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Lack of Robust Associations Between Prepandemic Coping Strategies and Frontolimbic Circuitry With Depression and Anxiety Symptoms During the COVID-19 Pandemic: A Preregistered Longitudinal Study

Bailey Holt-Gosselin[1, 2], Emily M. Cohodes[1], Sarah McCauley[1], Jordan C. Foster[1], Paola Odriozola[1], Sadie J. Zacharek[1], Sahana Kribakaran[1, 2], Jason T. Haberman[1], H. R. Hodges[1], and Dylan G. Gee[1]

[1] Department of Psychology, Yale University

[2] Interdepartmental Neuroscience Graduate Program, Yale University

The COVID-19 pandemic is an ongoing stressor that has resulted in the exacerbation of mental health problems worldwide. However, longitudinal studies that identify preexisting behavioral and neurobiological factors associated with mental health outcomes during the pandemic are lacking. Here, we examined associations between prepandemic coping strategy engagement and frontolimbic circuitry with internalizing symptoms during the pandemic. In 85 adults (71.8% female; age 18–30 years), we assessed prototypically adaptive coping strategies (Connor–Davidson Resilience Scale), resting-state functional magnetic resonance imaging functional connectivity (FC) of frontolimbic circuitry, and depression and anxiety symptoms (Beck Depression Inventory, Screen for Child Anxiety-Related Emotional Disorders–Adult, respectively). We conducted general linear models to test preregistered hypotheses that (1) lower coping engagement prepandemic and (2) weaker frontolimbic FC prepandemic would predict elevated symptoms during the pandemic; and (3) coping would interact with FC to predict symptoms during the pandemic. Depression and anxiety symptoms worsened during the pandemic (ps $< .001$). Prepandemic adaptive coping engagement and frontolimbic FC were not associated with depression or anxiety symptoms during the pandemic (uncorrected ps $> .05$). Coping interacted with insula-rostral anterior cingulate cortex (ACC) FC ($p = .003$, pFDR $= .014$) and with insula-ventral ACC FC ($p < .001$, pFDR $< .001$) to predict depression symptoms, but these findings did not survive FDR correction after removal of outliers. Findings from our preregistered study suggest that specific prepandemic factors, particularly adaptive coping and frontolimbic circuitry, are not robustly associated with emotional responses to the pandemic. Additional studies that identify preexisting neurobehavioral factors implicated in mental health outcomes during global health crises are needed.

Keywords: COVID-19, anxiety, depression, coping, frontolimbic circuitry

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Dylan G. Gee https://orcid.org/0000-0002-3685-2710

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Correspondence concerning this article should be addressed to Dylan G. Gee, Department of Psychology, Yale University, 2 Hillhouse Avenue, New Haven, CT 06520, United States. Email: dylan.gee@yale.edu

The coronavirus disease (COVID-19) pandemic is an ongoing stressor that has resulted in millions of deaths (World Health Organization, 2021) and significant increases in anxiety and depression worldwide (Xiong et al., 2020). Few longitudinal studies have identified specific behavioral and neurobiological factors that are associated with mental health outcomes during this global stressor. Identifying factors that may buffer against or exacerbate the effects of stressful events on mental health is essential for contributing to the development and improvement of early detection and intervention programs. In the present study, we addressed current gaps in knowledge by using a multimodal approach to examine whether prepandemic coping strategy engagement and functional connectivity (FC) between frontolimbic brain regions relate to anxiety and depression symptoms during the pandemic. We leverage a sample of young adults, an age group shown to be at particularly elevated risk for poor mental health during the pandemic (Varma et al., 2021), who reported on their mental health in an early stage of the pandemic (May–June 2020).

Engagement in prototypically adaptive coping strategies (e.g., adopting a positive view of stress and change, acceptance of one's own negative feelings) has been shown to play a role in determining whether an individual will develop adverse mental health conditions following stress exposure (Connor & Davidson, 2003). In particular, individuals who more frequently engage in prototypically adaptive coping strategies are less likely to develop symptoms of depression and anxiety in the face of heightened stress (Robinson et al., 2014; Wermelinger Ávila et al., 2017). Thus, existing research indicates that adaptive coping strategy engagement may lower the risk of elevated depression and anxiety symptoms in response to the global pandemic. Recent work has demonstrated that greater use of prototypically adaptive coping strategies (e.g., positive reframing, emotional support) and lower use of prototypically maladaptive coping strategies (e.g., self-blame, behavioral disengagement) are associated with less severe psychiatric symptoms during the COVID-19 pandemic (Ran et al., 2020; Schmitt et al., 2021; Shechory Bitton & Laufer, 2021; Song et al., 2021; Valero-Moreno et al., 2021). However, there is also evidence of no association between use of prototypically adaptive coping strategies and psychiatric symptoms during the pandemic (Holt-Gosselin et al., 2021). It is important to delineate the precise impact of engagement in coping strategies on clinical symptom severity during stressful events to ultimately identify individuals at heightened risk and to inform the optimization of behavioral treatments.

In addition to behavioral factors, preexisting neurobiological factors may be associated with the development and/or exacerbation of anxiety and depression symptoms during stressful events. In particular, FC between brain regions involved in emotion regulation may play a role in mental health following the onset of a stressor (VanTieghem & Tottenham, 2018). Prior work has shown that the amygdala, anterior cingulate cortex (ACC), insula, and medial prefrontal cortex (mPFC) are key frontolimbic regions implicated in the development of psychiatric symptoms; specifically, altered FC between the ACC–insula (Helm et al., 2018; Klumpp et al., 2013; Mulders et al., 2015; Peterson et al., 2014), ACC–amygdala (Arnold Anteraper et al., 2014; Etkin et al., 2009, 2010; Matthews et al., 2008; Musgrove et al., 2015; Prater et al., 2013), insula–amygdala (Manoliu et al., 2014; Mulders et al., 2015; Veer et al., 2010), and amygdala–mPFC (Prater et al., 2013) have been linked to elevated symptoms of anxiety and depression. Similarly, there is robust evidence that frontolimbic FC is implicated in responses to chronic stress (VanTieghem & Tottenham, 2018). Together, these findings suggest that alterations in frontolimbic FC may be associated with greater risk for the development and/or exacerbation of anxiety and depression symptoms during the COVID-19 pandemic. Relatedly, it is possible that individual differences in frontolimbic FC may interact with coping strategy use to predict psychiatric symptoms during the pandemic. That is, the relation between coping engagement and symptom severity during the pandemic may depend on frontolimbic FC. A recent study revealed that the use of prototypically maladaptive coping strategies interacted with preexisting amygdala volume to predict depression symptoms during the pandemic (Holt-Gosselin et al., 2021). However, FC among frontolimbic regions has not been examined in relation to coping strategy engagement and psychiatric symptoms during the pandemic. Investigating the complex relations among coping, frontolimbic FC, and psychiatric symptoms during the pandemic has the potential to provide important insight regarding for whom engagement in coping strategies during stressful events may be most effective and beneficial.

Despite robust evidence of the negative impact of the pandemic on mental health (Xiong et al., 2020), the extent to which specific neurobehavioral factors (e.g., coping strategy engagement and frontolimbic FC) are associated with psychiatric symptoms during the pandemic remains unknown. The present study tested three preregistered hypotheses in a sample of young adults with varying levels of depression and anxiety symptoms. First, we hypothesized that a lower tendency to engage in prototypically adaptive coping strategies prepandemic would be associated with elevated anxiety and depression symptoms during the pandemic. Second, we hypothesized that weaker prepandemic frontolimbic FC would be associated with higher anxiety and depression symptoms during the pandemic. Third, we hypothesized that coping strategy engagement would interact with frontolimbic FC to predict anxiety and depression symptoms during the pandemic. We also conducted preregistered exploratory analyses to examine the associations among coping strategy engagement, frontolimbic FC, and specific anxiety symptoms (e.g., panic, social, generalized, etc.). Elucidating these relations is an important step toward the identification of individuals who are at elevated risk for mental health problems during the COVID-19 pandemic.

Method

Transparency and Openness

The analysis plan was preregistered in June 2021 on the Open Science Framework (DOI: https://doi.org/10.17605/OSF.IO/YKQMV; Holt-Gosselin et al., 2021) before any statistical analyses were conducted and after data collection. Prior to the preregistration, several coauthors had access to certain variables used in the present study for other analyses that are unrelated to the present study. There were no deviations from the analysis plan. Analyses were conducted using R studio Version 3.6.1. Materials and analysis code for this study are available by emailing the corresponding author.

Study Design and Participants

Prepandemic data used for the present investigation were collected at Yale University between January 2017 and January 2020. Data were acquired as part of an ongoing study examining the neural mechanisms underlying fear reduction in children, adolescents, and adults. The study protocol was approved by the institutional review board at Yale University. All participants identified as being potentially eligible for the broader study provided written, informed consent according to the procedures set forth by the Human Investigation Committee at Yale University and conducted according to the principles of the Declaration of Helsinki. Participants were recruited via flyers distributed throughout the community and online advertisements in the New Haven, Connecticut, area. Inclusion criteria included the following: 18–30 years old, free of current psychotropic medication, IQ > 80, free of lifetime history of head trauma resulting in loss of consciousness for > 5 min, right-handed, free of MRI contraindications, and free of chronic medical illness and neurological disorder. Only measures relevant to the current analyses are presented.

