doi.org/10.1196/annals.1440.011

Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in*

Cognitive Sciences, *11*(2), 49–57. https://doi.org/10.1016/j.tics.2006.11.004

Buckner, R. L., Krienen, F. M., Castellanos, A., Diaz, J. C., & Yeo, B. T. T. (2011). The

organization of the human cerebellum estimated by intrinsic functional

connectivity. *Journal of Neurophysiology*, *106*(5), 2322–2345.

https://doi.org/10.1152/jn.00339.2011

Bueno-Notivol, J., Gracia-García, P., Olaya, B., Lasheras, I., López-Antón, R., &

Santabárbara, J. (2021). Prevalence of depression during the COVID-19 outbreak:

A meta-analysis of community-based studies. *International Journal of Clinical*

and Health Psychology, *21*(1), 100196.

https://doi.org/10.1016/j.ijchp.2020.07.007

Cabeza, R., & Nyberg, L. (2000). Imaging Cognition II: An Empirical Review of 275

PET and fMRI Studies. *Journal of Cognitive Neuroscience*, *12*(1), 1–47.

https://doi.org/10.1162/08989290051137585

Carp, J. (2012). The secret lives of experiments: Methods reporting in the fMRI

　　literature. *NeuroImage*, *63*(1), 289–300.

　　https://doi.org/10.1016/j.neuroimage.2012.07.004

Champagne, D. L., Bagot, R. C., van Hasselt, F., Ramakers, G., Meaney, M. J., de Kloet,

　　E. R., Joëls, M., & Krugers, H. (2008). Maternal Care and Hippocampal

　　Plasticity: Evidence for Experience-Dependent Structural Plasticity, Altered

　　Synaptic Functioning, and Differential Responsiveness to Glucocorticoids and

　　Stress. *The Journal of Neuroscience*, *28*(23), 6037.

　　https://doi.org/10.1523/JNEUROSCI.0526-08.2008

Ciric, R., Wolf, D. H., Power, J. D., Roalf, D. R., Baum, G. L., Ruparel, K., Shinohara,

　　R. T., Elliott, M. A., Eickhoff, S. B., Davatzikos, C., Gur, R. C., Gur, R. E.,

　　Bassett, D. S., & Satterthwaite, T. D. (2017). Benchmarking of participant-level

　　confound regression strategies for the control of motion artifact in studies of

　　functional connectivity. *NeuroImage*, *154*, 174–187.

　　https://doi.org/10.1016/j.neuroimage.2017.03.020

Cooney, G., Dwan, K., Greig, C., Lawlor, D., Rimer, J., Waugh, F., McMurdo, M., &

　　Mead, G. (2013). Exercise for depression. *Cochrane Database of Systematic

　　Reviews*, *9*. https://doi.org/10.1002/14651858.CD004366.pub6

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven

　　attention in the brain. *Nature Reviews Neuroscience*, *3*(3), 201–215.

　　https://doi.org/10.1038/nrn755

Cox, R. W. (1996). AFNI: Software for Analysis and Visualization of Functional

Magnetic Resonance Neuroimages. *Computers and Biomedical Research*, *29*(3),

162–173. https://doi.org/10.1006/cbmr.1996.0014

Douw, L., Wakeman, D. G., Tanaka, N., Liu, H., & Stufflebeam, S. M. (2016). State-

dependent variability of dynamic functional connectivity between frontoparietal

and default networks relates to cognitive flexibility. *Neuroscience*, *339*, 12–21.

https://doi.org/10.1016/j.neuroscience.2016.09.034

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

Academy of Sciences*, *113*(28), 7900–7905.

https://doi.org/10.1073/pnas.1602413113

Eser, M. T., & Asku, G. (2021). *Beck Depression Inventory-II: A Study for meta

analytical reliability generalization*. *11*(3), 88–101.

https://doi.org/10.14527/pegegog.2021.00

Ettman, C. K., Abdalla, S. M., Cohen, G. H., Sampson, L., Vivier, P. M., & Galea, S.

