Resting-state Directional Connectivity and Anxiety and Depression Symptoms in Adult Cannabis Users

Supplementary Information

Subject inclusion and exclusion criteria used in Dataset 1

The subject inclusion criteria were: (I) right-handed; (II) lifetime cannabis dependence (for CU participants); and (III) positive urine test for delta-9-tetrahydrocannabinol (THC -COOH) (for CU participants). The exclusion criteria were: (I) higher than moderate level of nicotine dependence as determined by the score on the Fagerstrom Test for Nicotine Dependence (Heatherton et al., 1991); (II) breath alcohol concentration greater than 0.05 g/210 L; (III) positive urine test for drugs other than cannabis; (IV) meeting DSM-IV (American Psychiatric Association, 2000) criteria for alcohol dependence. Participants with diagnosis of lifetime alcohol abuse were not excluded because of high comorbidity between cannabis use and alcohol consumption (Duncan et al., 2015). A prior history of abuse or dependence on drugs other than alcohol was not used as an exclusion criterion because HCP did not provide these diagnoses.

Group matching in Dataset 1

Based on the inclusion/exclusion criteria, 28 CU participants were identified from the 1206 participants. Then, twenty-eight non-drug-using controls were manually selected from the remaining participants in order to match the 28 CU participants, in sex, age, education, alcohol use, tobacco use, and self-reported lifetime use of other non-cannabis drugs. Specifically, one control participant was selected to match one CU participant, with sex as the first priority, age, and education as the second priority, and alcohol use, tobacco use, and self-reported lifetime use of other non-cannabis drugs as the third priority in matching.

Subject inclusion and exclusion criteria used in Dataset 2

The subject inclusion criteria of this study were: (I) right-handed; (II) 20-25 years old (but participants slightly older than 25 years old were also scanned); (III) current cannabis dependence (for CU participants) as determined by the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) and (IV) positive urine test for delta9-THC (for CU participants). The exclusion criteria were: (I) history of a major Axis I psychiatric disorder; (II) any alcohol or cannabis use during the past 24h (self-report); and (III) positive urine test for cocaine, morphine, amphetamine, benzodiazepine, and methamphetamine.

Group matching in Dataset 2

CU participants and controls were matched on sex, age, cigarette smoking status (yes/no), alcohol use-related problems (AUDIT; (Saunders et al., 1993)) and educational level during recruitment, such that near significant group differences were followed by a more targeted recruitment strategy as the study progressed.

Internalizing measures for Dataset 2

Our efforts underscored to us the merit in recent calls for greater harmonization of assessments across studies. Our priority in choosing internalizing measures was face validity with DSM clinical symptoms of depression and anxiety. We are studying psychopathology, but many survey instruments created to probe innate constructs of “depression” and “anxiety” do not necessarily well assess psychiatric syndromes. Given the potential heterogeneity produced by the limitation that the two datasets did not collect data on depression and anxiety using the same survey instruments, we attempted to maximally harmonize the overall DSM-like constructs across datasets using the available measures. For Dataset 1, the ASR DSM-Oriented scales for Depressive Problems and Anxiety Problems exhibit acceptable item-level content overlap with DSM criteria for major depression and

generalized anxiety, respectively. Dataset 2 did not include any measures sufficiently similar to ASR, so we attempted to identify included scales or items that would best approximate said DSM criteria.

Several different self-report instruments assessed recent symptoms of depression and anxiety at the same visit as the neuroimaging. The DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure-Adult (DSM-CC, https://www.psychiatry.org/psychiatrists/practice/dsm/educational-resources/assessment-measures) consists of 23 screening questions on a 1-4 severity scale for mental health domains that are important across psychiatric diagnoses such as depression, anxiety, sleep, etc. (American Psychiatric Association, 2013). Rather than the original past two-week period, the instrument was modified to query symptoms experienced in the prior six months. It includes two questions for depression (loss of interest and feeling down/depressed) and three for anxiety (nervous/anxious/worried, panic/frightened, and anxious avoidance). The Beck Depression Inventory (BDI) provides a sum score across 21 depression items experienced during the past two weeks (Beck et al., 1996). The State-Trait Anxiety Inventory (STAI) assesses various yes/no anxiety symptoms in two time intervals: the State subscale (STAI-S) includes 20 symptoms experienced “right now”, while the Trait subscale (STAI-T) includes a partially overlapping set of 20 symptoms experienced “generally” (Spielberger et al., 1970).

We sought to combine these measures to create a single summary phenotype within each domain of depression and anxiety, respectively, for incorporation into the imaging analyses. For depression, the sum of the two DSM-CC depression items was moderately correlated with the BDI total score ($r=0.55$, $p<0.001$). We created an overall depression measure by summing all of these. The relationships were more complicated among the anxiety measures. STAI-S and STAI-T were moderately correlated with each other ($r=0.48$, $p<0.001$) but differentially correlated with the sum of the DSM-CC anxiety items ($r=0.16$, $p=0.19$ and $r=0.45$, $p<0.001$, respectfully). We conducted a series of exploratory factor analyses in Mplus version 8 (Muthén and Muthén, 1998-2017) to examine the overlap and covariance

structure for groups of items within and across STAI-S and STAI-T. The model that included the three DSM-CC items and the 40 STAI items had 11 eigenvalues > 1. We iteratively examined the factor loadings on each set of items and removed those that did not load on any of the main factors (loading < 0.5) and refit, each time finding a simpler and more interpretable structure. The final model, containing two broad factors, suggested creating an overall anxiety measure by summing the three DSM-CC items with selected items from each of STAI-S and STAI-T representing similar symptomatic content. The selected items are listed in table S2.

rsfMRI data preprocessing pipeline for Dataset 2

Steps involved (1) skull-stripping of the T1 structural images; (2) removal of rsfMRI outliers using the Analysis of Functional NeuroImages (AFNI) (Cox, 1996) "3dDespike" command; (3) slice timing correction using Statistical Parametric Mapping 12 (SPM12) software (http://www.fil.ion.ucl.ac.uk/spm/); (4) rsfMRI and MPRAGE deoblique using the AFNI "3dWarp" command; (5) MPRAGE and fMRI reorientation to the orientation of the standard template image (MNI152) using the FSL (Jenkinson et al., 2012) "fslreorient2std" command; (6) FSL "FEAT" pre-stats module using rigid-body realignment of the fMRI timeseries, calculation of parameters for registration to the MPRAGE and subsequent parameters for linear and non-linear transformation to Montreal Neurological Institute(MNI) standard space, spatial smoothing with a Gaussian kernel of 5 mm FWHM (no highpass or lowpass filtering at this step); (7) the contents of the output folder from the previous FEAT step served as input to ICA-AROMA (Pruim et al., 2015) for removal of head-motion related artifacts using nonaggressive denoising applied to the spatially smoothed rsfMRI images on which ICA-AROMA used the spatial realignment and registration parameters from the previous FEAT step; (8) removal of other artifactual signal from the ICA-AROMA-denoised fMRI timeseries using the aCompCor procedure as implemented in CONN software, generating 5 principal components from unsmoothed white matter and 5 principal components from unsmoothed

cerebrospinal fluid (CSF) regions of interest, and subsequent SPM12 multiple regression model to remove these components from the fMRI timeseries; (9) SPM12 coregistration of the MPRAGE into the space of the mean unsmoothed fMRI image that was generated by a previous SPM12 Realignment of the unsmoothed rsfMRI timeseries; (10) warping of the coregistered-MPRAGE image into standard MNI space using SPM12 Normalisation, and subsequent application of the normalization parameters generated by this step to warp the ICA-AROMA-and-aCompCor-denoised fMRI timeseries into MNI space; (11) application of a temporal high-pass filter of 125 s (i.e., 0.008 Hz) to the MNI-standard-space-fMRI timeseries (using a separate FSL FEAT step without any other options other than this filtering); and (12) because of the fact that the rsfMRI only had 2 dummy scans prior to the acquisition of the fMRI timeseries, two more rsfMRI volumes were removed from the beginning of the fMRI timeseries.

Group independent component analysis (ICA)

The resting state networks (RSNs) specific to the participants in the present study were verified using Group ICA of fMRI Toolbox (GIFT) v3.0b (http://icatb.sourceforge.net/) (Calhoun et al., 2001). Among the available algorithms in GIFT, constrained ICA (Lin et al., 2010) was selected. Constrained ICA, a semiblind ICA approach, uses prior information (i.e., DMN, SAN, and amygdala templates in this study) to identify the independent components that best match the supplied templates. Thus, the number of output independent components are the same as the number of supplied templates in constrained ICA.

The DMN and SAN templates used in this study were from the GIFT Toolbox. Since an amygdala template was not included in the GIFT SAN template, the amygdala template was obtained using seed-based method. The seeds were left and right-amygdala regions of interest provided in the CONN software (adopted from FSL Harvard-Oxford Atlas). The seed-based correlation analysis was conducted using the FSL SCA Matlab script. The amygdala template was obtained by averaging the

brain networks across the two seeds and all the participants. This ICA analysis was conducted separately for the Datasets 1 and 2 and worked well for both datasets. For each participant, each of the three networks of interest was converted to z-maps (McKeown et al., 1998). Each z-score represents the number of SDs from the map mean (McKeown et al., 1998). The group average z-map from Dataset 1, the group average z-map from Dataset 2, and the group average z-map from Dataset 1+2 (i.e., mean of the previous two z-maps) were also obtained for each of the networks of interest. The group average z-map from Dataset 1+2 for the networks of interest are shown in Figure 1.

Further description of DCM

DCM models the ECs among neuronal populations at the composite neuron-activity level, supported by *in vivo* probe experiments and thus reflects composite neuronal connectivity (Park et al., 2018; Stephan et al., 2010). Specifically, ECs are modeled as interactions among hidden neuronal states (populations) using differential equations (Stephan et al., 2010). The dynamics of these modeled neuronal states predict the signals at the observed hemodynamic level (predicted fMRI signals) using a forward model (Stephan et al., 2010). The neuronal state model ECs and the parameters of the forward model are optimized by minimizing the difference between the predicted fMRI signals and the observed fMRI signals using Bayesian inference and Bayesian model selection (Stephan et al., 2010).

Spectral DCM has been developed specifically to infer EC in rsfMRI. Compared to task-based DCM, the number of parameters to be estimated is smaller in the spectral DCM because of no external inputs. The number of parameters is further reduced by obtaining the principal components of the FC matrix (FCs are used as priors of ECs among the DCM nodes) (Friston et al., 2014). It has been shown (Friston et al., 2014; Razi, 2017), both theoretically and practically, that spectral DCM is relatively computationally efficient.

Atlas details of DCM nodes

The anatomical locations in MNI coordinates of the putative a priori regions were determined using the Anatomical Automatic Labeling (AAL2) atlas (Rolls et al., 2015). The anatomical locations of DMN-mPFC and DMN-LP were determined using the medial orbitofrontal cortex and angular gyrus atlases (Andrews-Hanna et al., 2014) respectively. Same-named atlases in AAL2 were used for the remaining seven regions.

Computational details of Bayesian-PP

The Bayesian-PP regarding if an EC exists is assessed by comparing two models (they only differ in whether this EC exists or not) in terms of their log-evidence (i.e., log-Bayes-factor) (Friston and Penny, 2011). A softmax function is used to convert the log-evidence to the Bayesian-PP (Sokolov et al., 2019). Some typical Bayes-factors (0, 1, 3, 10) correspond to Bayesian-PPs (0, 0.63, 0.95, 1), reflecting no evidence, mediocre evidence, strong evidence, and very strong evidence respectively. Bayesian-PP for a linear regression beta is similar.

Further description of linear regression within PEB

The advantage of the linear regression analysis within the PEB framework is that the covariance between DCM parameters is automatically computed. In linear regression analysis, the *beta* coefficient is the slope of the regression line, i.e., the degree of change in the outcome variable per unit change of the predictor variable.

Correlation between the anxiety and depression scores

Pearson correlation analyses revealed that the anxiety score and the depression score was significant correlated for both datasets ($R>0.93$; $p<0.005$, see Figure S1 for the scatter plots).

Secondary DCM analyses harmonizing the EC results from the two datasets

To quantify the difference in ECs between CU and Control groups common to both datasets, an extra PEB analysis was conducted using a two-way ANOVA PEB analysis with Group (with two-level: CU and Control) and Dataset (with two-level: Datasets 1 and 2) as factors. Thus the differential effects (such as effects from scanner, preprocessing, and cohort) in the Dataset factor were explicitly modeled. For an EC, If the Group×Dataset Interaction was not reliable (Bayesian-PP<0.95) but the main effect of Group was reliable (Bayesian-PP>0.95), then the group difference in this EC is considered to be common to both datasets. Linear regression analyses were also conducted to test the linear relationship between each EC and each of the three anxiety/depression z-scores for both CU and Control groups combined with the Dataset included as a covariate.

Results of the secondary DCM

Group comparison based on a two-way ANOVA analysis

We conducted a two-way ANOVA analysis to evaluate the group differences (CU vs. Control) in ECs common for both datasets. In this analysis, the effect of Dataset (e.g. scanner, preprocessing, and cohort) was explicitly modeled. For each EC, the main effects of Dataset (1 vs 2), Group (CU vs. Control), their interaction, together with the average EC across both groups and both datasets, and the corresponding Bayesian-PP are shown in Table S2. Among the 81 ECs, two ECs showed no (Bayesian-PP=0) Group×Dataset interaction effects but reliable (Bayesian-PP=1) main effects of Group. Specifically, the CU group was greater (Bayesian-PP=1) in right amygdala → left amygdala EC, and smaller (Bayesian-PP=1) in left insula → left amygdala EC than the Control group. These two ECs are depicted in Figure S2.