Participants who completed the prepandemic survey measures were contacted during an early phase of the pandemic (May–June 2020) with an invitation to complete surveys related to their experiences and mental health during the pandemic (from approximately mid-March 2020 to the time of questionnaire completion). This timeframe is of particular importance, as there were already over 90,000 COVID-19-related deaths in the United States (The Institute for Health Metrics and Evaluation [IHME], 2021), and the majority of Americans reported that they were adhering to social distancing procedures (i.e., staying home and avoiding other people; Ipsos, 2021). The final sample was composed of 85 adult participants who had complete prepandemic and pandemic follow-up survey data, while 72 participants had complete prepandemic survey, prepandemic imaging, and follow-up survey data. We included the highest number of participants with complete data for all analyses (i.e., n = 85 for Hypothesis 1; n = 72 for Hypotheses 2–3).

Depression and Anxiety Symptoms

At prepandemic and pandemic follow-up, self-reported depression and anxiety symptoms were assessed using the Beck Depression Inventory (BDI-II; Beck et al., 1996) and Screen for Child Anxiety-Related Emotional Disorders–Adult (SCARED-A; Bögels & van Melick, 2004), respectively. The BDI-II (Beck et al., 1996; García-Batista et al., 2018; Segal et al., 2008) and SCARED-A (Birmaher et al., 1997) have demonstrated good reliability and validity. Cronbach's α for the BDI total score for prepandemic and pandemic follow-up for the present study is 0.92 and 0.90, respectively. Cronbach's α for the SCARED-A total score for prepandemic and pandemic follow-up for the present study is 0.94 and 0.94, respectively.

The BDI-II consists of 21 items on a 4-point Likert scale, with a total score ranging from 0 to 63. A total score of 0–13 is considered typical, 14–19 is mild, 20–28 is moderate, and 29–63 is severe. The question assessing self-harm and suicidality (item 9) was not collected at pandemic follow-up due to the inability to monitor clinical risk remotely; thus, item 9 also was removed from the prepandemic BDI-II total score, resulting in the total score ranging from 0 to 60.

The SCARED-A is adapted from the original Screen for Child Anxiety-Related Emotional Disorders–Child (SCARED-C), which is used to assess anxiety in children. The SCARED-A questions are similar to that of the SCARED-C, only rephrased to better suit adult participants. The SCARED-A consists of 71 items on a 3-point Likert scale, with a total score ranging from 0 to 142. A total score of 23 or higher may indicate the presence of an anxiety disorder (Angulo et al., 2017). There are nine subscales: panic disorder (13 items), generalized anxiety disorder (GAD; 9 items), social phobia (9 items), separation anxiety disorder (12 items), obsessive–compulsive disorder (9 items), posttraumatic stress disorder (4 items), specific phobia consisting of animal phobia (3 items), blood injection-injury phobia (7 items), and situational environmental phobia (5 items). For the present study, items 3 ("I'm worried about my partner leaving me"), 13 ("I follow my partner wherever s/he goes"), and 17 ("I'm worried about the closeness of my relationship with my children") were removed due to these not being applicable to all participants (thus, the total score range for the present study was 0–136).

Coping Strategies

The tendency to engage in coping strategies associated with resilience (prepandemic) was measured using the Connor–Davidson Resilience Scale (CD-RISC; Connor & Davidson, 2003). The CD-RISC consists of 25 items on a 5-point Likert scale, with a total score ranging from 0 to 100. It contains five subscales thought to reflect behaviors and beliefs associated with positive adaptation in the face of adversity: personal competence and tenacity (8 items, Subscale 1), tolerance of negative affect and stress (7 items, Subscale 2), accepting of change positively (5 items, Subscale 3), sense of control (3 items, Subscale 4), and spirituality (2 items, Subscale 5). The CD-RISC has demonstrated good reliability and validity (Connor & Davidson, 2003; Mealer et al., 2016; Xie et al., 2016). Cronbach's α for the total score for the present study is 0.91.

Imaging Acquisition

Prepandemic, whole-brain images were acquired at the Yale University Brain Imaging Center on a 3.0 Tesla Siemens Prisma scanner using a 32-channel head coil. Structural T1-weighted 3D gradient echo MPRAGE sequence MRI scans were acquired: TR = 2,500 ms, TE = 2.88 ms, inversion time TI = 1,060 ms, flip angle = 8°, field of view = 256 × 256 mm, matrix size = 256 × 256, 176 axial slices, voxel size = 1.0 mm isotropic.

Two fieldmaps were acquired in opposing phase-encoding directions along the anterior–posterior axis: TR = 8,860 ms, TE = 80 ms, field of view = 216 × 216 mm, multiband factor = 6, echo spacing = 0.56 ms, voxel size = 2.4 mm isotropic. Functional scans were acquired using a multiband echo-planar imaging (EPI) sequence: TR = 800 ms, TE = 30 ms, 60 axial slices, flip angle = 52°, multiband factor = 6, echo spacing = 0.56 ms, voxel size = 2.4 mm isotropic, volumes = 375 (for each 5-min resting-state scan).

Participants completed two 5-min resting-state fMRI scans, where they were instructed to fixate on a white crosshair on a black screen. Head motion was restricted with foam pads, and OptoAcoustics noise-canceling headphones were used to minimize external scanner noises and allow participants to hear instructions during the scan (Kahana et al., 2004).

Preprocessing and Functional Connectivity Analyses

Raw images were converted to Brain Imaging Data Structure (BIDS; Gorgolewski et al., 2016) using heudiconv (www.github.com/nipy/heudiconv). Preprocessing was performed using the Default Preprocessing Pipeline in CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012). The first eight volumes were removed to account for time needed to reach magnetic field stabilization. The following preprocessing steps were included: (a) realignment and unwarping, (b) outlier detection and scrubbing using an intermediate framewise displacement of above 0.9 mm or global signal changes above 5 *SD*s such that participants were excluded if more than 50% of volumes were scrubbed (Power et al., 2014), consistent with standard CONN practices (Nieto-Castanon, 2020), (c) segmentation of grey matter, white matter, and cerebrospinal fluid, (d) normalization to Montreal Neurological Institute (MNI) space, and (e) spatial smoothing with an 8 mm full-width half-maximum (FWHM) Gaussian kernel. In our sample, there were no participants excluded based on an insufficient number of volumes after scrubbing. To increase the signal-to-noise ratio, a temporal band-pass filter was applied to remove low-frequency signal drift below 0.01 Hz and to remove high-frequency noise above 0.1 Hz.

Given strong a priori hypotheses about the role of frontolimbic and limbic networks in internalizing symptoms (Arnold Anteraper et al., 2014; Etkin et al., 2009, 2010; Helm et al., 2018; Klumpp et al., 2013; Manoliu et al., 2014; Matthews et al., 2008; Mulders et al., 2015; Musgrove et al., 2015; Peterson et al., 2014; Prater et al., 2013; Veer et al., 2010) and emotional responses to stress (VanTieghem & Tottenham, 2018), a region of interest (ROI)-ROI approach was used to quantify frontolimbic and limbic functional connectivity (FC) from the resting-state scans. To assess frontolimbic FC, we specifically examined FC between the amygdala and ventromedial prefrontal cortex (vmPFC). To assess limbic FC, we examined FC between the insula and anterior cingulate cortex (ACC), the amygdala and ACC, and the insula and amygdala. The mask for the basolateral amygdala was derived from the Juelich histological atlas (stereotaxic probabilistic maps of cytoarchitectonic boundaries generated by Amunts et al., 2005); masks for the anterior vmPFC, subgenual cingulate (sgACC), rostral ACC (rACC), and ventral ACC (vACC) were derived from the Mackey and Petrides atlas (Mackey & Petrides, 2014; separate regions were examined due to evidence that these regions are differentially implicated in internalizing symptoms; Etkin et al., 2011; Helm et al., 2018); and the mask for the insula was derived from the Automated Anatomical Labeling (AAL) atlas (Rolls et al., 2020). The blood oxygen-level dependent (BOLD) signal time course from each bilateral ROI (amygdala, vmPFC, sgACC, rACC, vACC, insula) was extracted. Each bilateral ROI was computed by averaging across the left and right hemispheres. FC between the eight ROI–ROI pairs (i.e., amygdala-vmPFC, amygdala-sgACC, amygdala-rACC, amygdala-vACC, insula-amygdala, insula-rACC, insula-sgACC, insula-vACC) was calculated using Statistical Parametric Mapping Version 12 (SPM12) and CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) software packages. Mean head motion was included as a covariate in first-level analyses in CONN. Pearson's correlation coefficients were calculated for each ROI–ROI pair, which were converted to *Z* scores using Fisher's transformation.

Primary Analyses

Hypothesis 1: Prepandemic coping strategy engagement and symptoms during the pandemic

We conducted general linear models to assess associations between prepandemic coping strategy engagement and symptoms during the pandemic. Separate models were conducted for each of the two dependent variables (anxiety and depression symptoms). Prepandemic coping strategy engagement was the independent variable. The following covariates were included: age at pandemic follow-up, sex, prepandemic depression and anxiety symptoms, and time between the prepandemic visit and pandemic follow-up.

Hypothesis 2: Prepandemic frontolimbic functional connectivity and symptoms during the pandemic

We conducted general linear models to examine associations between prepandemic frontolimbic FC and symptoms during the pandemic. Separate models were conducted for each of the two dependent variables (anxiety and depression symptoms). FC between each ROI–ROI pair of interest was an independent variable in separate models. Eight comparisons (number of ROI–ROI FC pairs) were controlled for using false discovery rate (FDR; Benjamini & Hochberg, 1995). The following covariates were included: age at pandemic follow-up, sex, prepandemic depression and anxiety symptoms, and time between the prepandemic visit and pandemic follow-up.