(2020). Prevalence of Depression Symptoms in US Adults Before and During the

COVID-19 Pandemic. *JAMA Network Open*, *3*(9), e2019686–e2019686.

https://doi.org/10.1001/jamanetworkopen.2020.19686

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses

using G*Power 3.1: Tests for correlation and regression analyses. *Behavior

Research Methods*, *41*(4), 1149–1160. https://doi.org/10.3758/BRM.41.4.1149

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible

statistical power analysis program for the social, behavioral, and biomedical

sciences. *Behavior Research Methods*, *39*(2), 175–191.

https://doi.org/10.3758/BF03193146

First, M. B. (1997). *Structured clinical interview for DSM-IV axis I disorders.*

Forman, S. D., Cohen, J. D., Fitzgerald, M., Eddy, W. F., Mintun, M. A., & Noll, D. C.

(1995). Improved Assessment of Significant Activation in Functional Magnetic

Resonance Imaging (fMRI): Use of a Cluster-Size Threshold. *Magnetic*

Resonance in Medicine, *33*(5), 636–647.

https://doi.org/10.1002/mrm.1910330508

Fox, M., Snyder Abraham Z., Vincent Justin L., Corbetta Maurizio, Van Essen David C.,

& Raichle Marcus E. (2005). The human brain is intrinsically organized into

dynamic, anticorrelated functional networks. *Proceedings of the National*

Academy of Sciences, *102*(27), 9673–9678.

https://doi.org/10.1073/pnas.0504136102

Frost, C. P., Meyerand, M. E., Birn, R. M., Hoks, R. M., Walsh, E. C., & Abercrombie,

H. C. (2018). Childhood Emotional Abuse Moderates Associations Among

Corticomotor White Matter Structure and Stress Neuromodulators in Women

With and Without Depression. *Frontiers in Neuroscience*, *12*.

https://www.frontiersin.org/article/10.3389/fnins.2018.00256

Gaffey, A. E., Walsh, E. C., Ladd, C. O., Hoks, R. M., & Abercrombie, H. C. (2019).

Alterations in Systemic and Cognitive Glucocorticoid Sensitivity in Depression.

Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, *4*(3), 310–

320. https://doi.org/10.1016/j.bpsc.2018.11.007

Gomes de Assis, G., & Cieszczyk, P. (2020). Exercise—A unique endogenous regulator of irisin, BDNF, leptin and cortisol against depression. *Baltic Journal of Health and Physical Activity*, *12*(2), 1–8. https://doi.org/10.29359/BJHPA.12.4.01

Greicius, M. (2008). Resting-state functional connectivity in neuropsychiatric disorders. *Current Opinion in Neurology*, *21*(4). https://journals.lww.com/co-neurology/Fulltext/2008/08000/Resting_state_functional_connectivity_in.7.aspx

Gusnard, D., Erbil, A., Shulman Gordon L., & Raichle Marcus E. (2001). Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proceedings of the National Academy of Sciences*, *98*(7), 4259–4264. https://doi.org/10.1073/pnas.071043098

Heim, C., Newport, D. J., Mletzko, T., Miller, A. H., & Nemeroff, C. B. (2008). The link between childhood trauma and depression: Insights from HPA axis studies in humans. *Psychoneuroendocrinology*, *33*(6), 693–710. https://doi.org/10.1016/j.psyneuen.2008.03.008

Hellyer, P. J., Shanahan, M., Scott, G., Wise, R. J. S., Sharp, D. J., & Leech, R. (2014). The Control of Global Brain Dynamics: Opposing Actions of Frontoparietal Control and Default Mode Networks on Attention. *The Journal of Neuroscience*, *34*(2), 451. https://doi.org/10.1523/JNEUROSCI.1853-13.2014

Henckens, M. J. A. G., van Wingen, G. A., Joëls, M., & Fernández, G. (2012). Corticosteroid Induced Decoupling of the Amygdala in Men. *Cerebral Cortex*, *22*(10), 2336–2345. https://doi.org/10.1093/cercor/bhr313

Hermans, E. J., Henckens, M. J. A. G., Joëls, M., & Fernández, G. (2014). Dynamic

adaptation of large-scale brain networks in response to acute stressors. *Trends in*

Neurosciences, *37*(6), 304–314. https://doi.org/10.1016/j.tins.2014.03.006

Holsen, L. M., Lancaster, K., Klibanski, A., Whitfield-Gabrieli, S., Cherkerzian, S.,

Buka, S., & Goldstein, J. M. (2013). HPA-axis hormone modulation of stress

response circuitry activity in women with remitted major depression.