Linear relationships between EC and each of the three anxiety/depression z-scores for both CU and Control participants combined

For each of the three analyses, the Dataset was included as a covariate. The linear regression coefficient (*beta*) for each EC and corresponding Bayesian-PP are shown in Table S3. The six ECs showing reliable (Bayesian-PP=1) linear relationship with at least one of the three negative affect z-scores are depicted in Figure S3. Two of these nine ECs also showed reliable group difference (see the right panel of Figure S2). For five of these six ECs, the reliable linear relationships were preserved when the group was included as a covariate (see Table S3). The evidence on the positive linear relationship between the right amygdala to left amygdala EC and the anxiety z-score changed from very strong (Baysian-PP=1) to mediocre (Baysian-PP=0.5184) after the group was included as a covariate.

Results of the secondary analyses consistent with Major DCM results

Two ECs (i.e., right amygdala → left amygdala and left insula → left amygdala ECs) found by the secondary analyses showed consistency with the main results. The consistent results are summarized in Table S4.

Other discussions

In Dataset 2 (continuous cannabis use parameters were available in Dataset 2 but not in Dataset 1), the right-amygdala → left-amygdala EC was reliably (Bayesian-PP=1) and negatively correlated with the days of use per week. This result could be related to a chronic effect of cannabis (people who use large amounts of cannabis chronically have higher residual effect in their system) (Filbey et al., 2018). In such a situation, cannabis may "numb" emotional experience (temporary relief of anxiety and depression symptoms). This speculation can be verified in future studies by comparing CU/CUD individuals in intoxicated and non-intoxicated states.

In Dataset 2, greater left amygdala to left amygdala EC was associated with greater abstinence days. Self-connection (such as the left amygdala to left amygdala EC) was reported only recently (Van de Steen et al., 2020; Zeidman et al., 2019). According to (Zeidman et al., 2019), the greater the self-connection, the greater self-inhibited the region. Thus, within the CU group, the abstinence was longer in the participants with left-amygdala more self-inhibited (i.e., less sensitive to the inputs from the network).

According to a recent technical guidance (Zeidman et al., 2019) published by the DCM authors, a self-connection (e.g, left insula to left insula EC) can be interpreted as an interaction between pyramidal cells and interneurons which play a regulatory role by controlling the excitatory-inhibitory balance in the local brain region (Zeidman et al., 2019). This technical guidance also showed an example showing the meaningfulness of the self-connection. In addition, a canonical cortical microcircuit has been demonstrated (Bastos et al., 2012), in which excitatory and inhibitory neurons in the granular, infragranular, and supragranular layers interact to yield outputs that go to higher cortical areas as well as lower cortical areas, brainstem, and thalamus. According to (Zeidman et al., 2019), the greater the self-connection, the greater self-inhibited the region (i.e., less sensitive to the inputs from the network). Consistently, self-connection results have been reported in a recently published DCM study (Van de Steen et al., 2020).

With more and more studies starting to use more than one datasets to test scientific hypotheses in the neuroimaging literature, there is an increasing need of methods for harmonizing different datasets. The two-way ANOVA analysis was based on the PEB approach, and is a method for harmonizing DCM based EC results. Consistent with the main analysis conducted separately in each dataset, this two-way ANOVA analysis showed that the right amygdala to left amygdala EC was greater in the CU group than the Control group and that this group difference was not dependent on the dataset (no Group×Dataset interaction and no main effect of Dataset). These results suggest that the group

difference on the right amygdala to left amygdala EC can be generalized across the datasets. However, the two-way ANOVA analysis also found several instances of an EC showing a Group×Dataset interaction, suggesting that the degree of between dataset generalization is limited. The existence of Group×Dataset interaction, consistent with the fact that the two datasets were different in several aspects (e.g., cohort, scanner, and preprocessing), justified the main analyses (two separate group analyses within each dataset).

The composite anxiety/depression z-score was the mean of the anxiety z-score and the depression z-score. Consistently, in Dataset 1, we found that the right amygdala → left amygdala EC showed mediocre evidence (Bayesian-PP=0.5029) in the positive linear relationship with the composite anxiety/depression z-score. Correspondingly, this EC showed very strong evidence (Bayesian-PP=1) in the positive linear relationship with the depression z-score but no evidence (Bayesian-PP=0) in the linear relationship with the anxiety z-score.

Our use of DCM afforded mechanistic insights not possible with simple functional connectivity. Although we could have used DCM to adjudicate between two specific *a priori* directional models (see Nicholson et al., 2017 as an example), such as information flow between amygdala and its cortical regulators, we did not believe extant literature provided sufficient grounds for this constraint. We thus opted instead for Bayesian model reduction (BMR) (Friston et al., 2016) to detect the optimal model among all possible models that are reduced (or restricted) forms of the full model. Importantly, aberrations in "top-down" versus "bottom-up" information flow to and from neuroendocrine effectors could nevertheless be evident in the best-fitting model with BMR. For example, greater right amygdala → left amygdala EC with cannabis use history in both datasets suggests a mechanism for exaggerated bottom-up processing. Moreover, in the optimal model found in Dataset 2, the ACC → left amygdala EC could reflect additional alteration in top-down processing with cannabis use. Conversely, the mPFC → right insula EC might reflect neither top-down processing nor bottom-up processing.

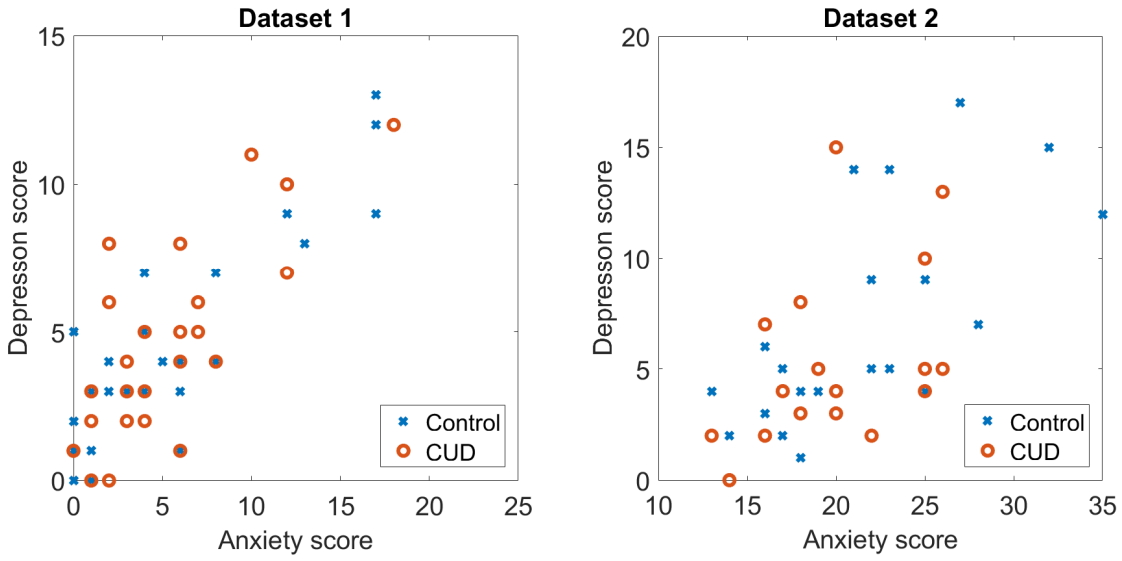

Figure S1: The scatter plots showing the relationship between the anxiety score and depression score in Dataset 1 (left panel, the correlation between the anxiety score and the depression score was significant in the CU group [n=28, R=0.93; p<0.001], in the Control group [n=28, R=0.77; p<0.001], and in both groups combined [n=56, R=0.88; p<0.001]) and Dataset 2 (right panel, the correlation between the anxiety score and the depression score was significant in the CU group [n=21, R=0.68;p<0.001], in the Control group [n=21, R=0.56;p= 0.008], and in both groups combined [n=42, R=0.64;p<0.001]).

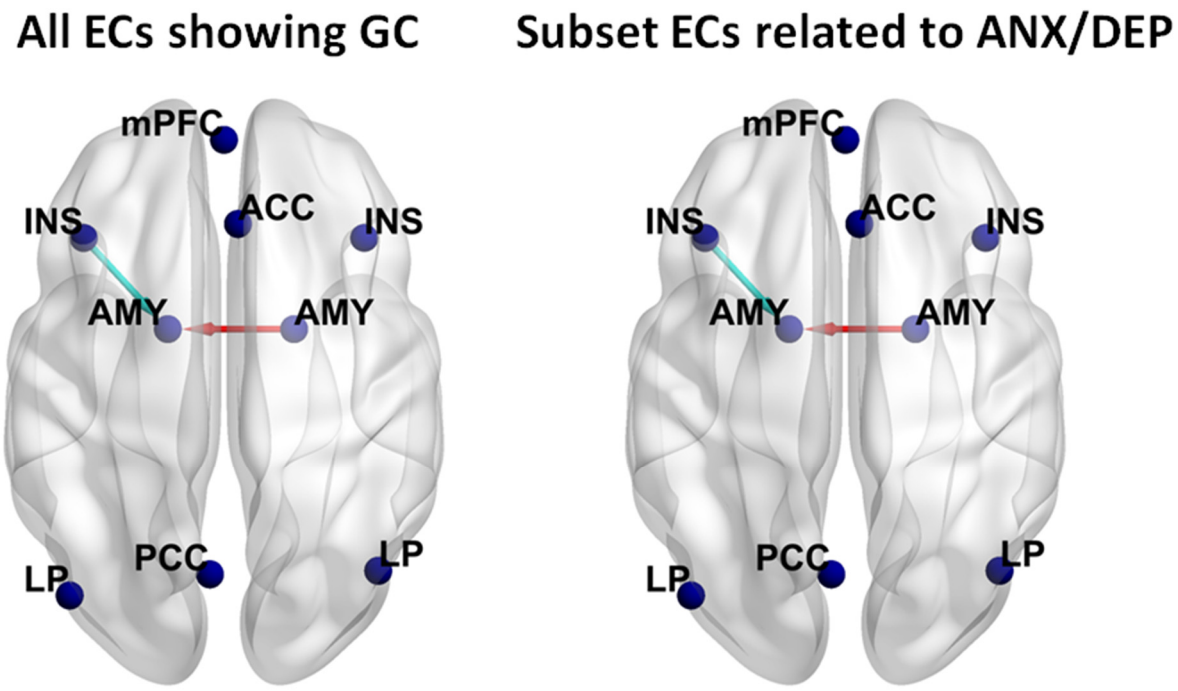

Figure S2: The lines with arrows representing the group difference (GC, CU minus Control) in ECs in the two-way ANOVA analysis for the combined datasets (n=49 for CU group and n=41 for Control group). All ECs showing group differences are shown in the left panel, and sub-set ECs showing group differences which are linearly related to at least one of the three negative affect z-scores (anxiety [ANX], depression [DEP], and composite ANX/DEP z-scores) are shown in the right panel. A red line denotes that this EC was greater in the CU group than the Control group; and a light blue line denotes that this EC was smaller in the CU group than the Control group. Left side in the figure is left hemisphere of the brain, and right side of figure is right hemisphere of brain.

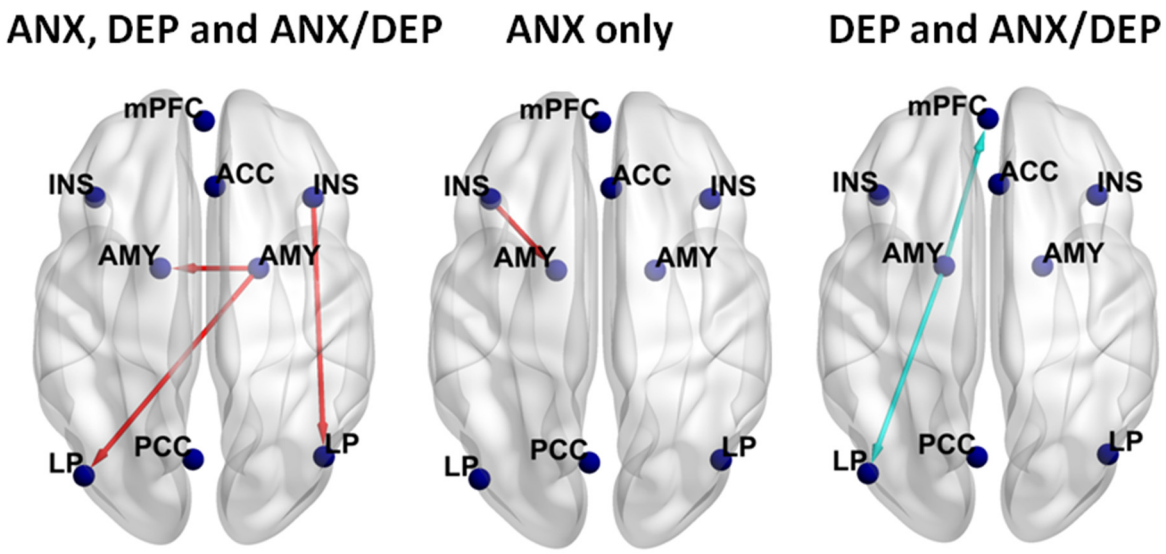

Figure S3: The lines with arrows representing ECs which showed linear relationships with at least one of the three negative affect z-scores (anxiety [ANX], depression [DEP], and composite ANX/DEP z-scores) across all both CU and Control participants in the combined datasets with the dataset as the covariate (in each dataset, both CU and Control participants) in combined datasets (n=98). ECs showing linear relationship with all the three negative affect z-scores are shown in the left panel, EC showing linear relationship with ANX z-score only is shown in the middle panel, and ECs showing linear relationship with both DEP and composite ANX/DEP z-scores are shown in the right panel. None of the ECs showed linear relationship with any of the negative affect z-scores other than shown in the figure. A red line denotes that this EC had positive linear relationship with at least one of three negative affect z-scores; and a light blue line denotes that this EC had negative linear relationship with at least one of three negative affect z-scores. Left side in the figure is left hemisphere of the brain, and right side of figure is right hemisphere of brain.