Hypothesis 3: Prepandemic frontolimbic functional connectivity as a potential moderator of the association between coping strategy engagement and symptoms during the pandemic

We conducted general linear models to examine whether frontolimbic FC moderated the association between coping engagement and symptoms during the pandemic. Separate models were conducted for each of the two dependent variables (anxiety and depression symptoms). The interaction between FC for each ROI–ROI pair of interest and coping engagement was an independent variable in separate models. The main effects of FC and coping engagement were also included in each model. Eight comparisons (number of ROI–ROI FC pairs) were controlled for using FDR (Benjamini & Hochberg, 1995). The following covariates were included: age at pandemic follow-up, sex, prepandemic depression and anxiety symptoms, and time between the prepandemic visit and pandemic follow-up.

Exploratory Analyses

For all significant findings that survived FDR correction, we also reran the analyses after removal of outliers (defined as any value 3 *SD*s above or below the mean for a given measure). For depression symptoms during the pandemic (measured by the BDI-II), there was one outlier. There were no other outliers for any other variable. Additionally, we conducted preregistered exploratory analyses using general linear models to examine the associations among coping strategy engagement, frontolimbic FC, and specific symptom subscales derived from the SCARED-A (i.e., panic, social anxiety, obsessive-compulsive, generalized anxiety, separation

anxiety, posttraumatic stress, specific phobia). Analyses were identical to those of Hypotheses 1–3, using anxiety symptom subscales as the dependent variables in separate models. Eight comparisons (number of anxiety subscales) were controlled for using FDR (Benjamini & Hochberg, 1995).

Results

Demographic and Clinical Characteristics

Descriptive statistics for demographic characteristics, clinical symptoms, and coping strategies for the sample with complete survey data ($n = 85$, 71.8% female) and the sample with complete survey and imaging data ($n = 72$, 72.2% female) prepandemic and during the pandemic are reported in Table 1. See Supplemental Tables 1 and 2 for differences in prepandemic measures between participants who completed the pandemic follow-up versus participants who did not complete the pandemic follow-up.

Symptom Changes From Prepandemic to During the Pandemic

Participants' depression and anxiety symptoms worsened during the pandemic as compared to prepandemic, $t(83) = -4.338$, $p < .001$; $t(83) = -5.174$, $p < .001$, respectively; Figure 1, Table 1. With regard to subtypes of anxiety (Supplemental Figure 1, Table 1), panic, social anxiety, obsessive-compulsive, generalized anxiety, separation anxiety, and specific phobia symptoms worsened during the pandemic as compared to prepandemic, $t(83) = -4.615$, $p < .001$; $t(83) = -2.790$, $p = .006$; $t(83) = -4.90$, $p < .001$; $t(83) = -2.37$, $p = .020$; $t(83) = -3.843$, $p < .001$; $t(83) = -4.610$, $p < .001$, respectively. In contrast, posttraumatic stress symptoms did not change, $t(83) = -0.260$, $p = .796$. See Supplemental Material for comparable findings using the sample with complete survey and imaging data ($n = 72$).

Hypothesis 1: Prepandemic coping strategy engagement and symptoms during the pandemic

Prepandemic coping strategy engagement was not associated with overall anxiety or depression symptoms during the pandemic (uncorrected ps $> .05$).

Hypothesis 2: Prepandemic frontolimbic functional connectivity and symptoms during the pandemic

Prepandemic frontolimbic FC was not associated with overall anxiety or depression symptoms during the pandemic (uncorrected ps $> .05$).

Hypothesis 3: Prepandemic frontolimbic functional connectivity as a potential moderator of the association between coping strategy engagement and symptoms during the pandemic

Prepandemic frontolimbic FC moderated the relation between prepandemic coping strategies and depression symptoms during the pandemic (Figure 2, Table 2). Specifically, there were interactions between prepandemic coping strategy engagement and prepandemic insula-rACC FC ($\beta = 2.317$, $p = .003$, pFDR $= .014$, Figure 2a), as well as with insula-vACC FC ($\beta = 2.989$, $p < .001$, pFDR $< .001$, Figure 2b), in predicting depression symptoms. However, after removal of one outlier, neither of these findings survived FDR correction.

No significant findings were observed in regard to overall anxiety symptoms (uncorrected ps $> .05$).

Exploratory Findings

Exploratory analyses for Hypothesis 1 showed that prepandemic coping strategy engagement was not associated with specific anxiety symptoms during the pandemic (uncorrected ps $> .05$).

Exploratory analyses for Hypothesis 2 showed that prepandemic frontolimbic FC was associated with specific anxiety symptoms, although none of these findings survived FDR correction (Figure 3, Table 3). Particularly, weaker prepandemic insula-sgACC FC was associated with higher obsessive-compulsive symptoms during the pandemic ($p = .026$, pFDR $= .214$, Figure 3a). Weaker prepandemic amygdala-vACC FC was associated with higher separation anxiety symptoms during the pandemic ($p = .040$, pFDR $= .282$, Figure 3b).

Exploratory analyses for Hypothesis 3 revealed that prepandemic frontolimbic FC moderated the relation between prepandemic coping strategies and specific anxiety symptoms (Figure 4, Table 4). However, none of these findings survived FDR correction. Specifically, there was an interaction between prepandemic insula-vACC FC and coping strategy engagement in predicting panic symptoms ($\beta = 1.519$, $p = .017$, pFDR $= .133$, Figure 4a), as well as generalized anxiety symptoms ($\beta = 1.163$, $p = .049$, pFDR $= .133$, Figure 4b) during the pandemic. There was also an interaction between prepandemic amygdala-vmPFC FC and coping strategy engagement in predicting generalized anxiety symptoms during the pandemic ($\beta = 1.387$, $p = .032$, pFDR $= .129$, Figure 4c). There was an interaction between prepandemic amygdala-rACC FC and coping strategy engagement in predicting generalized anxiety symptoms during the pandemic ($\beta = 1.328$, $p = .027$, pFDR $= .129$, Figure 4d). Finally, there was an interaction between prepandemic insula-sgACC FC and coping strategy engagement in predicting obsessive-compulsive symptoms during the pandemic ($\beta = -1.298$, $p = .041$, pFDR $= .672$, Figure 4e).

Discussion

The present preregistered study examined relations among coping strategy engagement and frontolimbic circuitry prior to the COVID-19 pandemic with internalizing symptomology during the pandemic. As expected, participants' depression and anxiety symptoms worsened during the pandemic. Unexpectedly, prepandemic coping engagement and frontolimbic FC were not associated with depression or anxiety symptoms during the pandemic. Although we initially found an interaction between prepandemic frontolimbic FC and coping strategies in predicting depression symptoms during the pandemic, these findings did not survive FDR correction after removal of outliers. Exploratory analyses similarly revealed associations among prepandemic frontolimbic FC and coping engagement with specific anxiety symptoms during the pandemic, but these findings did not survive FDR correction. Altogether, findings suggest that adaptive coping and frontolimbic circuitry are not robustly implicated in emotional responses to major stressful life events (after accounting for age, sex at birth,

Table 1

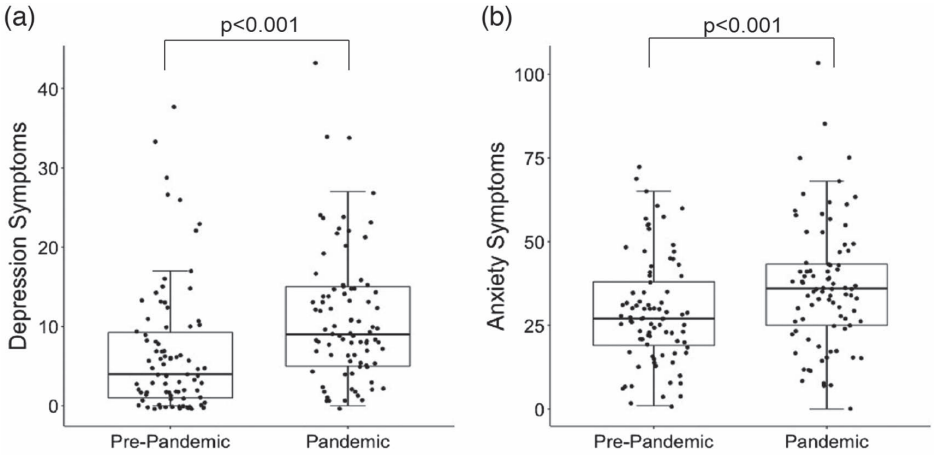
Descriptive Statistics for Demographic Characteristics, Clinical Symptoms, and Coping Strategies