Neuroscience, *250*, 733–742. https://doi.org/10.1016/j.neuroscience.2013.07.042

Holtzheimer, P. E., & Mayberg, H. S. (2011). Stuck in a rut: Rethinking depression and

its treatment. *Trends in Neurosciences*, *34*(1), 1–9.

https://doi.org/10.1016/j.tins.2010.10.004

Kaiser, R. H., Andrews-Hanna, J. R., Spielberg, J. M., Warren, S. L., Sutton, B. P.,

Miller, G. A., Heller, W., & Banich, M. T. (2015). Distracted and down: Neural

mechanisms of affective interference in subclinical depression. *Social Cognitive*

and Affective Neuroscience, *10*(5), 654–663. https://doi.org/10.1093/scan/nsu100

Kaiser, R. H., Andrews-Hanna, J. R., Wager, T. D., & Pizzagalli, D. A. (2015). Large-

Scale Network Dysfunction in Major Depressive Disorder: A Meta-analysis of

Resting-State Functional Connectivity. *JAMA Psychiatry*, *72*(6), 603–611.

https://doi.org/10.1001/jamapsychiatry.2015.0071

Kalafatakis, K., Russell, G. M., Ferguson, S. G., Grabski, M., Harmer, C. J., Munafò, M.

R., Marchant, N., Wilson, A., Brooks, J. C., Thakrar, J., Murphy, P., Thai, N. J.,

& Lightman, S. L. (2021). Glucocorticoid ultradian rhythmicity differentially

regulates mood and resting state networks in the human brain: A randomised

controlled clinical trial. *Psychoneuroendocrinology*, *124*, 105096.

https://doi.org/10.1016/j.psyneuen.2020.105096

Kirschbaum, C., Wust, S., & Hellhammer, D. (1992). Consistent sex differences in

cortisol responses to psychological stress. *Psychosomatic Medicine*, *54*(6), 648–

657. https://doi.org/10.1097/00006842-199211000-00004

Liu, N., Zhang, F., Wei, C., Jia, Y., Shang, Z., Sun, L., Wu, L., Sun, Z., Zhou, Y., Wang,

Y., & Liu, W. (2020). Prevalence and predictors of PTSS during COVID-19

outbreak in China hardest-hit areas: Gender differences matter. *Psychiatry

Research*, *287*, 112921. https://doi.org/10.1016/j.psychres.2020.112921

Lydon-Staley, D. M., Kuehner, C., Zamoscik, V., Huffziger, S., Kirsch, P., & Bassett, D.

S. (2019). Repetitive negative thinking in daily life and functional connectivity

among default mode, fronto-parietal, and salience networks. *Translational

Psychiatry*, *9*(1), 234. https://doi.org/10.1038/s41398-019-0560-0

Menon, V. (2011). Large-scale brain networks and psychopathology: A unifying triple

network model. *Trends in Cognitive Sciences*, *15*(10), 483–506.

https://doi.org/10.1016/j.tics.2011.08.003

Mulders, P. C., van Eijndhoven, P. F., Schene, A. H., Beckmann, C. F., & Tendolkar, I.

(2015). Resting-state functional connectivity in major depressive disorder: A

review. *Neuroscience & Biobehavioral Reviews*, *56*, 330–344.

https://doi.org/10.1016/j.neubiorev.2015.07.014

Murphy, A. C., Bertolero, M. A., Papadopoulos, L., Lydon-Staley, D. M., & Bassett, D.

S. (2020). Multimodal network dynamics underpinning working memory. *Nature

Communications*, *11*(1), 3035. https://doi.org/10.1038/s41467-020-15541-0

Nemeroff, C. B., Krishnan, K. R. R., Reed, D., Leder, R., Beam, C., & Dunnick, N. R. (1992). Adrenal Gland Enlargement in Major Depression: A Computed Tomographic Study. *Archives of General Psychiatry*, *49*(5), 384–387. https://doi.org/10.1001/archpsyc.1992.01820050048008

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*(1), 46–59. https://doi.org/10.1002/hbm.20131

Pariante, C. M. (2009). Risk Factors for Development of Depression and Psychosis. *Annals of the New York Academy of Sciences*, *1179*(1), 144–152. https://doi.org/10.1111/j.1749-6632.2009.04978.x