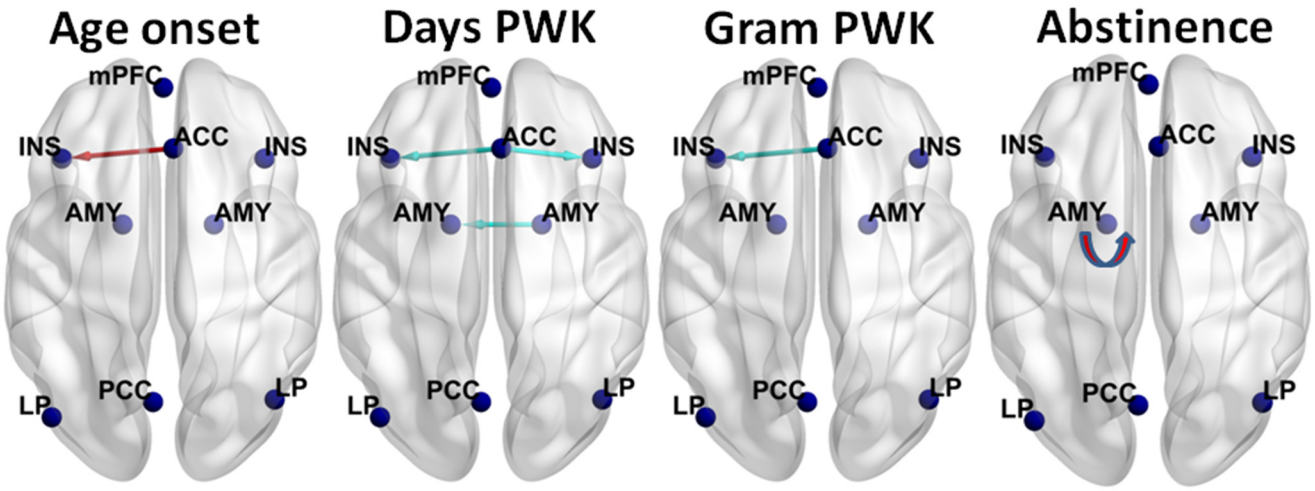

Figure S4: The lines with arrows representing ECs which showed linear relationships with at least one of the cannabis use measures (age onset, cannabis use days per week, cannabis use gram per week and abstinence days) across all participants (both CU and Control participants) in Dataset 2 (n=42). An EC showing linear relationship with the age onset is shown in the left panel, ECs showing linear relationship with the cannabis use days per week are shown in the second panel (from left), an EC showing linear relationship with the cannabis use gram per week is shown in the third panel (from left) and an EC showing linear relationship with the abstinence days is shown in the right panel. The ECs shown in this figure were those showing group differences demonstrated in Figure 2. See Table S9 for ECs showing linear relationship with the cannabis use measures but not showing difference between the CU and Control groups. None of the ECs showed linear relationship with lifetime cannabis use (# joints). A red line denotes that this EC had positive linear relationship with at least one of three negative affect z-scores; and a light blue line denotes that this EC had negative linear relationship with at least one of three negative affect z-scores. Left side in the figure is left hemisphere of the brain, and right side of figure is right hemisphere of brain.

Table S1. Items included in anxiety summary measure.

Survey	Item Number and Content Wording
DSM-CC	6. Feeling nervous, anxious, frightened, worried, or on edge
DSM-CC	7. Feeling panic or being frightened
DSM-CC	8. Avoiding situations that make you anxious
STAI-S	3. I am tense
STAI-S	4. I feel strained
STAI-S	7. I am presently worrying over possible misfortunes
STAI-S	9. I feel frightened
STAI-S	12. I feel nervous
STAI-S	13. I am jittery
STAI-S	17. I am worried
STAI-T	22. I feel nervous and restless
STAI-T	27. I am “calm, cool, and collected” (reverse coded)
STAI-T	29. I worry too much over something that really doesn’t matter
STAI-T	31. I have disturbing thoughts
STAI-T	37. Some unimportant thought runs through my mind and bothers me
STAI-T	40. I get in a state of tension or turmoil as I think over my recent concerns and interests

Table S2. The results of the group level PEB two-way ANOVA DCM analyses for comparison between CU and Control groups. EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Average across both CU and Control participants and both datasets (n=98)		Main effects of Dataset: Dataset 1(n=56) – Dataset 2 (n=42)		Main effects of Group: CU (n=49) – Control (n=49)		Group × Dataset Interaction	
Connectivity	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP
DMN-mPFC→DMN-mPFC	0.1315	1	-0.0873	1	0	0	-0.0010	0
DMN-mPFC→DMN-PCC	0.0985	1	-0.1932	1	0	0	0.0001	0
DMN-mPFC→L-DMN-LP	0.0004	0	-0.0360	0	-0.0001	0	0.0006	0
DMN-mPFC→R-DMN-LP	-0.0004	0	-0.0386	1	-0.0001	0	0.0005	0
DMN-mPFC→SAN-ACC	0.1420	1	-0.0986	1	0	0	-0.0001	0
DMN-mPFC→L-SAN-INS	-0.0004	0	0.0385	0.5323	0	0	0.0001	0
DMN-mPFC→R-SAN-INS	0.0010	0	0.0047	0	0	0	0	0
DMN-mPFC→L-AMY	-0.0002	0	0.0011	0	-0.0002	0	0	0
DMN-mPFC→R-AMY	-0.0001	0	-0.0029	0	0	0	0	0
DMN-PCC→DMN-mPFC	0.1615	1	0.1662	1	0	0	-0.0002	0
DMN-PCC→DMN-PCC	0	0	-0.0333	0.5171	0	0	0.0001	0
DMN-PCC→L-DMN-LP	0.0378	0	0.0365	0	0	0	-0.0139	0
DMN-PCC→R-DMN-LP	0.0489	1	0.0404	1	0	0	-0.0141	0.5165
DMN-PCC→SAN-ACC	0.0755	1	0.0713	1	0	0	0.0005	0
DMN-PCC→L-SAN-INS	-0.0043	0	-0.0046	0	0	0	0.0016	0
DMN-PCC→R-SAN-INS	-0.0045	0	-0.0043	0	0	0	0.0015	0
DMN-PCC→L-AMY	0.0001	0	-0.0003	0	0.0001	0	0	0
DMN-PCC→R-AMY	0.0026	0	0.0026	0	0	0	-0.0010	0
L-DMN-LP→DMN-mPFC	-0.1322	1	0.0197	0	0.0001	0	-0.0317	0
L-DMN-LP→DMN-PCC	-0.0363	0	0.0571	1	0	0	0.0020	0
L-DMN-LP→L-DMN-LP	0.1792	1	0.1006	1	-0.0042	0	0.0186	0
L-DMN-LP→R-DMN-LP	0.1805	1	0.1161	1	-0.0040	0	0.0168	0
L-DMN-LP→SAN-ACC	-0.0977	1	-0.0699	1	-0.0001	0	-0.0036	0
L-DMN-LP→L-SAN-INS	-0.0096	0	-0.0860	1	-0.0005	0	0.0044	0
L-DMN-LP→R-SAN-INS	0.0343	0	-0.0542	1	-0.0004	0	0.0005	0
L-DMN-LP→L-AMY	-0.0062	0	-0.0307	1	-0.0079	0	0.0001	0
L-DMN-LP→R-AMY	-0.0026	0	-0.0133	0	0.0003	0	-0.0003	0
R-DMN-LP→DMN-mPFC	-0.0568	0.5220	-0.0193	0	0.0001	0	-0.0322	1
R-DMN-LP→DMN-PCC	0.0369	0	0.0200	0	0	0	-0.0019	0
R-DMN-LP→L-DMN-LP	0.2212	1	0.0558	0.5042	-0.0043	0.5072	0.0186	1
R-DMN-LP→R-DMN-LP	0.2246	1	0.0644	1	-0.0041	0	0.0175	0.5268
R-DMN-LP→SAN-ACC	-0.1408	1	-0.0816	1	-0.0001	0	0.0040	0
R-DMN-LP→L-SAN-INS	-0.0643	1	-0.0513	0	-0.0005	0	-0.0032	0
R-DMN-LP→R-SAN-INS	-0.0348	0	-0.0265	0	-0.0004	0	0.0006	0
R-DMN-LP→L-AMY	0.0062	0	-0.0368	0	0.0080	0	-0.0001	0
R-DMN-LP→R-AMY	0.0026	0	-0.0138	0.5097	0.0003	0	-0.0004	0
SAN-ACC→DMN-mPFC	0.1784	1	-0.0006	0	0	0	0.0010	0
SAN-ACC→DMN-PCC	0.0013	0	0.1734	1	0	0	-0.0001	0
SAN-ACC→L-DMN-LP	-0.0265	0	0.1014	1	0.0001	0	-0.0006	0
SAN-ACC→R-DMN-LP	-0.0362	1	0.1256	1	0.0001	0	-0.0005	0
SAN-ACC→SAN-ACC	0.1177	1	-0.1445	1	0	0	0.0001	0
SAN-ACC→L-SAN-INS	0.0845	1	-0.1317	1	0	0	-0.0001	0
SAN-ACC→R-SAN-INS	0.1059	1	-0.0717	1	0	0	0	0
SAN-ACC→L-AMY	0.0001	0	-0.0011	0	0.0002	0	0	0
SAN-ACC→R-AMY	-0.0018	0	0.0004	0	0	0	0	0
L-SAN-INS→DMN-mPFC	-0.2671	1	0.3787	1	0	0	0.0038	0

L-SAN-INS→DMN-PCC	-0.2446	1	0.2795	1	0	0	0.1184	1
L-SAN-INS→L-DMN-LP	-0.1836	1	0.2394	1	0.0005	0	0.0011	0
L-SAN-INS→R-DMN-LP	-0.2534	1	0.2938	1	0.0004	0	-0.0053	0
L-SAN-INS→SAN-ACC	0.1735	1	0.0732	1	0	0	-0.0662	1
L-SAN-INS→L-SAN-INS	0.1816	1	-0.3166	1	0	0	0.0664	1
L-SAN-INS→R-SAN-INS	0.3778	1	-0.1335	1	0	0	-0.0004	0
L-SAN-INS→L-AMY	0.0007	0	0.0648	1	-0.0726	1	0	0
L-SAN-INS→R-AMY	0.0003	0	0.0015	0	0	0	0.0003	0
R-SAN-INS→DMN-mPFC	-0.4865	1	-0.0022	0	0	0	0.0035	0
R-SAN-INS→DMN-PCC	-0.4690	1	0.0022	0	0	0	-0.0876	1
R-SAN-INS→L-DMN-LP	-0.2270	1	0.1851	1	0.0005	0	-0.0024	0
R-SAN-INS→R-DMN-LP	-0.3036	1	0.1921	1	0.0004	0	-0.0015	0
R-SAN-INS→SAN-ACC	0.1331	1	0	0	0	0	0.0004	0
R-SAN-INS→L-SAN-INS	0.3207	1	-0.0054	0	0.0001	0	-0.0004	0
R-SAN-INS→R-SAN-INS	0.2676	1	-0.0849	1	0	0	0	0
R-SAN-INS→L-AMY	0.0007	0	-0.0041	0	0.0009	0	0	0
R-SAN-INS→R-AMY	0.0003	0	0.0015	0	0	0	0	0
L-AMY→DMN-mPFC	-0.2168	1	0.1728	1	0	0	-0.0001	0
L-AMY→DMN-PCC	-0.2835	1	0.1945	1	0	0	0	0
L-AMY→L-DMN-LP	-0.2691	1	0.1968	1	-0.0001	0	0.0001	0
L-AMY→R-DMN-LP	-0.2464	1	0.2160	1	0.0001	0	-0.0001	0
L-AMY→SAN-ACC	-0.1928	1	0	0	0	0	0	0
L-AMY→L-SAN-INS	0	0	-0.1361	1	0	0	0	0
L-AMY→R-SAN-INS	0.0001	0	-0.1194	1	0	0	0	0
L-AMY→L-AMY	-0.1070	1	0.0828	1	0.0873	1	-0.0975	1
L-AMY→R-AMY	0.2567	1	-0.1499	1	0	0	0	0
R-AMY→DMN-mPFC	-0.0794	1	0.1213	1	0	0	-0.0022	0
R-AMY→DMN-PCC	-0.1526	1	0.0983	1	0	0	0.0001	0
R-AMY→L-DMN-LP	-0.1494	1	0.1269	1	-0.0004	0	0.0013	0
R-AMY→R-DMN-LP	-0.1393	1	0.1440	1	-0.0002	0	0.0012	0
R-AMY→SAN-ACC	-0.1649	1	-0.0750	1	0	0	-0.0003	0
R-AMY→L-SAN-INS	-0.0678	1	-0.1236	1	0	0	0.0003	0
R-AMY→R-SAN-INS	0.0983	1	0.0016	0	0	0	0	0
R-AMY→L-AMY	0.1934	1	0.0025	0	0.1084	1	0	0
R-AMY→R-AMY	0.0695	1	-0.0009	0	0	0	0	0