Demographic, clinical, and coping characteristics	$n = 85$ (Hypothesis 1)	$n = 72$ (Hypotheses 2 and 3)
Sex at birth	*n* (%)	*n* (%)
Female	61 (71.76%)	52 (72.22%)
Male	24 (28.24%)	20 (27.78%)
Race/ethnicity[a]		
Non-Hispanic White	45 (52.94%)	40 (55.56%)
Hispanic or Latino	10 (11.76%)	8 (11.11%)
Black or African American	11 (12.94%)	9 (12.50%)
Asian	22 (25.88%)	16 (22.22%)
Native American, native Hawaiian, or Pacific Islander	1 (1.17%)	1 (1.34%)
Other/not listed	0	0
Prefer not to answer	0	0
Combined family income		
Less than $5,000	2 (2.35%)	2 (2.78%)
$5,000–$11,999	2 (2.35%)	2 (2.78%)
$12,000–$15,999	3 (3.53%)	3 (4.17%)
$16,000–$24,999	8 (9.41%)	8 (11.11%)
$25,000–$34,999	5 (5.88%)	5 (6.94%)
$35,000–$49,999	5 (5.88%)	4 (5.56%)
$50,000–$74,999	18 (21.17%)	17 (23.61%)
$75,000–$99,999	5 (5.88%)	3 (4.17%)
$100,000 and greater	26 (30.59%)	21 (29.17%)
Don't know	7 (8.24%)	5 (6.94%)
	M (*SD*)	*M* (*SD*)
Prepandemic years of education	14.65 (2.24)	14.70 (2.15)
Age at pandemic follow-up	24.10 (3.57)	24.09 (3.74)
Years between prepandemic visit and pandemic follow-up	1.51 (0.90)	1.45 (0.86)
Student and employment status at pandemic follow-up[b]	*n* (%)	*n* (%)
Working full-time	20 (23.52%)	17 (23.61%)
Working part-time	19 (22.35%)	15 (20.83%)
Looking for a job	10 (11.76%)	9 (12.50%)
Student	49 (57.65%)	44 (61.11%)
Unemployed	8 (9.41%)	8 (11.11%)
Stay at home caregiver	1 (1.17%)	1 (1.39%)
Retired	0	0
Other	5 (5.88%)	5 (6.94%)
Self-report symptoms	*M* (*SD*)	*M* (*SD*)
Prepandemic depression symptoms	6.80 (8.04)	7.04 (8.45)
Pandemic depression symptoms	11.05 (8.22)	11.35 (8.32)
Prepandemic anxiety symptoms	29.26 (16.02)	29.17 (16.36)
Pandemic anxiety symptoms	36.56 (18.61)	36.90 (18.65)
Prepandemic panic symptoms	3.12 (3.12)	3.07 (3.07)
Pandemic panic symptoms	4.62 (3.95)	4.53 (3.92)
Prepandemic social anxiety symptoms	5.52 (4.10)	5.63 (4.32)
Pandemic social anxiety symptoms	6.42 (4.09)	6.50 (4.17)
Prepandemic obsessive-compulsive symptoms	4.42 (2.59)	4.47 (2.69)
Pandemic obsessive-compulsive symptoms	5.61 (3.07)	5.69 (3.15)
Prepandemic generalized anxiety symptoms	8.38 (4.82)	8.33 (4.91)
Pandemic generalized anxiety symptoms	9.30 (4.69)	9.39 (4.69)
Prepandemic separation anxiety symptoms	2.72 (2.53)	2.68 (2.45)
Pandemic separation anxiety symptoms	3.98 (3.37)	4.10 (3.29)
Prepandemic posttraumatic stress symptoms	1.42 (1.51)	1.40 (1.55)
Pandemic posttraumatic stress symptoms	1.48 (1.73)	1.56 (1.78)
Prepandemic specific phobia symptoms	3.68 (3.27)	3.58 (3.14)
Pandemic specific phobia symptoms	5.17 (3.85)	5.14 (3.78)
Prepandemic coping strategies	72.33 (11.85)	73.46 (11.12)
Personal competence and tenacity (Subscale 1)	24.46 (4.56)	24.58 (4.47)
Tolerance of negative affect and stress (Subscale 2)	19.12 (4.02)	18.64 (3.72)
Positive acceptance of change, secure relationships (Subscale 3)	16.07 (2.64)	16.42 (2.34)
Sense of control (Subscale 4)	8.57 (2.33)	8.63 (2.35)
Spiritual influences (Subscale 5)	4.12 (2.22)	4.19 (2.22)

Note. Table describes information about demographic characteristics, self-reported clinical symptoms, and coping strategies. [a] Percentages for race/ethnicity do not sum to 100% due to multiracial reporting (i.e., some participants endorsed more than one race/ethnicity category). [b] Percentages for student/employment status do not sum to 100% due to some participants endorsing more than one category.

Figure 1

Symptom Changes From Prepandemic to During the Pandemic



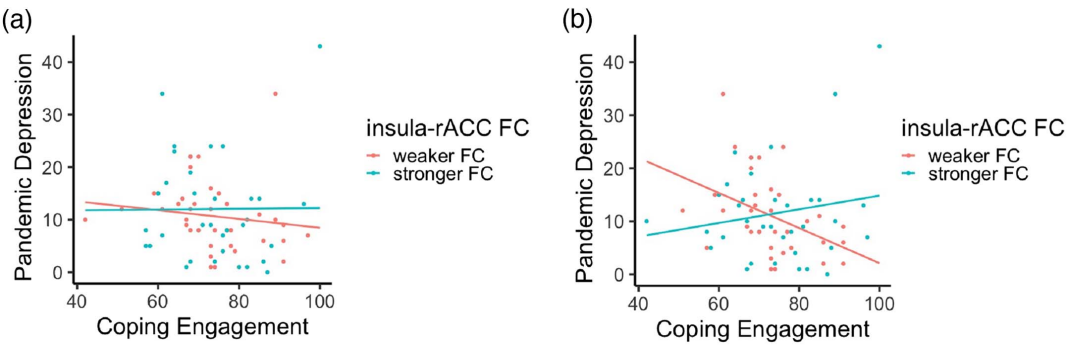
Note. Participants' (a) depression and (b) anxiety symptoms worsened during the pandemic as compared to prepandemic.

prepandemic symptoms, and interval between the timepoints), contrary to what was expected based on the extant literature. Nonetheless, this research can inform future work delineating the extent to which these specific factors that pre-date the COVID-19 pandemic may or may not modulate mental health during the pandemic. This line of research can facilitate the identification of individuals at high risk for developing mental health problems in response to global stressful events.

Contrary to our first preregistered hypothesis, prepandemic engagement in prototypically adaptive coping strategies (e.g., adopting a positive view of stress) was not associated with depression or anxiety symptoms during the pandemic, after controlling for age, sex at birth, prepandemic symptoms, and interval between the timepoints. While some studies have found that adaptive coping is linked to fewer psychiatric symptoms (Robinson et al., 2014; Wermelinger Ávila et al., 2017), including during the COVID-19 pandemic (Ran et al., 2020; Schmitt et al., 2021; Shechory Bitton & Laufer, 2021; Song et al., 2021; Valero-Moreno et al., 2021), our null findings align with other work showing no association (Holt-Gosselin et al., 2021). Relatedly, there is evidence that the use of prototypically maladaptive coping strategies (e.g., self-blame, denial) is more strongly related to psychiatric symptom severity than the use of adaptive coping strategies, both cross-sectionally and longitudinally (Aldao & Nolen-Hoeksema, 2012; Mahmoud et al., 2012; Moritz et al., 2016), including during the COVID-19 pandemic (Holt-Gosselin et al., 2021). This research suggests that it may be more beneficial for individuals to decrease their use of maladaptive strategies than to increase their use of adaptive

Figure 2

Prepandemic Frontolimbic Functional Connectivity as a Potential Moderator of the Association Between Coping Strategy Engagement and Symptoms During the Pandemic



Note. There were significant (corrected) interactions between prepandemic coping strategy engagement and (a) prepandemic insula-rACC FC, as well as with (b) insula-vACC FC in predicting depression symptoms during the pandemic. However, after removal of one outlier, neither of these findings survived false discovery rate (FDR) correction. FC = functional connectivity; rACC = rostral anterior cingulate cortex; vACC = ventral anterior cingulate cortex. See the online article for the color version of this figure.

Table 2

Prepandemic Frontolimbic Functional Connectivity as a Potential Moderator of the Association Between Coping Strategy Engagement and Symptoms During the Pandemic

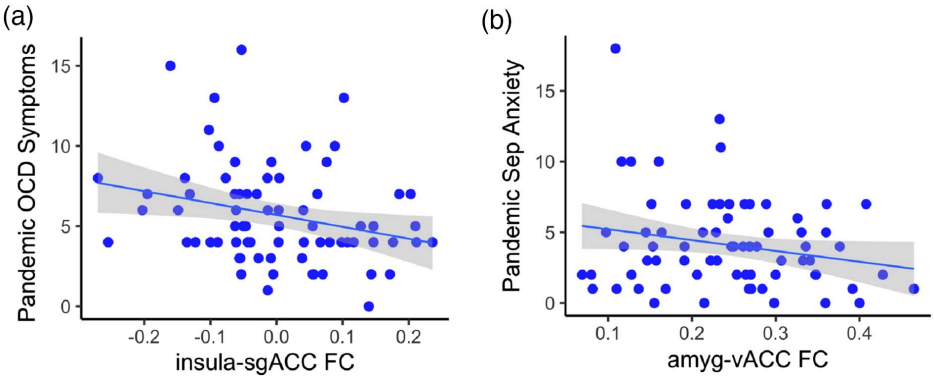
Dependent variable	Independent variables	β (95% CI)	*SE*	*t*	*p* value
Depression symptoms during the pandemic	Intercept	0 (−2.10 to 40.12)	10.56	1.80	.077
	Age during pandemic	−0.33 (−1.25 to −0.23)	0.25	−2.93	.005[a]
	Sex at birth	0.22 (0.08 to 7.89)	1.95	2.04	0.046[a]
	Time between prepandemic and pandemic	0.16 (−0.62 to 3.69)	1.08	1.43	.159
	Prepandemic depression symptoms	0.45 (0.20 to 0.70)	0.12	3.61	<.001[a]
	Prepandemic insula-rACC FC	−2.21 (−194.10 to −35.91)	39.58	−2.91	.005[a]
	Prepandemic coping strategies	0.04 (−0.20 to 0.26)	0.11	0.26	.793
	Prepandemic Coping Strategies × Prepandemic Insula-rACC FC	2.32 (0.53 to 2.58)	0.51	3.04	.003[a,b]
Depression symptoms during the pandemic	Intercept	0 (5.34 to 44.93)	9.90	2.54	.013
	Age during pandemic	−0.31 (−1.15 to −0.21)	0.24	−2.89	.005[a]
	Sex at birth	0.18 (−0.25 to 7.01)	1.82	1.86	.068
	Time between prepandemic and pandemic	0.15 (−0.55 to 3.45)	0.99	1.45	.151[a]
	Prepandemic depression symptoms	0.49 (0.25 to 0.72)	0.12	4.08	<.001[a]
	Prepandemic insula-vACC FC	−2.86 (−282.97 to −103.72)	44.85	−4.31	<.001[a]
	Prepandemic coping strategies	−0.09 (−0.30 to 0.15)	0.11	−0.63	.531
	Prepandemic Coping Strategies × Prepandemic Insula-vACC FC	2.99 (1.41 to 3.74)	0.59	4.40	<.001[a,b]