Pariante, C. M., & Lightman, S. L. (2008). The HPA axis in major depression: Classical theories and new developments. *Trends in Neurosciences*, *31*(9), 464–468. https://doi.org/10.1016/j.tins.2008.06.006

Parker, K. J., Schatzberg, A. F., & Lyons, D. M. (2003). Neuroendocrine aspects of hypercortisolism in major depression. *Hormones and Behavior*, *43*(1), 60–66. https://doi.org/10.1016/S0018-506X(02)00016-8

Peters, A. T., Burkhouse, K., Feldhaus, C. C., Langenecker, S. A., & Jacobs, R. H. (2016). Aberrant resting-state functional connectivity in limbic and cognitive control networks relates to depressive rumination and mindfulness: A pilot study among adolescents with a history of depression. *Journal of Affective Disorders*, *200*, 178–181. https://doi.org/10.1016/j.jad.2016.03.059

Peters, A. T., Jenkins, L. M., Stange, J. P., Bessette, K. L., Skerrett, K. A., Kling, L. R., Welsh, R. C., Milad, M. R., Phan, K. L., & Langenecker, S. A. (2019). Pre-scan

cortisol is differentially associated with enhanced connectivity to the cognitive

control network in young adults with a history of depression.

Psychoneuroendocrinology, *104*, 219–227.

https://doi.org/10.1016/j.psyneuen.2019.03.007

Peters, A. T., Van Meter, A., Pruitt, P. J., Briceño, E. M., Ryan, K. A., Hagan, M.,

Weldon, A. L., Kassel, M. T., Vederman, A., Zubieta, J.-K., McInnis, M.,

Weisenbach, S. L., & Langenecker, S. A. (2016). Acute cortisol reactivity

attenuates engagement of fronto-parietal and striatal regions during emotion

processing in negative mood disorders. *Psychoneuroendocrinology*, *73*, 67–78.

https://doi.org/10.1016/j.psyneuen.2016.07.215

Philippi, C. L., Cornejo, M. D., Frost, C. P., Walsh, E. C., Hoks, R. M., Birn, R., &

Abercrombie, H. C. (2018). Neural and behavioral correlates of negative self-

focused thought associated with depression. *Human Brain Mapping*, *39*(5), 2246–

2257. https://doi.org/10.1002/hbm.24003

Philippi, C. L., & Koenigs, M. (2014). The neuropsychology of self-reflection in

psychiatric illness. *Journal of Psychiatric Research*, *54*, 55–63.

https://doi.org/10.1016/j.jpsychires.2014.03.004

Philippi, C. L., Pessin, S., Reyna, L., Floyd, T., & Bruce, S. E. (2020). Cortical midline

structures associated with rumination in women with PTSD. *Journal of

Psychiatric Research*, *131*, 69–76.

https://doi.org/10.1016/j.jpsychires.2020.09.001

Philippi, C. L., Velez, C. S., Wade, B. S. C., Drennon, A. M., Cooper, D. B., Kennedy, J.

E., Bowles, A. O., Lewis, J. D., Reid, M. W., York, G. E., Newsome, M. R.,

Wilde, E. A., & Tate, D. F. (2021). Distinct patterns of resting-state connectivity in U.S. service members with mild traumatic brain injury versus posttraumatic stress disorder. *Brain Imaging and Behavior*, *15*(5), 2616–2626. https://doi.org/10.1007/s11682-021-00464-1

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*, *59*(3), 2142–2154. https://doi.org/10.1016/j.neuroimage.2011.10.018

Power, J. D., Schlaggar, B. L., & Petersen, S. E. (2014). Studying Brain Organization via Spontaneous fMRI Signal. *Neuron*, *84*(4), 681–696. https://doi.org/10.1016/j.neuron.2014.09.007

Power, J. D., Schlaggar, B. L., & Petersen, S. E. (2015). Recent progress and outstanding issues in motion correction in resting state fMRI. *NeuroImage*, *105*, 536–551. https://doi.org/10.1016/j.neuroimage.2014.10.044

Provenzano, J., Verduyn, P., Daniels, N., Fossati, P., & Kuppens, P. (2019). Mood congruency effects are mediated by shifts in salience and central executive network efficiency. *Social Cognitive and Affective Neuroscience*, *14*(9), 987–995. https://doi.org/10.1093/scan/nsz065