Table S3. The results of the linear regression analyses for combined datasets, testing the linear relationships between EC and each of the three negative affect z-scores for CU and Control participants combined for Dataset 2 (without or with group as a covariate). EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Linear relationship between EC and anxiety z-score (n=98)		Linear relationship between EC and depression z-score (n=98)		Linear relationship between EC and composite anxiety/depression z-score (n=98)		Linear relationship between EC and anxiety z-score with group as a covariate (n=98)		Linear relationship between EC and depression z-score with group as a covariate (n=98)		Linear relationship between EC and composite anxiety/depression z-score with group as a covariate (n=98)	
Connectivity	beta	PP	beta	PP	beta	PP	beta	PP	beta	PP	beta	PP
DMN-mPFC→DMN-mPFC	-0.0004	0	0	0	0	0	-0.0004	0	0	0	0	0
DMN-mPFC→DMN-PCC	0.0681	1	0	0	0.0001	0	0.0682	1	0	0	0.0001	0
DMN-mPFC→L-DMN-LP	0.0001	0	0	0	0	0	0.0002	0	0	0	0	0
DMN-mPFC→R-DMN-LP	-0.0004	0	0	0	0	0	-0.0004	0	0	0	0	0
DMN-mPFC→SAN-ACC	0	0	0.0001	0	0	0	0	0	0	0	0	0
DMN-mPFC→L-SAN-INS	-0.0001	0	0	0	0	0	-0.0001	0	0	0	0	0
DMN-mPFC→R-SAN-INS	-0.0001	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→L-AMY	0.0001	0	-0.0001	0	-0.0001	0	0.0001	0	-0.0001	0	-0.0001	0
DMN-mPFC→R-AMY	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→DMN-mPFC	0.0001	0	0	0	0	0	0.0001	0	0	0	0	0
DMN-PCC→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→L-DMN-LP	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→R-DMN-LP	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→SAN-ACC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→L-SAN-INS	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→R-SAN-INS	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→L-AMY	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→R-AMY	0	0	0	0	0	0	0	0	0	0	0	0
L-DMN-LP→DMN-mPFC	0.0147	0.502719	0.0002	0	0.0001	0	0.0144	0.503024	0.0002	0	0.0001	0
L-DMN-LP→DMN-PCC	0.0034	0	0	0	0.0047	0	0.0034	0	0	0	0.0047	0
L-DMN-LP→L-DMN-LP	-0.0050	0	0.0005	0	-0.0008	0	-0.0042	0	0.0004	0	-0.0008	0
L-DMN-LP→R-DMN-LP	-0.0044	0	0.0005	0	-0.0007	0	-0.0036	0	0.0004	0	-0.0007	0
L-DMN-LP→SAN-ACC	-0.0002	0	0.0017	0	-0.0001	0	-0.0001	0	0.0016	0	-0.0001	0
L-DMN-LP→L-SAN-INS	-0.0006	0	-0.0004	0	-0.0003	0	-0.0005	0	-0.0003	0	-0.0003	0
L-DMN-LP→R-SAN-INS	-0.0006	0	-0.0003	0	-0.0003	0	-0.0005	0	-0.0003	0	-0.0003	0
L-DMN-LP→L-AMY	0.0016	0	-0.0048	0	-0.0043	0	0.0031	0	-0.0044	0	-0.0040	0
L-DMN-LP→R-AMY	0.0004	0	0.0002	0	0.0002	0	0.0003	0	0.0002	0	0.0002	0
R-DMN-LP→DMN-mPFC	0.0139	0	-0.0002	0	-0.0001	0	0.0137	0	-0.0002	0	-0.0001	0
R-DMN-LP→DMN-PCC	-0.0035	0	0	0	-0.0048	0	-0.0035	0	0	0	-0.0048	0
R-DMN-LP→L-DMN-LP	-0.0043	0.502968	-0.0005	0	0.0008	0	-0.0055	0.502808	-0.0004	0	0.0008	0

R-DMN-LP→R-DMN-LP	-0.0037	0	-0.0005	0	0.0007	0	-0.0048	0	-0.0004	0	0.0007	0
R-DMN-LP→SAN-ACC	-0.0001	0	-0.0018	0	0.0001	0	-0.0001	0	-0.0016	0	0.0001	0
R-DMN-LP→L-SAN-INS	-0.0003	0	0.0004	0	0.0003	0	-0.0004	0	0.0003	0	0.0003	0
R-DMN-LP→R-SAN-INS	-0.0003	0	0.0003	0	0.0003	0	-0.0004	0	0.0003	0	0.0003	0
R-DMN-LP→L-AMY	-0.0016	0	0.0049	0	0.0043	0	-0.0031	0	0.0044	0	0.0041	0
R-DMN-LP→R-AMY	0.0002	0	-0.0002	0	-0.0002	0	0.0003	0	-0.0002	0	-0.0002	0
SAN-ACC→DMN-mPFC	0.0004	0	0	0	0	0	0.0004	0	0	0	0	0
SAN-ACC→DMN-PCC	-0.0001	0	0	0	-0.0001	0	-0.0001	0	0	0	-0.0001	0
SAN-ACC→L-DMN-LP	0.0001	0	0	0	0	0	0.0001	0	0	0	0	0
SAN-ACC→R-DMN-LP	0.0001	0	0	0	0	0	0.0001	0	0	0	0	0
SAN-ACC→SAN-ACC	0	0	-0.0001	0	0	0	0	0	-0.0001	0	0	0
SAN-ACC→L-SAN-INS	0	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→R-SAN-INS	0	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→L-AMY	-0.0001	0	0.0001	0	0.0001	0	-0.0001	0	0.0001	0	0.0001	0
SAN-ACC→R-AMY	0	0	0	0	0	0	0	0	0	0	0	0
L-SAN-INS→DMN-mPFC	0.0011	0	0	0	0	0	0.0006	0	0	0	0	0
L-SAN-INS→DMN-PCC	-0.0003	0	0	0	-0.0005	0	-0.0001	0	0	0	-0.0005	0
L-SAN-INS→L-DMN-LP	0.0157	0.529727	-0.0001	0	0.0001	0	0.0331	1	0	0	0.0001	0
L-SAN-INS→R-DMN-LP	0.0152	0	-0.0001	0	0.0001	0	0.0318	0	0	0	0.0001	0
L-SAN-INS→SAN-ACC	0.0005	0	-0.0002	0	0	0	0.0010	0	-0.0002	0	0	0
L-SAN-INS→L-SAN-INS	0.0018	0	0	0	0	0	0.0036	0	0	0	0	0
L-SAN-INS→R-SAN-INS	0.0017	0	0	0	0	0	0.0035	0	0	0	0	0
L-SAN-INS→L-AMY	0.0705	1	0.0006	0	0.0005	0	0.0742	1	0.0005	0	0.0005	0
L-SAN-INS→R-AMY	-0.0010	0	0	0	0	0	-0.0022	0	0	0	0	0
R-SAN-INS→DMN-mPFC	0.0028	0	0.0010	0	0.0014	0	0.0028	0	0.0010	0	0.0014	0
R-SAN-INS→DMN-PCC	0.0815	1	-0.0003	0	0.0861	1	0.0815	1	-0.0003	0	0.0865	1
R-SAN-INS→L-DMN-LP	0.0420	0	0.0330	0	0.0441	0	0.0417	0	0.0312	0	0.0441	0
R-SAN-INS→R-DMN-LP	0.0420	1	0.0325	1	0.0441	1	0.0418	1	0.0308	1	0.0441	1
R-SAN-INS→SAN-ACC	-0.0013	0	0.0327	0.502946	-0.0013	0	-0.0013	0	0.0298	0.502988	-0.0013	0
R-SAN-INS→L-SAN-INS	-0.0047	0	-0.0038	0	-0.0051	0	-0.0047	0	-0.0036	0	-0.0051	0
R-SAN-INS→R-SAN-INS	-0.0046	0	-0.0037	0	-0.0049	0	-0.0046	0	-0.0035	0	-0.0049	0
R-SAN-INS→L-AMY	-0.0001	0	0.0006	0	0.0005	0	-0.0003	0	0.0005	0	0.0005	0
R-SAN-INS→R-AMY	0.0028	0	0.0023	0	0.0030	0	0.0028	0	0.0021	0	0.0030	0
L-AMY→DMN-mPFC	0	0	-0.0696	1	-0.0788	1	0	0	-0.0738	1	-0.0792	1
L-AMY→DMN-PCC	0	0	-0.0003	0	-0.0003	0	0	0	-0.0003	0	-0.0003	0
L-AMY→L-DMN-LP	0	0	-0.0381	1	-0.0389	1	0	0	-0.0388	1	-0.0405	1
L-AMY→R-DMN-LP	0	0	-0.0385	0	-0.0396	0	0	0	-0.0392	0	-0.0411	0
L-AMY→SAN-ACC	0	0	-0.0012	0	-0.0012	0	0	0	-0.0012	0	-0.0012	0
L-AMY→L-SAN-INS	0	0	-0.0044	0	-0.0045	0	0	0	-0.0045	0	-0.0047	0
L-AMY→R-SAN-INS	0	0	-0.0042	0	-0.0044	0	0	0	-0.0043	0	-0.0045	0

L-AMY→L-AMY	0	0	0.0001	0	0.0001	0	0	0	0.0001	0	0.0001	0
L-AMY→R-AMY	0	0	0.0026	0	0.0027	0	0	0	0.0027	0	0.0028	0
R-AMY→DMN-mPFC	-0.0009	0	-0.0012	0	0.0001	0	-0.0009	0	-0.0012	0	0	0
R-AMY→DMN-PCC	0.0002	0	0.0003	0	0.0003	0	0.0002	0	0.0003	0	0.0003	0
R-AMY→L-DMN-LP	0.1033	1	0.0396	1	0.0948	1	0.1036	1	0.0405	1	0.0945	1
R-AMY→R-DMN-LP	0.1018	1	0.0380	0	0.0936	1	0.1020	1	0.0389	0	0.0932	1
R-AMY→SAN-ACC	0	0	0.0013	0	-0.0001	0	0	0	0.0013	0	0	0
R-AMY→L-SAN-INS	-0.0001	0	0.0043	0	-0.0002	0	-0.0001	0	0.0044	0	-0.0001	0
R-AMY→R-SAN-INS	-0.0001	0	0.0042	0	-0.0002	0	-0.0001	0	0.0043	0	-0.0001	0
R-AMY→L-AMY	0.0722	1	0.1427	1	0.1273	1	0.0332	0.518388	0.1300	1	0.1202	1
R-AMY→R-AMY	0.0001	0	-0.0026	0	0.0001	0	0.0001	0	-0.0026	0	0.0001	0

Table S4. Summary of the ECs showing consistency between the secondary analyses and main analyses. In Dataset 1, n=28 for CU group, n=28 for Control group, and n=56 for both groups combined; in Dataset 2, n=21 for CU group, n=21 for Control group, and n=42 for both groups combined; and in combined datasets, n=49 for CU group, n=49 for Control group, and n=98 for both groups combined.

EC	Results on EC	Found in
Right amygdala → left amygdala	• CU greater than Control • Across all participants (both CU and Control participants) in each dataset, greater EC was associated with greater depression z-score and greater anxiety/depression z-score	Dataset 1 Dataset 2 Combined datasets
	• Across all participants (both CU and Control participants) in Dataset 2, greater EC was associated with greater anxiety z-score	Dataset 2 Combined datasets
Left insula → left amygdala	• CU smaller than Control • Across all participants (both CU and Control participants) in Dataset 1, smaller EC was associated with smaller anxiety z-score	Dataset 1 Dataset 1+2

Table S5. The results of the group comparison (CU minus Control) in Dataset 1 (without a covariate, with alcohol and tobacco usages as covariates, and with anxiety/depression as a covariate). EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Average across both groups (n=56)		Group comparison (CU [n=28] minus Control [n=28]) without a covariate		Group comparison (CU [n=28] minus Control [n=28]) with alcohol and tobacco usages as covariates		Group comparison (CU [n=28] minus Control [n=28]) with anxiety z-score as a covariate		Group comparison (CU [n=28] minus Control [n=28]) with depression z-score as a covariate		Group comparison (CU [n=28] minus Control [n=28]) with composite anxiety/depression z-score as a covariate	
Connectivity	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP
DMN-mPFC→DMN-mPFC	0.0001	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→DMN-PCC	-0.0863	1	0.0001	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0
DMN-mPFC→L-DMN-LP	0.0038	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→R-DMN-LP	-0.0039	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→SAN-ACC	-0.0001	0	-0.0001	0	-0.0002	0	-0.0002	0	-0.0002	0	-0.0001	0
DMN-mPFC→L-SAN-INS	0.0820	1	0.0001	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0
DMN-mPFC→R-SAN-INS	-0.0002	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→L-AMY	0.0004	0	-0.0003	0	-0.0003	0	-0.0003	0	-0.0003	0	-0.0003	0
DMN-mPFC→R-AMY	0.0003	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→DMN-mPFC	0.3005	1	0.0005	0	0.0005	0	0.0005	0	0.0005	0	0.0005	0
DMN-PCC→DMN-PCC	-0.0002	0	-0.0002	0	-0.0002	0	-0.0001	0	-0.0001	0	-0.0001	0
DMN-PCC→L-DMN-LP	0.0960	1	-0.0164	0.5203	-0.0165	0.5203	-0.0164	0.5221	-0.0156	0.5207	-0.0164	0.5220
DMN-PCC→R-DMN-LP	0.0998	1	-0.0156	0	-0.0158	0	-0.0156	0	-0.0149	0	-0.0156	0
DMN-PCC→SAN-ACC	0.1349	1	-0.0004	0	-0.0004	0	-0.0004	0	-0.0004	0	-0.0004	0
DMN-PCC→L-SAN-INS	-0.0001	0	-0.0018	0	-0.0018	0	-0.0018	0	-0.0017	0	-0.0018	0
DMN-PCC→R-SAN-INS	-0.0001	0	-0.0017	0	-0.0017	0	-0.0017	0	-0.0016	0	-0.0017	0
DMN-PCC→L-AMY	-0.0001	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0
DMN-PCC→R-AMY	0	0	0.0011	0	0.0011	0	0.0011	0	0.0010	0	0.0011	0
L-DMN-LP→DMN-mPFC	-0.1126	1	0	0	0	0	0	0	0	0	0	0
L-DMN-LP→DMN-PCC	0.0224	0	0.0024	0	0.0024	0	0.0023	0	0.0024	0	0.0025	0
L-DMN-LP→L-DMN-LP	0.2572	1	0.0001	0	0	0	0.0001	0	0.0001	0	0.0001	0
L-DMN-LP→R-DMN-LP	0.2737	1	-0.0003	0	-0.0001	0	-0.0002	0	-0.0002	0	-0.0002	0
L-DMN-LP→SAN-ACC	-0.1524	1	-0.0047	0	-0.0057	0	-0.0061	0	-0.0062	0	-0.0049	0
L-DMN-LP→L-SAN-INS	-0.1020	1	0.0047	0	0.0027	0	0.0035	0	0.0036	0	0.0034	0
L-DMN-LP→R-SAN-INS	0.0058	0	0	0	0	0	0	0	0	0	0	0
L-DMN-LP→L-AMY	-0.0223	0.5299	-0.0088	0	-0.0082	0	-0.0089	0	-0.0085	0	-0.0085	0
L-DMN-LP→R-AMY	-0.0001	0	0	0	0	0	0	0	0	0	0	0
R-DMN-LP→DMN-mPFC	-0.0765	1	0	0	0	0	0	0	0	0	0	0
R-DMN-LP→DMN-PCC	0.0666	1	-0.0024	0	-0.0024	0	-0.0024	0	-0.0024	0	-0.0025	0
R-DMN-LP→L-DMN-LP	0.2588	1	-0.0001	0	0	0	-0.0001	0	-0.0001	0	-0.0001	0
R-DMN-LP→R-DMN-LP	0.2695	1	0.0003	0	0.0002	0	0.0002	0	0.0002	0	0.0002	0