Note. Table describes significant interactions between prepandemic coping strategies and frontolimbic functional connectivity in predicting depression symptoms during the pandemic. FC = functional connectivity; rACC = rostral anterior cingulate cortex; vACC = ventral anterior cingulate cortex; β = standardized β; CI = 95% confidence interval; *SE* = standard error.
[a] Significant ($p < .05$ uncorrected). [b] Predictor of interest that survived false discovery rate (FDR) correction.

strategies in the face of stressful events. Our coping measure merely assessed adaptive coping; therefore, we were unable to explore the impact of maladaptive coping. Future studies should investigate whether the use of potentially harmful (vs. adaptive) coping strategies is more closely related to mental health during the pandemic. Relatedly, it is important to clarify that our measure examining the tendency to engage in coping strategies associated with resilience (using the CD-RISC) does not assess "objective" resilience; rather it measures one's *perception* of their own behaviors and beliefs that are associated with resilience (e.g., positively adapting in the face of adversity). This discrepancy may also help to explain our null findings. Further, one possibility that may help to explain limited evidence for an association between adaptive coping and psychopathology is that systemic factors (e.g., racism, poverty) may exert a stronger influence on mental health during stress as compared to individual-level factors (e.g., adopting a positive view of stress), due to strong links between such systemic factors and mental health (Alegría et al., 2018), including during the pandemic (Fortuna et al., 2020). While our adaptive coping measure includes some questions assessing social environment (e.g., level of emotional support), most

Figure 3

Exploratory: Prepandemic Frontolimbic Functional Connectivity and Specific Anxiety Symptoms During the Pandemic



Note. (a) Weaker prepandemic insula-sgACC FC was significantly (uncorrected) associated with higher obsessive-compulsive symptoms during the pandemic. (b) Weaker prepandemic amygdala-vACC FC was significantly (uncorrected) associated with higher separation anxiety symptoms during the pandemic. OCD = obsessive–compulsive disorder; sep anxiety = separation anxiety; FC = functional connectivity; vACC = ventral anterior cingulate cortex; sgACC = subgenual anterior cingulate cortex. See the online article for the color version of this figure.

Table 3

Exploratory: Prepandemic Frontolimbic Functional Connectivity and Specific Anxiety Symptoms During the Pandemic

Dependent variable	Independent variables	β (95% CI)	*SE*	*t*	*p* value
Obsessive-compulsive symptoms during the pandemic	Intercept	0 [2.15, 9.77]	1.91	3.12	.003
	Age during pandemic	−0.21 [−0.33, −0.02]	0.08	−2.31	.024[a]
	Sex at birth	0 [−1.10, 1.17]	0.57	0.06	.955
	Time between prepandemic and pandemic	0.13 [−0.20, 1.14]	0.33	1.41	.164
	Prepandemic obsessive-compulsive symptoms	0.63 [0.54, 0.94]	0.10	7.40	<.001[a]
	Prepandemic insula-sgACC FC	−0.19 [−9.69, −0.61]	2.27	2.27	.027[a]
Separation anxiety symptoms during the pandemic	Intercept	0 [−2.03, 9.26]	2.83	1.28	.206
	Age during pandemic	−0.05 [−0.24, 0.16]	0.10	−0.41	.683
	Sex at birth	0.27 [0.46, 3.46]	0.75	2.62	.011[a]
	Time between prepandemic and pandemic	0.080 [−0.54, 1.15]	0.42	0.72	.474
	Prepandemic separation anxiety symptoms	0.43 [0.30, 0.85]	0.14	4.17	<.001[a]
	Prepandemic amygdala-vACC FC	0.23 [−15.20, −0.38]	3.71	−2.10	.040[a]

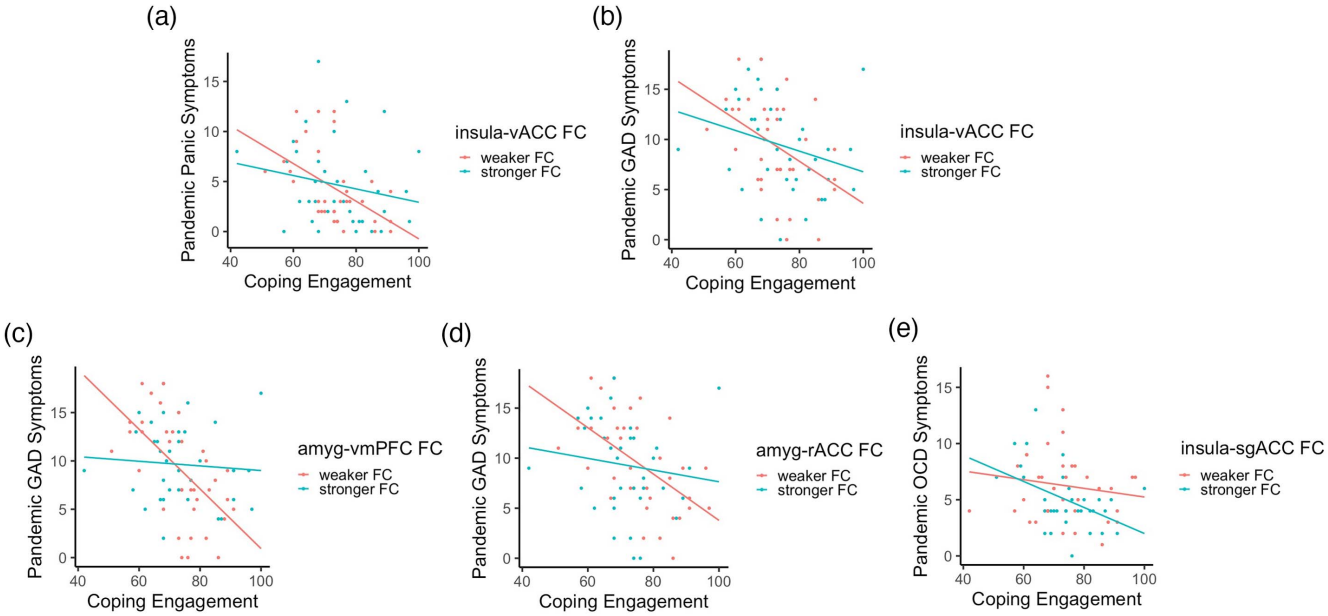
Note. Table describes significant associations between prepandemic frontolimbic functional connectivity and specific anxiety symptoms during the pandemic. FC = functional connectivity; sgACC = subgenual anterior cingulate cortex; vACC = ventral anterior cingulate cortex; β = standardized β; CI = 95% confidence interval; *SE* = standard error.
[a] Significant ($p < .05$ uncorrected).

items assess personal mindsets/beliefs. Hence, it is imperative that future research additionally examine the influence of system-level factors in predicting mental health in response to stress.

In contrast to our second preregistered hypothesis, prepandemic frontolimbic FC was not associated with overall anxiety or depression symptoms during the pandemic after controlling for age, sex at birth, prepandemic symptoms, and interval between the timepoints. However, findings from exploratory analyses showed that prepandemic frontolimbic FC was associated with specific anxiety symptoms, although these findings did not survive FDR

Figure 4

Exploratory: Prepandemic Frontolimbic Functional Connectivity as a Potential Moderator of the Association Between Coping Strategy Engagement and Specific Anxiety Symptoms During the Pandemic



Note. There was a significant (uncorrected) interaction between prepandemic insula-vACC FC and coping strategy engagement in predicting (a) panic symptoms as well as (b) generalized anxiety symptoms during the pandemic. There was also a significant (uncorrected) interaction between prepandemic amygdala-vmPFC FC and coping strategy engagement in predicting (c) generalized anxiety symptoms during the pandemic. There was a significant (uncorrected) interaction between prepandemic amygdala-rACC FC and coping strategy engagement in predicting (d) generalized anxiety symptoms during the pandemic. Finally, there was a significant (uncorrected) interaction between prepandemic insula-sgACC FC and coping strategy engagement in predicting (e) obsessive-compulsive symptoms during the pandemic. OCD = obsessive–compulsive disorder; GAD = generalized anxiety disorder; vACC = ventral anterior cingulate cortex; rACC = rostral anterior cingulate cortex; sgACC = subgenual anterior cingulate cortex; vmPFC = ventromedial prefrontal cortex; FC = functional connectivity. See the online article for the color version of this figure.