Reeder, S. B., Pineda, A. R., Wen, Z., Shimakawa, A., Yu, H., Brittain, J. H., Gold, G. E., Beaulieu, C. H., & Pelc, N. J. (2005). Iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL): Application with fast spin-echo imaging. *Magnetic Resonance in Medicine*, *54*(3), 636–644. https://doi.org/10.1002/mrm.20624

Rivera-Bonet, C. N., Birn, R. M., Ladd, C. O., Meyerand, M. E., & Abercrombie, H. C. (2021). Cortisol effects on brain functional connectivity during emotion processing in women with depression. *Journal of Affective Disorders*, *287*, 247–254. https://doi.org/10.1016/j.jad.2021.03.034

Rzepa, E., & McCabe, C. (2016). Decreased anticipated pleasure correlates with increased salience network resting state functional connectivity in adolescents with depressive symptomatology. *Journal of Psychiatric Research*, *82*, 40–47. https://doi.org/10.1016/j.jpsychires.2016.07.013

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. *The Journal of Neuroscience*, *27*(9), 2349. https://doi.org/10.1523/JNEUROSCI.5587-06.2007

Sezer, I., Pizzagalli, D. A., & Sacchet, M. D. (2022). Resting-state fMRI functional connectivity and mindfulness in clinical and non-clinical contexts: A review and synthesis. *Neuroscience & Biobehavioral Reviews*, *135*, 104583. https://doi.org/10.1016/j.neubiorev.2022.104583

Shah, S. M. A., Mohammad, D., Qureshi, M. F. H., Abbas, M. Z., & Aleem, S. (2021). Prevalence, Psychological Responses and Associated Correlates of Depression, Anxiety and Stress in a Global Population, During the Coronavirus Disease (COVID-19) Pandemic. *Community Mental Health Journal*, *57*(1), 101–110. https://doi.org/10.1007/s10597-020-00728-y

Sheline, Y. I., Barch, D. M., Price, J. L., Rundle, M. M., Vaishnavi, S. N., Snyder, A. Z., Mintun, M. A., Wang, S., Coalson, R. S., & Raichle, M. E. (2009). The default

mode network and self-referential processes in depression. *Proceedings of the National Academy of Sciences*, *106*(6), 1942–1947. https://doi.org/10.1073/pnas.0812686106

Soares, J. M., Marques, P., Magalhães, R., Santos, N. C., & Sousa, N. (2017). The association between stress and mood across the adult lifespan on default mode network. *Brain Structure and Function*, *222*(1), 101–112. https://doi.org/10.1007/s00429-016-1203-3

Sridharan, D., Levitin Daniel J., & Menon Vinod. (2008). A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proceedings of the National Academy of Sciences*, *105*(34), 12569–12574. https://doi.org/10.1073/pnas.0800005105

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *NeuroImage*, *44*(2), 489–501. https://doi.org/10.1016/j.neuroimage.2008.08.039

Stroud, L. R., Salovey, P., & Epel, E. S. (2002). Sex differences in stress responses: Social rejection versus achievement stress. *Biological Psychiatry*, *52*(4), 318–327. https://doi.org/10.1016/S0006-3223(02)01333-1

Taren, A. A., Gianaros, P. J., Greco, C. M., Lindsay, E. K., Fairgrieve, A., Brown, K. W., Rosen, R. K., Ferris, J. L., Julson, E., Marsland, A. L., & Creswell, J. D. (2017). Mindfulness Meditation Training and Executive Control Network Resting State Functional Connectivity: A Randomized Controlled Trial. *Psychosomatic Medicine*, *79*(6), 674–683. PubMed. https://doi.org/10.1097/PSY.0000000000000466

Thomason, M. E., Hamilton, J. P., & Gotlib, I. H. (2011). Stress-induced activation of the

    HPA axis predicts connectivity between subgenual cingulate and salience network

    during rest in adolescents. *Journal of Child Psychology and Psychiatry*, *52*(10),

    1026–1034. https://doi.org/10.1111/j.1469-7610.2011.02422.x

Tofoli, S. M. de C., Baes, C. von W., Martins, C. M. S., & Juruena, M. (2011). *Early life

    stress, HPA axis, and depression*. *4*(2), 229–234.