R-DMN-LP→SAN-ACC	-0.2052	1	0.0048	0	0.0058	0	0.0062	0	0.0063	0	0.0050	0
R-DMN-LP→L-SAN-INS	-0.1234	1	-0.0047	0	-0.0027	0	-0.0036	0	-0.0036	0	-0.0035	0
R-DMN-LP→R-SAN-INS	-0.0340	0.5135	0	0	0	0	0	0	0	0	0	0
R-DMN-LP→L-AMY	-0.0113	0	0.0089	0	0.0084	0	0.0090	0	0.0086	0	0.0087	0
R-DMN-LP→R-AMY	0.0002	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→DMN-mPFC	0.1467	1	0	0	0	0	0	0	0	0	0	0
SAN-ACC→DMN-PCC	0.1764	1	-0.0001	0	-0.0001	0	-0.0001	0	-0.0001	0	-0.0001	0
SAN-ACC→L-DMN-LP	0.0405	0	-0.0012	0	-0.0015	0	-0.0012	0	-0.0013	0	-0.0012	0
SAN-ACC→R-DMN-LP	0.0519	1	0.0012	0	0.0015	0	0.0012	0	0.0013	0	0.0012	0
SAN-ACC→SAN-ACC	-0.0013	0	-0.0814	1	-0.1007	1	-0.0813	1	-0.0842	1	-0.0801	1
SAN-ACC→L-SAN-INS	-0.0047	0	0	0	0.0001	0	0	0	0	0	0	0
SAN-ACC→R-SAN-INS	-0.0047	0	0.0001	0	0.0002	0	0.0001	0	0.0001	0	0.0001	0
SAN-ACC→L-AMY	-0.0003	0	0.0003	0	0.0003	0	0.0003	0	0.0003	0	0.0003	0
SAN-ACC→R-AMY	0.0028	0	-0.0001	0	-0.0001	0	-0.0001	0	-0.0001	0	-0.0001	0
L-SAN-INS→DMN-mPFC	0.1024	1	0.0002	0	0.0002	0	0.0002	0	0.0002	0	0.0002	0
L-SAN-INS→DMN-PCC	-0.0025	0	0.1461	1	0.1544	1	0.1466	1	0.1475	1	0.1467	1
L-SAN-INS→L-DMN-LP	0.0255	0.5343	0.0063	0	0.0053	0	0.0063	0	0.0063	0	0.0062	0
L-SAN-INS→R-DMN-LP	0.0073	0	-0.0064	0	-0.0053	0	-0.0064	0	-0.0064	0	-0.0063	0
L-SAN-INS→SAN-ACC	0.2275	1	-0.0387	0.5393	-0.0734	0.5393	-0.0394	0.5420	-0.0418	0.5435	-0.0386	0.5427
L-SAN-INS→L-SAN-INS	-0.1242	1	0.1094	1	0.1001	1	0.1090	1	0.1108	1	0.1083	1
L-SAN-INS→R-SAN-INS	0.2304	1	-0.0007	0	-0.0006	0	-0.0007	0	-0.0007	0	-0.0007	0
L-SAN-INS→L-AMY	0.1049	1	-0.0920	1	-0.0761	1	-0.0919	1	-0.0900	1	-0.0893	1
L-SAN-INS→R-AMY	-0.0005	0	0.0004	0	0.0004	0	0.0004	0	0.0004	0	0.0004	0
R-SAN-INS→DMN-mPFC	-0.4628	1	0	0	0	0	0	0	0	0	0	0
R-SAN-INS→DMN-PCC	-0.3963	1	-0.1086	1	-0.1175	1	-0.1100	1	-0.1095	1	-0.1077	1
R-SAN-INS→L-DMN-LP	-0.0289	0	-0.0005	0	-0.0005	0	-0.0005	0	-0.0005	0	-0.0005	0
R-SAN-INS→R-DMN-LP	-0.0826	1	0.0005	0	0.0005	0	0.0005	0	0.0005	0	0.0005	0
R-SAN-INS→SAN-ACC	0.1326	1	0.0005	0	0.0007	0	0.0007	0	0.0007	0	0.0006	0
R-SAN-INS→L-SAN-INS	0.2562	1	-0.0005	0	-0.0002	0	-0.0003	0	-0.0003	0	-0.0003	0
R-SAN-INS→R-SAN-INS	0.1661	1	0.0001	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0
R-SAN-INS→L-AMY	-0.0986	1	0.0010	0	0.0009	0	0.0010	0	0.0009	0	0.0010	0
R-SAN-INS→R-AMY	-0.0020	0	0	0	0	0	0	0	0	0	0	0
L-AMY→DMN-mPFC	0.0006	0	0	0	0	0	0	0	0	0	0	0
L-AMY→DMN-PCC	-0.0449	0.5602	0	0	0	0	0	0	0	0	0	0
L-AMY→L-DMN-LP	-0.0507	1	0	0	0.0011	0	0	0	0	0	0	0
L-AMY→R-DMN-LP	-0.0197	0	0	0	-0.0012	0	0	0	0	0	0	0
L-AMY→SAN-ACC	-0.1541	1	0	0	0.0771	0	0	0	0	0	0	0
L-AMY→L-SAN-INS	-0.1215	1	0	0	-0.0001	0	0	0	0	0	0	0
L-AMY→R-SAN-INS	-0.0987	1	0	0	-0.0001	0	0	0	0	0	0	0
L-AMY→L-AMY	0.0001	0	0	0	0	0	0	0	0	0	0	0

L-AMY→R-AMY	0.0959	1	0	0	0.0001	0	0	0	0	0	0	0
R-AMY→DMN-mPFC	-0.0005	0	0.0001	0	0.0002	0	0.0002	0	0.0002	0	0.0002	0
R-AMY→DMN-PCC	0.0017	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0	0.0001	0
R-AMY→L-DMN-LP	-0.0136	0	0.0031	0	0.0049	0	0.0056	0	0.0056	0	0.0051	0
R-AMY→R-DMN-LP	0.0139	0	-0.0031	0	-0.0050	0	-0.0057	0	-0.0057	0	-0.0052	0
R-AMY→SAN-ACC	-0.2161	1	0.0380	0.5493	-0.0005	0.5493	0.0792	1	0.0753	1	0.0441	0.5514
R-AMY→L-SAN-INS	-0.1716	1	0.0456	0.5571	0.0887	0.5571	0.0792	1	0.0798	1	0.0803	1
R-AMY→R-SAN-INS	0.0019	0	-0.0003	0	-0.0006	0	-0.0006	0	-0.0006	0	-0.0006	0
R-AMY→L-AMY	0.2162	1	0.1053	1	0.1154	1	0.1086	1	0.0996	1	0.1025	1
R-AMY→R-AMY	-0.0010	0	0.0002	0	0.0003	0	0.0004	0	0.0004	0	0.0004	0

Table S6. The results of the linear regression analyses testing the linear relationships between EC and each of the three negative affect z-scores for CU and Control participants combined for Dataset 1 (without or with group as a covariate). EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Linear relationship between EC and anxiety z-score (n=56)		Linear relationship between EC and depression z-score (n=56)		Linear relationship between EC and composite anxiety/depression z-score (n=56)		Linear relationship between EC and anxiety z-score with group as a covariate (n=56)		Linear relationship between EC and depression z-score with group as a covariate (n=56)		Linear relationship between EC and composite anxiety/depression z-score with group as a covariate (n=56)	
Connectivity	beta	PP	beta	beta	PP	beta	beta	PP	beta	PP	beta	PP
DMN-mPFC→DMN-mPFC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→L-DMN-LP	0	0	-0.0001	0	0	0	0	0	-0.0002	0	0	0
DMN-mPFC→R-DMN-LP	0	0	-0.0003	0	-0.0001	0	0	0	-0.0003	0	-0.0001	0
DMN-mPFC→SAN-ACC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→L-SAN-INS	0	0	0	0	0	0	0	0	0	0	0	0
DMN-mPFC→R-SAN-INS	-0.0010	0	0.0011	0	0.0012	0	-0.0010	0	0.0011	0	0.0012	0
DMN-mPFC→L-AMY	0.0001	0	-0.0001	0	0	0	0	0	-0.0001	0	0	0
DMN-mPFC→R-AMY	-0.0005	0	-0.0004	0	-0.0006	0	-0.0005	0	-0.0004	0	-0.0006	0
DMN-PCC→DMN-mPFC	0	0	-0.0002	0	-0.0002	0	0	0	-0.0002	0	-0.0002	0
DMN-PCC→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→L-DMN-LP	0	0	-0.0051	0	-0.0051	0	0	0	-0.0052	0	-0.0050	0
DMN-PCC→R-DMN-LP	0	0	0.0053	0	0.0052	0	0	0	0.0054	0	0.0051	0
DMN-PCC→SAN-ACC	0	0	0.0002	0	0.0002	0	0	0	0.0002	0	0.0002	0
DMN-PCC→L-SAN-INS	0	0	-0.0904	1	-0.0896	1	0	0	-0.0926	1	-0.0876	1
DMN-PCC→R-SAN-INS	0.0003	0	0.0003	0	0.0002	0	0.0003	0	0.0003	0	0.0002	0
DMN-PCC→L-AMY	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→R-AMY	0.0001	0	-0.0002	0	-0.0002	0	0.0001	0	-0.0003	0	-0.0002	0
L-DMN-LP→DMN-mPFC	0	0	0.0001	0	0	0	0	0	0.0001	0	0	0
L-DMN-LP→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
L-DMN-LP→L-DMN-LP	-0.0010	0	0.0007	0	-0.0036	0	-0.0014	0	0.0014	0	-0.0027	0
L-DMN-LP→R-DMN-LP	0.0015	0	0.0041	0.52158	-0.0004	0	0.0012	0	0.0048	0.52287	0.0005	0
L-DMN-LP→SAN-ACC	0	0	-0.0001	0	0	0	0	0	-0.0001	0	0	0
L-DMN-LP→L-SAN-INS	0	0	-0.0008	0	-0.0002	0	-0.0001	0	-0.0009	0	-0.0003	0
L-DMN-LP→R-SAN-INS	-0.0314	0	-0.0378	1	-0.0394	1	-0.0330	0	-0.0386	1	-0.0394	1
L-DMN-LP→L-AMY	0.0022	0	-0.0030	0	-0.0013	0	0	0	-0.0027	0	0	0
L-DMN-LP→R-AMY	-0.0152	0	-0.0135	0	-0.0180	0	-0.0145	0	-0.0125	0	-0.0185	0
R-DMN-LP→DMN-mPFC	-0.0001	0	0.0001	0	-0.0001	0	-0.0001	0	0.0001	0	-0.0001	0
R-DMN-LP→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
R-DMN-LP→L-DMN-LP	-0.0014	0	0.0052	0	0.0006	0	-0.0012	0	0.0058	0	-0.0002	0