Table 4

Exploratory: Prepandemic Frontolimbic Functional Connectivity as a Potential Moderator of the Association Between Coping Strategy Engagement and Specific Anxiety Symptoms During the Pandemic

Dependent variable	Independent variables	β (95% CI)	*SE*	*t*	*p* value
Panic symptoms during the pandemic	Intercept	0 [1.43, 17.80]	4.10	2.35	.022
	Age during pandemic	−0.09 [−0.30, 0.11]	0.10	−0.94	.352
	Sex at birth	0.04 [−1.19, 1.90]	0.78	0.46	.647
	Time between prepandemic and pandemic	0.07 [−0.56, 1.21]	0.44	0.73	.467
	Prepandemic panic symptoms	0.67 [0.59, 1.11]	0.13	6.57	<.001[a]
	Prepandemic insula-vACC FC	−1.45 [−84.63, −7.67]	19.26	−2.40	.020[a]
	Prepandemic coping strategies	−0.24 [−0.17, 0]	0.04	−1.88	.064
	Prepandemic Coping Strategies × Prepandemic Insula-vACC FC	1.52 [0.12, 1.12]	0.25	2.45	.017[a]
Generalized anxiety symptoms during the pandemic	Intercept	0 [−1.65, 20.36]	5.51	1.70	.094
	Age during pandemic	−0.27 [−5.71, −0.11]	0.12	−2.95	.004[a]
	Sex at birth	0.19 [2.62, 3.77]	0.88	2.30	.024[a]
	Time between prepandemic and pandemic	0.11 [−4.02, 1.60]	0.50	1.20	.236
	Prepandemic generalized anxiety symptoms	0.67 [4.14, 0.84]	0.11	5.84	<.001[a]
	Prepandemic insula-vACC FC	−1.04 [−8.28, 3.59]	21.63	−1.83	.072
	Prepandemic coping strategies	0.01 [−0.01, 0.12]	0.06	0.10	.924
	Prepandemic Coping Strategies × Prepandemic Insula-vACC FC	1.16 [0, 1.13]	0.28	2.00	.049[a]
Generalized anxiety symptoms during the pandemic	Intercept	0 [−0.47, 25.77]	6.57	1.92	.059
	Age during pandemic	−0.26 [−0.56, −0.10]	0.11	−2.90	.005[a]
	Sex at birth	0.16 [−0.16, 3.40]	0.89	1.81	.074
	Time between prepandemic and pandemic	0.05 [−0.71, 1.29]	0.50	0.58	.564
	Prepandemic generalized anxiety symptoms	0.65 [0.40, 0.84]	0.11	5.65	<.001[a]
	Prepandemic amygdala-vmPFC FC	−1.28 [−81.92, 0.92]	20.27	−2.04	.045[a]
	Prepandemic coping strategies	−0.08 [−0.18, 0.11]	0.07	−0.48	.634
	Prepandemic Coping Strategies × Prepandemic Amygdala-vmPFC FC	1.39 [0.05, 1.16]	0.28	2.19	.032[a]
Generalized anxiety symptoms during the pandemic	Intercept	0 [1.20, 32.49]	7.83	2.15	.035
	Age during pandemic	−0.28 [−0.59, −0.12]	0.12	−3.07	.003[a]
	Sex at birth	0.15 [−0.29, 3.33]	0.91	1.68	.098
	Time between prepandemic and pandemic	0.11 [−0.40, 1.61]	0.50	1.20	.236
	Prepandemic generalized anxiety symptoms	0.65 [0.40, 0.84]	0.11	5.70	<.001[a]
	Prepandemic amygdala-rACC FC	−1.31 [−93.63, −4.57]	22.29	−2.20	.031[a]
	Prepandemic coping strategies	−0.19 [−0.25, 0.09]	0.09	−0.93	.358
	Prepandemic Coping Strategies × Prepandemic Amygdala-rACC FC	1.33 [0.08, 1.26]	0.30	2.27	.027[a]
Obsessive-compulsive symptoms during the pandemic	Intercept	0 [1.21, 11.64]	2.61	2.46	.017
	Age during pandemic	−0.20 [−0.32, −0.01]	0.08	−2.16	.035[a]
	Sex at birth	−0.03 [−1.35, 0.97]	0.58	−0.32	.748
	Time between prepandemic and pandemic	0.14 [−0.16, 1.15]	0.33	1.51	.136
	Prepandemic obsessive-compulsive symptoms	0.64 [0.54, 0.94]	0.10	7.24	<.001[a]
	Prepandemic insula-sgACC FC	1.10 [−3.86, 65.40]	17.33	1.78	.081
	Prepandemic coping strategies	−0.03 [−0.06, 0.04]	0.03	−0.34	.736
	Prepandemic Coping Strategies × Prepandemic Insula-sgACC FC	−1.30 [−0.93, −0.02]	0.23	−2.09	.041[a]

Note. Table describes significant interactions between prepandemic coping strategies and frontolimbic functional connectivity in predicting specific anxiety symptoms during the pandemic. FC = functional connectivity; rACC = rostral anterior cingulate cortex; vACC = ventral anterior cingulate cortex; vmPFC = ventromedial prefrontal cortex; sgACC = subgenual anterior cingulate cortex; β = standardized β; CI = 95% confidence interval; *SE* = standard error.

[a] Significant ($p < .05$ uncorrected).

correction. Specifically, weaker insula-sgACC FC was associated with higher obsessive-compulsive symptoms during the pandemic, and weaker amygdala-vACC FC was associated with higher separation anxiety symptoms during the pandemic. When connections between the insula, amygdala, and ACC are disrupted, it can lead to the various visceral, affective, and cognitive features of anxiety (Paulus & Stein, 2006; Williams, 2016, 2017). Our exploratory findings are consistent with prior research showing altered insula-ACC FC in patients with obsessive–compulsive disorder (Fan et al., 2017; Tomiyama et al., 2022), and altered amygdala-ACC FC associated with fear-based anxiety disorders including separation anxiety among youth (Strawn et al., 2014). These exploratory results set the stage for subsequent studies to investigate whether particular anxiety symptoms experienced during stressful events are differentially associated with specific neural circuits.

In regard to our third preregistered hypothesis, although we found that prepandemic insula-ACC FC moderated the relation between prepandemic coping strategies and depression symptoms during the pandemic, these findings did not hold after removal of outliers. Relatedly, exploratory analyses revealed that prepandemic

frontolimbic (specifically insula-ACC, amygdala-ACC, amygdala-vmPFC) FC moderated the relation between prepandemic coping and specific anxiety symptoms (including panic, generalized anxiety, and obsessive-compulsive) during the pandemic, but these findings did not survive FDR correction. It is possible that we did not observe robust relations because FC is a more transient, variable measure (associated with more changes over time within individuals) as compared to other brain measures (e.g., structural connectivity; Osmanlıoğlu et al., 2020). Further, although we covaried for the time between the prepandemic visit and pandemic follow-up, the range was 0.3–3.4 years. Therefore, some individuals' neural measures, particularly those whose prepandemic visit took place a few years prior, may have undergone substantial changes. Further, it is important to note that participants completed two separate 5-min resting-state scans; it is possible that more resting-state data or longer scans would be needed to observe robust links between prepandemic neurobehavioral factors and psychiatric symptoms during the pandemic. While prior work has suggested that 5–7 min of resting-state data is sufficient and that multiple shorter runs may be optimal relative to a single longer resting-state scan (Teeuw et al., 2021; Van Dijk et al., 2010), it could be advantageous for future studies to collect resting-state scans for longer periods. Additionally, it is possible that other neural circuits (e.g., executive control network) outside of the circuitry examined in our preregistered hypotheses may also be associated with emotional responses to stress during the COVID-19 pandemic, as shown in Chahal et al. (2021). Future studies should investigate the potential role of other circuits in mental health outcomes during the pandemic.

Our study has several limitations. This study was observational and was not designed to address causal relations among prepandemic brain function and coping with psychiatric symptoms during the pandemic. Second, the majority of individuals' symptoms at the prepandemic and pandemic follow-up timepoints fell within low- to moderate-symptom ranges; findings may not extend to individuals with more severe symptoms. Third, our study primarily included non-Hispanic White individuals, and those of middle- to high-socioeconomic status. Thus, additional studies should examine a more racially, ethnically, and socioeconomically diverse sample, as research has shown that minoritized and disadvantaged populations are at elevated risk for negative impacts of the COVID-19 pandemic (Yip et al., 2022). Additionally, symptoms of depression and anxiety were assessed during the early phase of the pandemic (May–June 2020); thus, it is possible that there may indeed be associations between prepandemic neurobehavioral factors and psychiatric symptoms during later stages of the pandemic, when the uncertainty and stress became chronic for many individuals, likely due to a combination of factors such as long-term social isolation and substantial increases in COVID-19 cases. Despite these limitations, a key strength of our study is that all of our hypotheses (including exploratory) were preregistered prior to analyzing the data, which represents an important step toward open and transparent science.