    https://doi.org/10.3922/j.psns.2011.2.008

Vaisvaser, S., Lin, T., Admon, R., Podlipsky, I., Greenman, Y., Stern, N., Fruchter, E.,

    Wald, I., Pine, D., Tarrasch, R., Bar-Haim, Y., & Hendler, T. (2013). Neural

    traces of stress: Cortisol related sustained enhancement of amygdala-hippocampal

    functional connectivity. *Frontiers in Human Neuroscience*, *7*.

    https://www.frontiersin.org/article/10.3389/fnhum.2013.00313

Van Oort et al. (2017). How the brain connects in response to acute stress: A   review

    at the human brain systems level. *Neuroscience& Biobehavioral Reviews*, *83*,

    281–297.

Vincent, J. L., Kahn, I., Snyder, A. Z., Raichle, M. E., & Buckner, R. L. (2008). Evidence

    for a Frontoparietal Control System Revealed by Intrinsic Functional

    Connectivity. *Journal of Neurophysiology*, *100*(6), 3328–3342.

    https://doi.org/10.1152/jn.90355.2008

Vossel, S., Geng, J. J., & Fink, G. R. (2014). Dorsal and Ventral Attention Systems:

    Distinct Neural Circuits but Collaborative Roles. *The Neuroscientist*, *20*(2), 150–

    159. https://doi.org/10.1177/1073858413494269

Wang, J., Korczykowski, M., Rao, H., Fan, Y., Pluta, J., Gur, R. C., McEwen, B. S., &
Detre, J. A. (2007). Gender difference in neural response to psychological stress.
Social Cognitive and Affective Neuroscience, *2*(3), 227–239.
https://doi.org/10.1093/scan/nsm018

Weinstein, A. A., Deuster, P. A., Francis, J. L., Bonsall, R. W., Tracy, R. P., & Kop, W.
J. (2010). Neurohormonal and inflammatory hyper-responsiveness to acute mental
stress in depression. *Biological Psychology*, *84*(2), 228–234.
https://doi.org/10.1016/j.biopsycho.2010.01.016

Welberg, L. A. M., & Seckl, J. R. (2001). Prenatal Stress, Glucocorticoids and the
Programming of the Brain. *Journal of Neuroendocrinology*, *13*(2), 113–128.
https://doi.org/10.1111/j.1365-2826.2001.00601.x

Woolrich, M. W., Jbabdi, S., Patenaude, B., Chappell, M., Makni, S., Behrens, T.,
Beckmann, C., Jenkinson, M., & Smith, S. M. (2009). Bayesian analysis of
neuroimaging data in FSL. *Mathematics in Brain Imaging*, *45*(1, Supplement 1),
S173–S186. https://doi.org/10.1016/j.neuroimage.2008.10.055

Yan, C.-G., Cheung, B., Kelly, C., Colcombe, S., Craddock, R. C., Martino, A. D., Li, Q.,
Zuo, X.-N., Castellanos, F. X., & Milham, M. P. (2013). A comprehensive
assessment of regional variation in the impact of head micromovements on
functional connectomics. *NeuroImage*, *76*, 183–201.
https://doi.org/10.1016/j.neuroimage.2013.03.004

Yaple, Z. A., Stevens, W. D., & Arsalidou, M. (2019). Meta-analyses of the n-back
working memory task: FMRI evidence of age-related changes in prefrontal cortex

involvement across the adult lifespan. *NeuroImage*, *196*, 16–31.

https://doi.org/10.1016/j.neuroimage.2019.03.074

Yeo, B. T. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead,

M., Roffman, J. L., Smoller, J. W., Zöllei, L., Polimeni, J. R., Fischl, B., Liu, H.,

& Buckner, R. L. (2011). The organization of the human cerebral cortex estimated

by intrinsic functional connectivity. *Journal of Neurophysiology*, *106*(3), 1125–

1165. https://doi.org/10.1152/jn.00338.2011

Zhang, Y., Brady, M., & Smith, S. (2001). Segmentation of brain MR images through a

hidden Markov random field model and the expectation-maximization algorithm.

IEEE Transactions on Medical Imaging, *20*(1), 45–57.