R-DMN-LP→R-DMN-LP	0.0010	0	0.0081	0	0.0034	0	0.0014	0	0.0089	0	0.0025	0
R-DMN-LP→SAN-ACC	0.0001	0	-0.0001	0	0.0001	0	0.0001	0	-0.0001	0	0.0001	0
R-DMN-LP→L-SAN-INS	0.0003	0	0.0001	0	0.0006	0	0.0004	0	0.0001	0	0.0007	0
R-DMN-LP→R-SAN-INS	-0.0315	1	-0.0359	0	-0.0373	0	-0.0330	1	-0.0366	0	-0.0372	0
R-DMN-LP→L-AMY	-0.0022	0	0.0030	0	0.0013	0	0	0	0.0027	0	0	0
R-DMN-LP→R-AMY	-0.0157	0.52793	-0.0139	0.50817	-0.0185	0.53951	-0.0151	0.53032	-0.0129	0.50861	-0.0191	0.54104
SAN-ACC→DMN-mPFC	0	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→L-DMN-LP	0	0	0.0001	0	0	0	0	0	0.0001	0	0	0
SAN-ACC→R-DMN-LP	0	0	0.0003	0	0.0001	0	0	0	0.0003	0	0.0001	0
SAN-ACC→SAN-ACC	0	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→L-SAN-INS	0	0	0	0	0	0	0	0	0	0	0	0
SAN-ACC→R-SAN-INS	0.0010	0	-0.0011	0	-0.0011	0	0.0010	0	-0.0011	0	-0.0011	0
SAN-ACC→L-AMY	-0.0001	0	0.0001	0	0	0	0	0	0.0001	0	0	0
SAN-ACC→R-AMY	0.0005	0	0.0004	0	0.0005	0	0.0004	0	0.0004	0	0.0006	0
L-SAN-INS→DMN-mPFC	0	0	0	0	0	0	0	0	0	0	0	0
L-SAN-INS→DMN-PCC	0	0	0	0	0	0	0	0	0	0	0	0
L-SAN-INS→L-DMN-LP	0.0001	0	0.0005	0	-0.0001	0	0.0002	0	0.0006	0	-0.0002	0
L-SAN-INS→R-DMN-LP	-0.0001	0	0.0010	0	0.0005	0	-0.0001	0	0.0011	0	0.0004	0
L-SAN-INS→SAN-ACC	0	0	0	0	0	0	0	0	0	0	0	0
L-SAN-INS→L-SAN-INS	0	0	0	0	0.0001	0	0	0	0	0	0.0001	0
L-SAN-INS→R-SAN-INS	0.0037	0	-0.0041	0	-0.0042	0	0.0038	0	-0.0042	0	-0.0042	0
L-SAN-INS→L-AMY	0.0388	0.512	0.0003	0	0.0002	0	0	0	0.0003	0	0	0
L-SAN-INS→R-AMY	0.0018	0	0.0016	0	0.0021	0	0.0017	0	0.0015	0	0.0021	0
R-SAN-INS→DMN-mPFC	0.0010	0	0.0005	0	0.0007	0	0.0011	0	0.0005	0	0.0011	0
R-SAN-INS→DMN-PCC	-0.0003	0	-0.0001	0	-0.0002	0	-0.0003	0	-0.0001	0	-0.0003	0
R-SAN-INS→L-DMN-LP	0.0324	0	0.0163	0	0.0214	0	0.0339	0	0.0159	0	0.0362	0
R-SAN-INS→R-DMN-LP	0.0327	1	0.0171	0.53086	0.0224	0.56556	0.0341	1	0.0167	0.53383	0.0374	1
R-SAN-INS→SAN-ACC	-0.0010	0	-0.0005	0	-0.0006	0	-0.0010	0	-0.0005	0	-0.0011	0
R-SAN-INS→L-SAN-INS	-0.0038	0	-0.0018	0	-0.0024	0	-0.0039	0	-0.0018	0	-0.0041	0
R-SAN-INS→R-SAN-INS	-0.0001	0	-0.0057	0	-0.0065	0	-0.0001	0	-0.0057	0	-0.0081	0
R-SAN-INS→L-AMY	-0.0002	0	0.0004	0	0.0002	0	0.0001	0	0.0003	0	0.0001	0
R-SAN-INS→R-AMY	0.0039	0	0.0026	0	0.0035	0	0.0040	0	0.0025	0	0.0046	0
L-AMY→DMN-mPFC	0.0003	0	0.0011	0	0.0009	0	0.0003	0	0.0011	0	0.0010	0
L-AMY→DMN-PCC	-0.0001	0	-0.0003	0	-0.0003	0	-0.0001	0	-0.0003	0	-0.0003	0
L-AMY→L-DMN-LP	-0.0237	0.53252	-0.0359	1	-0.0446	1	-0.0232	0.53653	-0.0372	1	-0.0470	1
L-AMY→R-DMN-LP	-0.0095	0	-0.0343	0	-0.0306	0	-0.0090	0	-0.0355	0	-0.0329	0
L-AMY→SAN-ACC	-0.0003	0	-0.0010	0	-0.0009	0	-0.0003	0	-0.0011	0	-0.0010	0
L-AMY→L-SAN-INS	-0.1199	1	-0.0039	0	-0.1117	1	-0.1197	1	-0.0041	0	-0.1121	1
L-AMY→R-SAN-INS	-0.0011	0	-0.0037	0	-0.0033	0	-0.0010	0	-0.0038	0	-0.0035	0

L-AMY→L-AMY	0	0	0.0001	0	0	0	0	0	0.0001	0	0.0001	0
L-AMY→R-AMY	0.0006	0	0.0023	0	0.0021	0	0.0006	0	0.0024	0	0.0022	0
R-AMY→DMN-mPFC	-0.0001	0	0	0	0	0	-0.0007	0	0	0	0	0
R-AMY→DMN-PCC	0	0	0	0	0	0	0.0002	0	0	0	0	0
R-AMY→L-DMN-LP	0.0462	0.59465	0.0932	1	0.0958	1	0.0591	1	0.0933	1	0.0949	1
R-AMY→R-DMN-LP	0.0456	0.57035	0.0915	1	0.0940	1	0.0576	0.51547	0.0916	1	0.0930	1
R-AMY→SAN-ACC	0.0001	0	0	0	0	0	0.0007	0	0	0	0	0
R-AMY→L-SAN-INS	0.0003	0	0.0001	0	0	0	0.0026	0	0	0	0	0
R-AMY→R-SAN-INS	-0.0019	0	0.0025	0	0.0026	0	0.0002	0	0.0025	0	0.0025	0
R-AMY→L-AMY	0.0001	0	0.0887	1	0.0384	0.5029	0	0	0.0801	1	0	0
R-AMY→R-AMY	-0.0012	0	-0.0010	0	-0.0013	0	-0.0026	0	-0.0009	0	-0.0013	0

Table S7. The results of the group comparison (CU minus Control) in Dataset 2 (without a covariate, with alcohol and tobacco usages as covariates, and with anxiety/depression as a covariate). EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Average across both groups (n=42)		Group comparison (CU [n=21] minus Control [n=21]) without a covariate		Group comparison (CU [n=21] minus Control [n=21]) with alcohol and tobacco usages as covariates		Group comparison (CU [n=21] minus Control [n=21]) with anxiety z-score as a covariate		Group comparison (CU [n=21] minus Control [n=21]) with depression z-score as a covariate		Group comparison (CU [n=21] minus Control [n=21]) with composite anxiety/depression z-score as a covariate	
Connectivity	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP	EC (Hz)	PP
DMN-mPFC→DMN-mPFC	0.1760	1	-0.0030	0	0.0002	0	0.0001	0	0.0002	0	0.0003	0
DMN-mPFC→DMN-PCC	0.2403	1	0.0004	0	0.0010	0	0	0	0	0	0.0016	0
DMN-mPFC→L-DMN-LP	0.0005	0	-0.0040	0	-0.0047	0	0.0001	0	0	0	-0.0842	1
DMN-mPFC→R-DMN-LP	-0.0006	0	0.0034	0	0.0041	0	0	0	0.0001	0	-0.0001	0
DMN-mPFC→SAN-ACC	0.2007	1	0.0057	0	0.0076	0	0.0048	0	0.0045	0	0	0
DMN-mPFC→L-SAN-INS	-0.0027	0	0.0574	0.5293	0.0488	0	-0.0010	0	0.0836	1	0.0738	1
DMN-mPFC→R-SAN-INS	0.0035	0	0.0540	1	0.0466	1	-0.0003	0	0.0755	1	0.0819	1
DMN-mPFC→L-AMY	0.0007	0	0.0012	0	0.0008	0	0	0	0.0012	0	0.0010	0
DMN-mPFC→R-AMY	0	0	0.0014	0	0.0050	0	0.0005	0	0	0	-0.0001	0
DMN-PCC→DMN-mPFC	0	0	0	0	-0.0036	0	0	0	-0.0001	0	0	0
DMN-PCC→DMN-PCC	0	0	0	0	-0.0391	1	0	0	0	0	-0.0002	0
DMN-PCC→L-DMN-LP	0	0	0	0	-0.0040	0	0	0	0	0	-0.0002	0
DMN-PCC→R-DMN-LP	0	0	0	0	0.0033	0	0	0	0	0	0	0
DMN-PCC→SAN-ACC	0	0	-0.0003	0	0.0024	0	-0.0006	0	-0.0006	0	0	0
DMN-PCC→L-SAN-INS	0	0	0.0001	0	-0.0208	1	0.0001	0	0.0001	0	0.0001	0
DMN-PCC→R-SAN-INS	0	0	0.0001	0	-0.0172	0	0	0	0	0	0.0001	0
DMN-PCC→L-AMY	-0.0001	0	-0.0002	0	-0.0004	0	0	0	-0.0002	0	-0.0001	0
DMN-PCC→R-AMY	0	0	0	0	0.0009	0	-0.0001	0	0	0	0	0
L-DMN-LP→DMN-mPFC	-0.0415	0.5428	0.0004	0	0.0115	0	0.0001	0	0.0006	0	0.0004	0
L-DMN-LP→DMN-PCC	0.0378	0.5045	0	0	-0.0002	0	0	0	0	0	0.0021	0
L-DMN-LP→L-DMN-LP	0.1850	1	0.0004	0	-0.0749	1	0.0001	0	0.0005	0	0.0015	0
L-DMN-LP→R-DMN-LP	-0.0030	0	-0.0002	0	-0.0069	0	0	0	-0.0003	0	-0.0001	0
L-DMN-LP→SAN-ACC	-0.0026	0	0.0032	0	-0.0010	0	0.0062	0	0.0055	0	0.0001	0
L-DMN-LP→L-SAN-INS	0.1029	1	-0.0012	0	-0.0063	0	-0.0013	0	-0.0006	0	-0.0011	0
L-DMN-LP→R-SAN-INS	0.0611	0.5236	-0.0008	0	0.0060	0	-0.0003	0	-0.0001	0	-0.0013	0
L-DMN-LP→L-AMY	0.0011	0	0.0018	0	-0.0328	1	0	0	0.0016	0	0.0014	0
L-DMN-LP→R-AMY	-0.0010	0	-0.0001	0	0.0015	0	0.0006	0	-0.0001	0	-0.0001	0
R-DMN-LP→DMN-mPFC	-0.0972	1	-0.0003	0	0.0454	1	-0.0001	0	-0.0005	0	-0.0003	0
R-DMN-LP→DMN-PCC	-0.1148	1	0	0	0.0002	0	0	0	0	0	-0.0017	0
R-DMN-LP→L-DMN-LP	0.0046	0	-0.0003	0	-0.0070	0	-0.0001	0	-0.0004	0	-0.0013	0
R-DMN-LP→R-DMN-LP	0.2029	1	0.0002	0	-0.0324	1	0	0	0.0003	0	0.0001	0