In sum, we provide novel insights regarding the relations among prepandemic coping strategies and alterations within frontolimbic circuitry with internalizing symptoms during the pandemic in a sample of young adults. Contrary to our preregistered hypotheses, there were no robust associations among prepandemic adaptive coping and frontolimbic circuitry with depression or anxiety symptoms during the pandemic. Future studies that build upon the current work are warranted to more fully elucidate these complex relations. Specifically, longitudinal studies that ascertain neurobiological and behavioral predictors of mental health outcomes may help to identify individuals at high risk for developing mental health problems in response to stressful events, and to contribute to the development and optimization of interventions.

References

Aldao, A., & Nolen-Hoeksema, S. (2012). When are adaptive strategies most predictive of psychopathology? *Journal of Abnormal Psychology*, *121*(1), 276–281. https://doi.org/10.1037/a0023598

Alegría, M., NeMoyer, A., Falgàs Bagué, I., Wang, Y., & Alvarez, K. (2018). Social determinants of mental health: Where we are and where we need to go. *Current Psychiatry Reports*, *20*(11), Article 95. https://doi.org/10.1007/s11920-018-0969-9

Amunts, K., Kedo, O., Kindler, M., Pieperhoff, P., Mohlberg, H., Shah, N. J., Habel, U., Schneider, F., & Zilles, K. (2005). Cytoarchitectonic mapping of the human amygdala, hippocampal region and entorhinal cortex: Intersubject variability and probability maps. *Anatomy and Embryology*, *210*(5–6), 343–352. https://doi.org/10.1007/s00429-005-0025-5

Angulo, M., Rooks, B. T., Gill, M., Goldstein, T., Sakolsky, D., Goldstein, B., Monk, K., Hickey, M. B., Diler, R. S., Hafeman, D., Merranko, J., Axelson, D., & Birmaher, B. (2017). Psychometrics of the screen for adult anxiety related disorders (SCAARED)- A new scale for the assessment of DSM-5 anxiety disorders. *Psychiatry Research*, *253*, 84–90. https://doi.org/10.1016/j.psychres.2017.02.034

Arnold Anteraper, S., Triantafyllou, C., Sawyer, A. T., Hofmann, S. G., Gabrieli, J. D., & Whitfield-Gabrieli, S. (2014). Hyper-connectivity of subcortical resting-state networks in social anxiety disorder. *Brain Connectivity*, *4*(2), 81–90. https://doi.org/10.1089/brain.2013.0180

Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. (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

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series A, (Statistics in Society)*, *57*(1), 289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

Birmaher, B., Khetarpal, S., Brent, D., Cully, M., Balach, L., Kaufman, J., & Neer, S. M. (1997). The screen for child anxiety related emotional disorders (SCARED): Scale construction and psychometric characteristics. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*(4), 545–553. https://doi.org/10.1097/00004583-199704000-00018

Bögels, S. M., & van Melick, M. (2004). The relationship between child-report, parent self-report, and partner report of perceived parental rearing behaviors and anxiety in children and parents. *Personality and Individual Differences*, *37*(8), 1583–1596. https://doi.org/10.1016/j.paid.2004.02.014

Chahal, R., Kirshenbaum, J. S., Miller, J. G., Ho, T. C., & Gotlib, I. H. (2021). Higher executive control network coherence buffers against puberty-related increases in internalizing symptoms during the COVID-19 pandemic. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(1), 79–88. https://doi.org/10.1016/j.bpsc.2020.08.010

Connor, K. M., & Davidson, J. R. (2003). Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). *Depression and Anxiety*, *18*(2), 76–82. https://doi.org/10.1002/da.10113

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, *15*(2), 85–93. https://doi.org/10.1016/j.tics.2010.11.004

Etkin, A., Prater, K. E., Hoeft, F., Menon, V., & Schatzberg, A. F. (2010). Failure of anterior cingulate activation and connectivity with the amygdala during implicit regulation of emotional processing in generalized anxiety

disorder. *The American Journal of Psychiatry*, *167*(5), 545–554. https://doi.org/10.1176/appi.ajp.2009.09070931

Etkin, A., Prater, K. E., Schatzberg, A. F., Menon, V., & Greicius, M. D. (2009). Disrupted amygdalar subregion functional connectivity and evidence of a compensatory network in generalized anxiety disorder. *Archives of General Psychiatry*, *66*(12), 1361–1372. https://doi.org/10.1001/archgenpsychiatry.2009.104

Fan, J., Zhong, M., Zhu, X., Gan, J., Liu, W., Niu, C., Liao, H., Zhang, H., Yi, J., & Tan, C. (2017). Resting-state functional connectivity between right anterior insula and right orbital frontal cortex correlate with insight level in obsessive–compulsive disorder. *NeuroImage : Clinical*, *15*, 1–7. https://doi.org/10.1016/j.nicl.2017.04.002

Fortuna, L. R., Tolou-Shams, M., Robles-Ramamurthy, B., & Porche, M. V. (2020). Inequity and the disproportionate impact of COVID-19 on communities of color in the United States: The need for a trauma-informed social justice response. *Psychological Trauma: Theory, Research, Practice, and Policy*, *12*(5), 443–445. https://doi.org/10.1037/tra0000889

García-Batista, Z. E., Guerra-Peña, K., Cano-Vindel, A., Herrera-Martínez, S. X., & Medrano, L. A. (2018). Validity and reliability of the Beck Depression Inventory (BDI-II) in general and hospital population of Dominican Republic. *PLOS ONE*, *13*(6), Article e0199750. https://doi.org/10.1371/journal.pone.0199750

Gorgolewski, K. J., Auer, T., Calhoun, V. D., Craddock, R. C., Das, S., Duff, E. P., Flandin, G., Ghosh, S. S., Glatard, T., Halchenko, Y. O., Handwerker, D. A., Hanke, M., Keator, D., Li, X., Michael, Z., Maumet, C., Nichols, B. N., Nichols, T. E., Pellman, J., . . . Poldrack, R. A. (2016). The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. *Scientific Data*, *3*(1), Article 160044. https://doi.org/10.1038/sdata.2016.44

Helm, K., Viol, K., Weiger, T. M., Tass, P. A., Grefkes, C., Del Monte, D., & Schiepek, G. (2018). Neuronal connectivity in major depressive disorder: A systematic review. *Neuropsychiatric Disease and Treatment*, *14*, 2715–2737. https://doi.org/10.2147/NDT.S170989

Holt-Gosselin, B., Tozzi, L., Ramirez, C. A., Gotlib, I. H., & Williams, L. M. (2021). Coping strategies, neural structure, and depression and anxiety during the COVID-19 pandemic: A longitudinal study in a naturalistic sample spanning clinical diagnoses and subclinical symptoms. *Biological Psychiatry Global Open Science*, *1*(4), 261–271. https://doi.org/10.1016/j.bpsgos.2021.06.007

Ipsos. (2021). *COVID-19 one year later: American reemergence?* https://www.ipsos.com/en-us/news-polls/axios-ipsos-coronavirus-index

Kahana, Y., Kots, A., Mican, S., Chambers, J., & Bullock, D. (2004). Optoacoustical ear defenders with active noise reduction in an MRI communication system. *INTER-NOISE and NOISE-CON congress and conference proceedings* (Vol. 2004, Issue 9, pp. 1009–1024). Institute of Noise Control Engineering.

Klumpp, H., Post, D., Angstadt, M., Fitzgerald, D. A., & Phan, K. L. (2013). Anterior cingulate cortex and insula response during indirect and direct processing of emotional faces in generalized social anxiety disorder. *Biology of Mood & Anxiety Disorders*, *3*(1), Article 7. https://doi.org/10.1186/2045-5380-3-7

Mackey, S., & Petrides, M. (2014). Architecture and morphology of the human ventromedial prefrontal cortex. *European Journal of Neuroscience*, *40*(5), 2777–2796. https://doi.org/10.1111/ejn.12654

Mahmoud, J. S., Staten, R., Hall, L. A., & Lennie, T. A. (2012). The relationship among young adult college students' depression, anxiety, stress, demographics, life satisfaction, and coping styles. *Issues in Mental Health Nursing*, *33*(3), 149–156. https://doi.org/10.3109/01612840.2011.632708

Manoliu, A., Meng, C., Brandl, F., Doll, A., Tahmasian, M., Scherr, M., Schwerthöffer, D., Zimmer, C., Förstl, H., Bäuml, J., Riedl, V., Wohlschläger, A. M., & Sorg, C. (2014). Insular dysfunction within the salience network is associated with severity of symptoms and aberrant inter-network connectivity in major depressive disorder. *Frontiers in Human Neuroscience*, *7*, Article 930. https://doi.org/10.3389/fnhum.2013.00930

Matthews, S. C., Strigo, I. A., Simmons, A. N., Yang, T. T., & Paulus, M. P. (2008). Decreased functional coupling of the amygdala and supragenual cingulate is related to increased depression in unmedicated individuals with current major depressive disorder. *Journal of Affective Disorders*, *111*(1), 13–20. https://doi.org/10.1016/j.jad.2008.05.022

Mealer, M., Schmiege, S. J., & Meek, P. (2016). The Connor-Davidson Resilience Scale in critical care nurses: A psychometric analysis. *Journal of Nursing Measurement*, *24*(1), 28–39. https://doi.org/10.1891/1061-3749.24.1.28

Moritz, S., Jahns, A. K., Schröder, J., Berger, T., Lincoln, T. M., Klein, J. P., & Göritz, A. S. (2016). More adaptive versus less maladaptive coping: What is more predictive of symptom severity? Development of a new scale to investigate coping profiles across different psychopathological syndromes. *Journal of Affective Disorders*, *191*, 300–307. https://doi.org/10.1016/j.jad.2015.11.027

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 and Biobehavioral Reviews*, *56*, 330–344. https://doi.org/10.1016/j.neubiorev.2015.07.014

Musgrove, D. R., Eberly, L. E., Klimes-Dougan, B., Basgoze, Z., Thomas, K. M., Mueller, B. A., Houri, A., Lim, K. O., & Cullen, K. R. (2015). Impaired bottom-up effective connectivity between Amygdala and Subgenual anterior cingulate cortex in unmedicated adolescents with major depression: Results from a dynamic causal modeling analysis. *Brain Connectivity*, *5*(10), 608–619. https://doi.org/10.1089/brain.2014.0312

Nieto-Castanon, A. (2020). *Handbook of functional connectivity magnetic resonance imaging methods in CONN*. Hilbert Press. https://doi.org/10.56441/hilbertpress.2207.6598

Osmanlıoğlu, Y., Alappatt, J. A., Parker, D., & Verma, R. (2020). Connectomic consistency: A systematic stability analysis of structural and functional connectivity. *Journal of Neural Engineering*, *17*(4), Article 045004. https://doi.org/10.1088/1741-2552/ab947b

Paulus, M. P., & Stein, M. B. (2006). An insular view of anxiety. *Biological Psychiatry*, *60*(4), 383–387. https://doi.org/10.1016/j.biopsych.2006.03.042

Peterson, A., Thome, J., Frewen, P., & Lanius, R. A. (2014). Resting-state neuroimaging studies: A new way of identifying differences and similarities among the anxiety disorders? *Canadian Journal of Psychiatry*, *59*(6), 294–300. https://doi.org/10.1177/070674371405900602

Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *NeuroImage*, *84*, 320–341. https://doi.org/10.1016/j.neuroimage.2013.08.048

Prater, K. E., Hosanagar, A., Klumpp, H., Angstadt, M., & Phan, K. L. (2013). Aberrant amygdala-frontal cortex connectivity during perception of fearful faces and at rest in generalized social anxiety disorder. *Depression and Anxiety*, *30*(3), 234–241. https://doi.org/10.1002/da.22014

Ran, L., Wang, W., Ai, M., Kong, Y., Chen, J., & Kuang, L. (2020). Psychological resilience, depression, anxiety, and somatization symptoms in response to COVID-19: A study of the general population in China at the peak of its epidemic. *Social Science & Medicine*, *262*, Article 113261. https://doi.org/10.1016/j.socscimed.2020.113261

Robinson, J. S., Larson, C. L., & Cahill, S. P. (2014). Relations between resilience, positive and negative emotionality, and symptoms of anxiety and depression. *Psychological Trauma: Theory, Research, Practice, and Policy*, *6*(Suppl. 1), S92–S98. https://doi.org/10.1037/a0033733

Rolls, E. T., Huang, C. C., Lin, C. P., Feng, J., & Joliot, M. (2020). Automated anatomical labelling atlas 3. *NeuroImage*, *206*, Article 116189. https://doi.org/10.1016/j.neuroimage.2019.116189

Schmitt, A. A., Jr., Brenner, A. M., Primo de Carvalho Alves, L., Claudino, F. C. A., Fleck, M. P. A., & Rocha, N. S. (2021). Potential predictors of

depressive symptoms during the initial stage of the COVID-19 outbreak among Brazilian adults. *Journal of Affective Disorders*, *282*, 1090–1095. https://doi.org/10.1016/j.jad.2020.12.203

Segal, D. L., Coolidge, F. L., Cahill, B. S., & O'Riley, A. A. (2008). Psychometric properties of the Beck Depression Inventory II (BDI-II) among community-dwelling older adults. *Behavior Modification*, *32*(1), 3–20. https://doi.org/10.1177/0145445507303833

Shechory Bitton, M., & Laufer, A. (2021). Mental health and coping in the shadow of the COVID-19 pandemic: The israeli case. *Frontiers in Public Health*, *8*, Article 568016. https://doi.org/10.3389/fpubh.2020.568016

Song, S., Yang, X., Yang, H., Zhou, P., Ma, H., Teng, C., Chen, H., Ou, H., Li, J., Mathews, C. A., Nutley, S., Liu, N., Zhang, X., & Zhang, N. (2021). Psychological resilience as a protective factor for depression and anxiety among the public during the outbreak of COVID-19. *Frontiers in Psychology*, *11*, Article 618509. https://doi.org/10.3389/fpsyg.2020.618509

Strawn, J. R., Dominick, K. C., Patino, L. R., Doyle, C. D., Picard, L. S., & Phan, K. L. (2014). Neurobiology of pediatric anxiety disorders. *Current Behavioral Neuroscience Reports*, *1*(3), 154–160. https://doi.org/10.1007/s40473-014-0014-1

Teeuw, J., Hulshoff Pol, H. E., Boomsma, D. I., & Brouwer, R. M. (2021). Reliability modelling of resting-state functional connectivity. *NeuroImage*, *231*, Article 117842. https://doi.org/10.1016/j.neuroimage.2021.117842

The Institute for Health Metrics and Evaluation. (2021). *IHME COVID-19 projections*. https://covid19.healthdata.org/

Tomiyama, H., Murayama, K., Nemoto, K., Hasuzawa, S., Mizobe, T., Kato, K., Matsuo, A., Ohno, A., Kang, M., Togao, O., Hiwatashi, A., Ishigami, K., & Nakao, T. (2022). Alterations of default mode and cingulo-opercular salience network and frontostriatal circuit: A candidate endophenotype of obsessive–compulsive disorder. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *116*, Article 110516. https://doi.org/10.1016/j.pnpbp.2022.110516

Valero-Moreno, S., Lacomba-Trejo, L., Tamarit, A., Pérez-Marín, M., & Montoya-Castilla, I. (2021). Psycho-emotional adjustment in parents of adolescents: A cross-sectional and longitudinal analysis of the impact of the COVID pandemic. *Journal of Pediatric Nursing*, *59*, e44–e51. https://doi.org/10.1016/j.pedn.2021.01.028

Van Dijk, K. R., Hedden, T., Venkataraman, A., Evans, K. C., Lazar, S. W., & Buckner, R. L. (2010). Intrinsic functional connectivity as a tool for human connectomics: Theory, properties, and optimization. *Journal of Neurophysiology*, *103*(1), 297–321. https://doi.org/10.1152/jn.00783.2009

VanTieghem, M. R., & Tottenham, N. (2018). Neurobiological programming of early life stress: Functional development of amygdala-prefrontal circuitry and vulnerability for stress-related psychopathology. *Current Topics in Behavioral Neurosciences*, *38*, 117–136. https://doi.org/10.1007/7854_2016_42

Varma, P., Junge, M., Meaklim, H., & Jackson, M. L. (2021). Younger people are more vulnerable to stress, anxiety and depression during COVID-19 pandemic: A global cross-sectional survey. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *109*, Article 110236. https://doi.org/10.1016/j.pnpbp.2020.110236

Veer, I. M., Beckmann, C. F., van Tol, M. J., Ferrarini, L., Milles, J., Veltman, D. J., Aleman, A., van Buchem, M. A., van der Wee, N. J., & Rombouts, S. A. (2010). Whole brain resting-state analysis reveals decreased functional connectivity in major depression. *Frontiers in Systems Neuroscience*, *4*, Article 41. https://doi.org/10.3389/fnsys.2010.00041

Wermelinger Ávila, M. P., Lucchetti, A. L., & Lucchetti, G. (2017). Association between depression and resilience in older adults: A systematic review and meta-analysis. *International Journal of Geriatric Psychiatry*, *32*(3), 237–246. https://doi.org/10.1002/gps.4619

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connectivity*, *2*(3), 125–141. https://doi.org/10.1089/brain.2012.0073

Williams, L. M. (2016). Precision psychiatry: A neural circuit taxonomy for depression and anxiety. *The Lancet Psychiatry*, *3*(5), 472–480. https://doi.org/10.1016/S2215-0366(15)00579-9

Williams, L. M. (2017). Defining biotypes for depression and anxiety based on large-scale circuit dysfunction: A theoretical review of the evidence and future directions for clinical translation. *Depression and Anxiety*, *34*(1), 9–24. https://doi.org/10.1002/da.22556

World Health Organization. (2021). *WHO coronavirus disease (COVID-19) dashboard*. https://covid19.who.int/

Xie, Y., Peng, L., Zuo, X., & Li, M. (2016). The psychometric evaluation of the Connor-Davidson Resilience Scale using a Chinese military sample. *PLOS ONE*, *11*(2), Article e0148843. https://doi.org/10.1371/journal.pone.0148843

Xiong, J., Lipsitz, O., Nasri, F., Lui, L. M. W., Gill, H., Phan, L., Chen-Li, D., Iacobucci, M., Ho, R., Majeed, A., & McIntyre, R. S. (2020). Impact of COVID-19 pandemic on mental health in the general population: A systematic review. *Journal of Affective Disorders*, *277*, 55–64. https://doi.org/10.1016/j.jad.2020.08.001

Yip, S. W., Jordan, A., Kohler, R. J., Holmes, A., & Bzdok, D. (2022). Multivariate, transgenerational associations of the COVID-19 pandemic across minoritized and marginalized communities. *JAMA Psychiatry*, *79*(4), 350–358. https://doi.org/10.1001/jamapsychiatry.2021.4331

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