R-DMN-LP→SAN-ACC	-0.0033	0	-0.0026	0	0.0008	0	-0.0052	0	-0.0046	0	-0.0001	0
R-DMN-LP→L-SAN-INS	-0.0217	0	0.0010	0	0.0047	0	0.0011	0	0.0005	0	0.0009	0
R-DMN-LP→R-SAN-INS	0.0237	0	0.0007	0	-0.0043	0	0.0003	0	0	0	0.0011	0
R-DMN-LP→L-AMY	-0.0005	0	-0.0015	0	-0.0016	0	0	0	-0.0013	0	-0.0011	0
R-DMN-LP→R-AMY	-0.0017	0	0.0001	0	0.0271	1	-0.0005	0	0.0001	0	0.0001	0
SAN-ACC→DMN-mPFC	0.1753	1	-0.0003	0	-0.0389	1	-0.0030	0	-0.0004	0	-0.0005	0
SAN-ACC→DMN-PCC	-0.1143	1	0	0	0	0	0.0004	0	0	0	-0.0015	0
SAN-ACC→L-DMN-LP	-0.1362	1	-0.0003	0	-0.0049	0	-0.0040	0	-0.0002	0	-0.0014	0
SAN-ACC→R-DMN-LP	-0.1281	1	0.0002	0	0.0038	0	0.0032	0	0.0001	0	0.0003	0
SAN-ACC→SAN-ACC	0.2206	1	-0.0024	0	-0.0004	0	-0.0018	0	-0.0042	0	0.0001	0
SAN-ACC→L-SAN-INS	0.1586	1	-0.0855	1	-0.0027	0	-0.0657	1	-0.0874	1	-0.0862	1
SAN-ACC→R-SAN-INS	0.1531	1	-0.0779	1	0.0039	0	-0.0573	0.5	-0.0799	1	-0.0780	1
SAN-ACC→L-AMY	-0.0007	0	0.1033	1	0.0600	1	-0.0002	0	0.1033	1	0.1075	1
SAN-ACC→R-AMY	-0.0002	0	0.0001	0	-0.0017	0	0.0009	0	0.0001	0	0.0001	0
L-SAN-INS→DMN-mPFC	-0.4846	1	-0.0394	0.5301	-0.0501	0	0.0002	0	-0.0912	1	-0.0924	1
L-SAN-INS→DMN-PCC	-0.4352	1	0	0	0.0004	0	-0.0001	0	0	0	-0.0100	0
L-SAN-INS→L-DMN-LP	-0.4209	1	-0.0006	0	0.0293	1	0.0004	0	-0.0002	0	-0.0054	0
L-SAN-INS→R-DMN-LP	-0.3854	1	0.0002	0	0.0276	0	-0.0007	0	-0.0002	0	-0.0008	0
L-SAN-INS→SAN-ACC	0.0959	1	0.0223	0.5431	0.0002	0	0.0405	1	0.0381	1	0.0355	0.5
L-SAN-INS→L-SAN-INS	0.3510	1	0.0005	0	-0.0001	0	0.0017	0	-0.0074	0	-0.0036	0
L-SAN-INS→R-SAN-INS	0.4161	1	0.0095	0	0.0054	0	0.0068	0	0.0119	0	0.0158	0
L-SAN-INS→L-AMY	-0.0043	0	-0.0088	0	-0.0089	0	0.0003	0	-0.0074	0	-0.0064	0
L-SAN-INS→R-AMY	-0.0011	0	0.0001	0	-0.0096	0	-0.0033	0	-0.0001	0	-0.0003	0
R-SAN-INS→DMN-mPFC	-0.4510	1	-0.0342	0.5575	-0.0412	1	0.0006	0	-0.0811	1	-0.0821	1
R-SAN-INS→DMN-PCC	-0.4744	1	0	0	-0.0005	0	0	0	0	0	-0.0101	0.5
R-SAN-INS→L-DMN-LP	-0.4445	1	0.0008	0	0.0394	0	0.0007	0	0.0006	0	0.0077	0
R-SAN-INS→R-DMN-LP	-0.3386	1	-0.0002	0	0.0208	1	-0.0002	0	0	0	-0.0006	0
R-SAN-INS→SAN-ACC	0.0920	1	0.0177	0	-0.0008	0	0.0332	0	0.0310	0	0.0318	0.5
R-SAN-INS→L-SAN-INS	0.3257	1	-0.0193	0.5228	-0.0036	0	-0.0071	0	-0.0306	1	-0.0254	0.5
R-SAN-INS→R-SAN-INS	0.3843	1	-0.0102	0	-0.0020	0	-0.0018	0	-0.0116	0	-0.0083	0
R-SAN-INS→L-AMY	0.0048	0	0.0098	0	0.0100	0	-0.0002	0	0.0082	0	0.0072	0
R-SAN-INS→R-AMY	0.0012	0	-0.0001	0	-0.0051	0.5154	0.0033	0	0	0	-0.0002	0
L-AMY→DMN-mPFC	-0.3037	1	-0.0840	1	0.0005	0	-0.0838	1	-0.0832	1	-0.0871	1
L-AMY→DMN-PCC	-0.3837	1	-0.0003	0	0	0	-0.0003	0	-0.0003	0	-0.0002	0
L-AMY→L-DMN-LP	-0.3724	1	-0.0884	1	-0.0137	0.4930	-0.0863	1	-0.0875	1	-0.1027	1
L-AMY→R-DMN-LP	-0.4061	1	-0.0023	0	-0.0003	0	-0.0024	0	-0.0023	0	-0.0026	0
L-AMY→SAN-ACC	-0.1947	1	-0.0019	0	0.0001	0	-0.0018	0	-0.0017	0	-0.0023	0
L-AMY→L-SAN-INS	0.1017	1	-0.0132	0	0.0004	0	-0.0136	0	-0.0130	0	-0.0148	0
L-AMY→R-SAN-INS	0.1303	1	0.0146	0	-0.0005	0	0.0150	0	0.0144	0	0.0163	0
L-AMY→L-AMY	-0.1610	1	0.1539	1	0.0001	0	0.0407	0.5	0.1583	1	0.1383	1

L-AMY→R-AMY	0.3327	1	-0.0009	0	-0.0511	1	-0.0009	0	-0.0009	0	-0.0011	0
R-AMY→DMN-mPFC	-0.1667	1	-0.0002	0	0.0665	1	0.0004	0	-0.0003	0	-0.0001	0
R-AMY→DMN-PCC	-0.1990	1	0	0	-0.0004	0	-0.0001	0	0	0	-0.0007	0
R-AMY→L-DMN-LP	-0.2724	1	-0.0002	0	0.0017	0	0.0006	0	-0.0002	0	-0.0005	0
R-AMY→R-DMN-LP	-0.1802	1	0.0002	0	-0.0015	0	-0.0005	0	0.0002	0	0	0
R-AMY→SAN-ACC	0	0	-0.0010	0	-0.0031	0	-0.0026	0	-0.0019	0	0	0
R-AMY→L-SAN-INS	0.0740	1	0.0008	0	0.0381	1	-0.0025	0	0.0004	0	0.0004	0
R-AMY→R-SAN-INS	0.1160	1	-0.0002	0	0.0228	0	0.0035	0	-0.0002	0	0.0004	0
R-AMY→L-AMY	0.1230	1	0.0871	1	0.0577	1	0	0	0.0427	1	-0.0005	0
R-AMY→R-AMY	0.0897	1	0.0001	0	-0.0021	0	0.0988	1	0.0001	0	0	0

Table S8. The results of the linear regression analyses testing the linear relationships between EC and each of the three negative affect z-scores for CU and Control participants combined for Dataset 2 (without or with group as a covariate). EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Linear relationship between EC and anxiety z-score (n=42)		Linear relationship between EC and depression z-score (n=42)		Linear relationship between EC and composite anxiety/depression z-score (n=42)		Linear relationship between EC and anxiety z-score with group as a covariate (n=42)		Linear relationship between EC and depression z-score with group as a covariate (n=42)		Linear relationship between EC and composite anxiety/depression z-score with group as a covariate (n=42)	
Connectivity	beta	PP	beta	PP	beta	PP	beta	PP	beta	PP	beta	PP
DMN-mPFC→DMN-mPFC	0.0021	0	0	0	0.0004	0	0.0051	0	0.0001	0	0.0022	0
DMN-mPFC→DMN-PCC	0.1521	1	0.0063	0	0.1072	1	0.1509	1	0.0063	0	0.1048	1
DMN-mPFC→L-DMN-LP	0.0029	0	0	0	0.0003	0	0.0068	0	0	0	0.0025	0
DMN-mPFC→R-DMN-LP	0.0006	0	-0.0017	0	0.0029	0	-0.0028	0	-0.0020	0	0.0034	0
DMN-mPFC→SAN-ACC	-0.0398	0.50799	0	0	-0.0002	0	-0.0454	0.50985	0	0	-0.0019	0
DMN-mPFC→L-SAN-INS	-0.0133	0	-0.0001	0	-0.0012	0	-0.0303	0	0.0001	0	-0.0119	0
DMN-mPFC→R-SAN-INS	-0.0154	0.52325	-0.0002	0	0.0013	0	-0.0332	1	-0.0001	0	-0.0092	0.4958
DMN-mPFC→L-AMY	-0.0014	0	0.0013	0	0.0012	0	-0.0012	0	0.0012	0	0.0009	0
DMN-mPFC→R-AMY	-0.0009	0	0.0006	0	0.0004	0	-0.0022	0	0.0011	0	-0.0004	0
DMN-PCC→DMN-mPFC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→DMN-PCC	0	0	-0.0008	0	0	0	0	0	-0.0008	0	0	0
DMN-PCC→L-DMN-LP	0	0	0	0	0	0	-0.0001	0	0	0	0	0
DMN-PCC→R-DMN-LP	-0.0004	0	0.0002	0	-0.0004	0	-0.0003	0	0.0003	0	-0.0007	0
DMN-PCC→SAN-ACC	0	0	0	0	0	0	0	0	0	0	0	0
DMN-PCC→L-SAN-INS	0.0001	0	0	0	0	0	0.0001	0	0	0	0	0
DMN-PCC→R-SAN-INS	0.0001	0	0	0	0	0	0.0001	0	0	0	-0.0001	0
DMN-PCC→L-AMY	0.0002	0	-0.0002	0	-0.0002	0	0.0002	0	-0.0002	0	-0.0001	0
DMN-PCC→R-AMY	0	0	-0.0001	0	-0.0001	0	0	0	-0.0001	0	-0.0001	0
L-DMN-LP→DMN-mPFC	0.0002	0	0	0	0.0003	0	0.0004	0	0.0001	0	0.0004	0
L-DMN-LP→DMN-PCC	0.0002	0	0.0082	0	0.0003	0	0.0002	0	0.0082	0	0.0001	0
L-DMN-LP→L-DMN-LP	0.0004	0	0	0	0.0001	0	0.0008	0	0	0	0.0001	0
L-DMN-LP→R-DMN-LP	0.0036	0	-0.0022	0	0.0040	0	0.0031	0	-0.0027	0	0.0071	0
L-DMN-LP→SAN-ACC	0.0004	0	0	0	0	0	0.0005	0	0	0	-0.0001	0
L-DMN-LP→L-SAN-INS	-0.0011	0	-0.0001	0	-0.0003	0	-0.0010	0	0.0001	0	-0.0004	0
L-DMN-LP→R-SAN-INS	-0.0005	0	-0.0002	0	0.0003	0	-0.0005	0	-0.0001	0	0.0007	0
L-DMN-LP→L-AMY	-0.0020	0	0.0018	0	0.0015	0	-0.0021	0	0.0016	0	0.0010	0
L-DMN-LP→R-AMY	0	0	0.0008	0	0.0006	0	0	0	0.0014	0	0.0006	0
R-DMN-LP→DMN-mPFC	0.1119	1	0.0002	0	0.1059	1	0.1156	1	0.0004	0	0.1064	1
R-DMN-LP→DMN-PCC	0.0001	0	-0.0069	0	-0.0001	0	0.0001	0	-0.0069	0	0.0001	0
R-DMN-LP→L-DMN-LP	-0.0034	0	0.0003	0	-0.0013	0	-0.0037	0	0.0006	0	-0.0013	0

R-DMN-LP→R-DMN-LP	-0.0894	1	0.0016	0	-0.0023	0	-0.0874	1	0.0017	0	-0.0049	0
R-DMN-LP→SAN-ACC	0.0019	0	-0.0002	0	0.0010	0	0.0018	0	-0.0004	0	0.0010	0
R-DMN-LP→L-SAN-INS	0.0152	0	-0.0014	0	0.0061	0	0.0153	0	-0.0028	0	0.0063	0
R-DMN-LP→R-SAN-INS	-0.0155	0	0.0019	0	-0.0068	0	-0.0157	0	0.0032	0	-0.0073	0
R-DMN-LP→L-AMY	0.0015	0	-0.0015	0	-0.0013	0	0.0016	0	-0.0013	0	-0.0009	0
R-DMN-LP→R-AMY	0.0011	0	0.0491	0.56669	0.0450	0.50505	0.0011	0	0.0900	1	0.0423	0.50543
SAN-ACC→DMN-mPFC	-0.0003	0	0.0018	0	-0.0003	0	-0.0005	0	-0.0001	0	-0.0005	0
SAN-ACC→DMN-PCC	-0.0910	1	-0.0063	0	-0.0458	0.54313	-0.0933	1	-0.0061	0	-0.0940	1
SAN-ACC→L-DMN-LP	-0.0005	0	0.0023	0	-0.0002	0	-0.0007	0	0	0	-0.0002	0
SAN-ACC→R-DMN-LP	-0.0025	0	-0.0003	0	-0.0029	0	-0.0022	0	0.0020	0	-0.0051	0
SAN-ACC→SAN-ACC	-0.0002	0	-0.0017	0	0.0001	0	-0.0002	0	0	0	0.0002	0
SAN-ACC→L-SAN-INS	0.0017	0	-0.0111	0	0.0008	0	0.0016	0	0.0001	0	0.0011	0
SAN-ACC→R-SAN-INS	-0.0005	0	-0.0117	0.50234	-0.0009	0	-0.0005	0	-0.0002	0	-0.0015	0
SAN-ACC→L-AMY	0.0015	0	0.0524	0.57627	0.0400	0.50223	0.0015	0	0.0413	0.52365	-0.0007	0
SAN-ACC→R-AMY	0.0001	0	-0.0014	0	-0.0004	0	0.0001	0	-0.0010	0	-0.0004	0
L-SAN-INS→DMN-mPFC	0.1276	1	0.1107	1	0.1386	1	0.1389	1	0.1178	1	0.1562	1
L-SAN-INS→DMN-PCC	0.1563	1	0.0538	1	0.1373	1	0.1584	1	0.0542	1	0.1452	1
L-SAN-INS→L-DMN-LP	0.0799	1	-0.0015	0	-0.0013	0	0.0832	1	-0.0014	0	-0.0011	0
L-SAN-INS→R-DMN-LP	0.0670	1	0.0116	0	0.0278	0.55295	0.0626	1	0.0139	0	0.0479	1
L-SAN-INS→SAN-ACC	-0.0018	0	0.0011	0	0.0010	0	-0.0022	0	0.0011	0	0.0008	0
L-SAN-INS→L-SAN-INS	0.0075	0	0.0071	0	0.0063	0	0.0061	0	0.0068	0	0.0052	0
L-SAN-INS→R-SAN-INS	-0.0135	0.50413	-0.0064	0	-0.0071	0	-0.0178	0.50846	-0.0076	0	-0.0074	0
L-SAN-INS→L-AMY	0.0094	0	-0.0085	0	-0.0074	0	0.0099	0	-0.0078	0	-0.0047	0
L-SAN-INS→R-AMY	0.0004	0	-0.0032	0	-0.0026	0	0.0003	0	-0.0062	0	-0.0025	0
R-SAN-INS→DMN-mPFC	0.1315	1	0.0994	1	0.1407	1	0.1417	1	0.1055	1	0.1562	1
R-SAN-INS→DMN-PCC	0.1053	1	0.0436	0	0.1010	1	0.1070	1	0.0440	0	0.1018	1
R-SAN-INS→L-DMN-LP	0.0776	1	-0.0010	0	-0.0015	0	0.0797	1	-0.0012	0	-0.0016	0
R-SAN-INS→R-DMN-LP	0.0528	0.50088	0.0113	0.50215	0.0229	0	0.0500	0.50165	0.0138	0.50299	0.0395	0
R-SAN-INS→SAN-ACC	0.0043	0	0.0007	0	0.0011	0	0.0047	0	0.0009	0	0.0012	0
R-SAN-INS→L-SAN-INS	0.0066	0	0.0047	0	0.0070	0	0.0079	0	0.0057	0	0.0077	0
R-SAN-INS→R-SAN-INS	-0.0168	0	-0.0070	0	-0.0079	0	-0.0179	0	-0.0063	0	-0.0069	0
R-SAN-INS→L-AMY	0.0148	0.50569	0.0093	0	0.0080	0	0.0129	0.50348	0.0086	0	0.0051	0
R-SAN-INS→R-AMY	0.0007	0	0.0044	0	0.0040	0	0.0007	0	0.0079	0	0.0038	0
L-AMY→DMN-mPFC	-0.0019	0	0	0	0.0002	0	-0.0018	0	0	0	0.0002	0
L-AMY→DMN-PCC	0.0003	0	0.0005	0	0	0	0.0003	0	0.0005	0	0	0
L-AMY→L-DMN-LP	-0.0024	0	0	0	0.0003	0	-0.0024	0	0	0	0.0003	0
L-AMY→R-DMN-LP	0.0023	0	-0.0001	0	0	0	0.0022	0	-0.0001	0	0.0002	0
L-AMY→SAN-ACC	0.0019	0	0	0	-0.0002	0	0.0018	0	0	0	-0.0002	0
L-AMY→L-SAN-INS	0.0117	0	0	0	-0.0014	0	0.0114	0	0	0	-0.0013	0
L-AMY→R-SAN-INS	0.0119	0.50611	0	0	0.0016	0	0.0115	0.50232	0	0	0.0015	0

L-AMY→L-AMY	-0.0003	0	0.0001	0	0.0001	0	-0.0003	0	0.0001	0	0.0001	0
L-AMY→R-AMY	0.0008	0	0	0	0.0466	0.50327	0.0008	0	0.0001	0	0.0424	0.50755
R-AMY→DMN-mPFC	-0.0001	0	-0.0001	0	-0.0002	0	-0.0001	0	-0.0002	0	-0.0003	0
R-AMY→DMN-PCC	-0.0001	0	-0.0028	0	-0.0001	0	-0.0001	0	-0.0028	0	0	0
R-AMY→L-DMN-LP	0.1109	1	-0.0002	0	-0.0002	0	0.1077	1	-0.0002	0	-0.0002	0
R-AMY→R-DMN-LP	0.1232	1	0.0009	0	-0.0012	0	0.1258	1	0.0010	0	-0.0023	0
R-AMY→SAN-ACC	-0.0001	0	0.0001	0	0.0001	0	-0.0002	0	0.0001	0	0.0001	0
R-AMY→L-SAN-INS	-0.0733	1	0.0008	0	0.0009	0	-0.0720	1	0.0008	0	0.0009	0
R-AMY→R-SAN-INS	-0.0681	1	-0.0008	0	-0.0010	0	-0.0655	1	-0.0009	0	-0.0011	0
R-AMY→L-AMY	0.0830	1	0.1605	1	0.1506	1	0.0465	0.53191	0.1632	1	0.1534	1
R-AMY→R-AMY	0	0	-0.0002	0	-0.0002	0	0	0	-0.0004	0	-0.0001	0

Table S9. The results of the group level PEB DCM analyses for Dataset 2: linear regression between EC and cannabis use measures in the CU group. EC=effective connectivity, PP=posterior probability, L=left, and R=right.

	Linear relationship between EC and age of onset (n=21)		Linear relationship between EC and days per week (n=21)		Linear relationship between EC and gram per week (n=21)		Linear relationship between EC and abstinence days (n=21)	
Connectivity	beta	PP	*beta*	PP	*beta*	PP	*beta*	PP
DMN-mPFC→DMN-mPFC	-0.0002	0	0.0014	0	0.0012	0	-0.0020	0
DMN-mPFC→DMN-PCC	-0.0001	0	-0.0001	0	-0.0523	1	-0.0797	1
DMN-mPFC→L-DMN-LP	0.0001	0	0.0014	0	0.0014	0	0.0025	0
DMN-mPFC→R-DMN-LP	-0.0012	0	-0.0016	0	-0.0006	0	0.0003	0
DMN-mPFC→SAN-ACC	0.0005	0	-0.0014	0	-0.0011	0	0.0002	0
DMN-mPFC→L-SAN-INS	-0.0001	0	0.0124	0.5399	0.0308	1	0.0013	0
DMN-mPFC→R-SAN-INS	0.0008	0	0.0102	0	0.0259	0.5394	-0.0005	0
DMN-mPFC→L-AMY	-0.0845	1	-0.0003	0	0	0	0	0
DMN-mPFC→R-AMY	-0.0001	0	-0.0006	0	-0.0005	0	0	0
DMN-PCC→DMN-mPFC	0	0	0	0	0	0	0.0002	0
DMN-PCC→DMN-PCC	0	0	0	0	-0.0001	0	0	0
DMN-PCC→L-DMN-LP	0	0	0.0001	0	0	0	-0.0004	0
DMN-PCC→R-DMN-LP	0.0001	0	0	0	-0.0001	0	0	0
DMN-PCC→SAN-ACC	-0.0001	0	0	0	0	0	0	0
DMN-PCC→L-SAN-INS	-0.0001	0	0	0	0	0	-0.0001	0
DMN-PCC→R-SAN-INS	0	0	0	0	0	0	0	0
DMN-PCC→L-AMY	-0.0002	0	0	0	0	0	0	0
DMN-PCC→R-AMY	0	0	0	0	0	0	0	0
L-DMN-LP→DMN-mPFC	-0.0003	0	0.0889	1	0.0009	0	-0.0033	0
L-DMN-LP→DMN-PCC	-0.0001	0	0.0001	0	0.0004	0	0.0003	0
L-DMN-LP→L-DMN-LP	0	0	-0.0011	0	0.0010	0	0.0024	0
L-DMN-LP→R-DMN-LP	-0.0015	0	0.0651	1	0	0	-0.1040	1
L-DMN-LP→SAN-ACC	0.0008	0	0.0004	0	-0.0008	0	0.0387	0.52357
L-DMN-LP→L-SAN-INS	0.0005	0	-0.0209	0.5206	-0.0062	0	0.0060	0
L-DMN-LP→R-SAN-INS	0.0004	0	-0.0210	0.5155	-0.0060	0.5200	-0.0055	0
L-DMN-LP→L-AMY	0.0016	0	-0.0005	0	-0.0001	0	0	0
L-DMN-LP→R-AMY	0	0	0.0002	0	-0.0004	0	0.0004	0
R-DMN-LP→DMN-mPFC	0.0002	0	0.0843	1	0.0200	0.5249	0.0058	0
R-DMN-LP→DMN-PCC	0.0001	0	0.0001	0	-0.0004	0	-0.0007	0
R-DMN-LP→L-DMN-LP	0	0	-0.0006	0	-0.0001	0	0.0020	0
R-DMN-LP→R-DMN-LP	-0.0495	1	0.0010	0	-0.0006	0	-0.0863	1
R-DMN-LP→SAN-ACC	0.0544	1	0.0008	0	0.0001	0	-0.1309	1
R-DMN-LP→L-SAN-INS	-0.0003	0	0.0061	0	0.0017	0	0.0658	1
R-DMN-LP→R-SAN-INS	-0.0004	0	-0.0063	0	-0.0014	0	0.0257	0
R-DMN-LP→L-AMY	-0.0013	0	0.0003	0	0.0001	0	0.0003	0
R-DMN-LP→R-AMY	0	0	0.0004	0	0.0001	0	-0.0017	0
SAN-ACC→DMN-mPFC	0.0013	0	0	0	-0.0016	0	-0.0002	0
SAN-ACC→DMN-PCC	-0.0001	0	-0.0001	0	-0.0002	0	-0.0366	0.50516
SAN-ACC→L-DMN-LP	0.0014	0	0.0855	1	0.0138	0.5068	-0.0053	0
SAN-ACC→R-DMN-LP	-0.0475	1	0.1398	1	0.0642	1	-0.0334	0.5101
SAN-ACC→SAN-ACC	-0.0017	0	0	0	0.0015	0	0.0019	0
SAN-ACC→L-SAN-INS	0.0364	1	-0.0733	1	-0.0210	1	0.0120	0
SAN-ACC→R-SAN-INS	0.0242	0.5147	-0.0598	1	-0.0109	0	0.0062	0.50662
SAN-ACC→L-AMY	0.0234	0.5289	0.0004	0	0	0	-0.0002	0
SAN-ACC→R-AMY	-0.0005	0	0	0	0.0007	0	0.0009	0
L-SAN-INS→DMN-mPFC	0.0014	0	0.1290	1	0.0406	1	-0.0185	0.51665

L-SAN-INS→DMN-PCC	0.0003	0	0.1115	1	-0.0024	0	-0.0811	1
L-SAN-INS→L-DMN-LP	-0.0001	0	0.0027	0	0.0004	0	0.0644	1
L-SAN-INS→R-DMN-LP	0.0069	0	0.0707	1	-0.0043	0	0.0013	0
L-SAN-INS→SAN-ACC	-0.0037	0	0.0001	0	-0.0001	0	-0.0788	1
L-SAN-INS→L-SAN-INS	-0.0024	0	0.0045	0	0.0049	0	0.0083	0
L-SAN-INS→R-SAN-INS	-0.0017	0	-0.0019	0	-0.0023	0	-0.0152	0
L-SAN-INS→L-AMY	-0.0074	0	0.0023	0	0.0007	0	0.0805	1
L-SAN-INS→R-AMY	0.0001	0	0	0	-0.0001	0	0.0009	0
R-SAN-INS→DMN-mPFC	-0.0016	0	0.1202	1	0.0389	1	-0.0149	0
R-SAN-INS→DMN-PCC	-0.0004	0	0.0999	1	0.0027	0	-0.0638	1
R-SAN-INS→L-DMN-LP	0.0001	0	0.0142	0.5206	-0.0009	0	0.0481	0.51398
R-SAN-INS→R-DMN-LP	-0.0077	0	0.0711	1	0.0052	0	0.0027	0
R-SAN-INS→SAN-ACC	0.0041	0	0.0004	0	0.0005	0	-0.0979	1
R-SAN-INS→L-SAN-INS	0.0027	0	-0.0019	0	-0.0031	0	0.0142	0
R-SAN-INS→R-SAN-INS	0.0018	0	-0.0085	0.5019	-0.0072	0.5132	-0.0094	0
R-SAN-INS→L-AMY	0.0083	0	-0.0026	0	-0.0008	0	0.0706	1
R-SAN-INS→R-AMY	-0.0002	0	0.0002	0	0.0002	0	0.0007	0
L-AMY→DMN-mPFC	0.0007	0	0.0001	0	0	0	0.0019	0
L-AMY→DMN-PCC	0.0661	1	0	0	0	0	-0.0003	0
L-AMY→L-DMN-LP	0.0010	0	0	0	0	0	0.0029	0
L-AMY→R-DMN-LP	-0.0009	0	-0.0001	0	0	0	-0.0022	0
L-AMY→SAN-ACC	0.0524	1	0	0	0	0	-0.0020	0
L-AMY→L-SAN-INS	-0.0047	0	-0.0692	1	-0.0458	1	0.0551	1
L-AMY→R-SAN-INS	0.0053	0	-0.0621	1	-0.0410	1	0.0462	0.50192
L-AMY→L-AMY	0.0001	0	0	0	0	0	0.1469	1
L-AMY→R-AMY	0.0202	0.5192	0	0	0	0	-0.0009	0
R-AMY→DMN-mPFC	-0.0496	1	0.1290	1	-0.0008	0	-0.0020	0
R-AMY→DMN-PCC	0	0	0.0002	0	-0.0400	1	0.0413	0.51607
R-AMY→L-DMN-LP	0.0007	0	-0.0015	0	-0.0429	1	-0.1287	1
R-AMY→R-DMN-LP	-0.0001	0	0.0015	0	0.0006	0	0.0030	0
R-AMY→SAN-ACC	-0.0008	0	0.0013	0	0.0008	0	0.0028	0
R-AMY→L-SAN-INS	-0.0036	0	0.0086	0	-0.0305	1	-0.0515	1
R-AMY→R-SAN-INS	0.0037	0	-0.0093	0	-0.0194	0.5034	-0.0199	0
R-AMY→L-AMY	-0.0005	0	-0.0769	1e	-0.0238	0.5360	-0.0002	0
R-AMY→R-AMY	-0.0002	0	0.0006	0	0.0004	0	0.0013	0

Table S10: Measures of alcohol and tobacco usage, for the included CU and Control participants in Dataset 2.

Parameter	CU (n=21)	Control (n=21)	Statistical results
Lifetime alcohol use (n standard drinks)	539.3 ± 485.1 (35 to 2000)	303.4 ± 316.4 (0 to 1200)	t=1.866 p=0.069
Lifetime cigarettes smoked (n)	7764.9 ± 18815.0 (1 to 85000)	4711.8 ± 7542.2 (0 to 29000)	t=0.690 p=0.494
Cigarettes smoked per day (n)	5.1 ± 5.9 (0 to 15)	3.5 ± 4.9 (0 to 15)	t=0.956 p=0.345

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