

Supporting Information for

Enhanced amygdala-cingulate connectivity associates with better mood in both healthy and depressive individuals after sleep deprivation

Ya Chai, Philip Gehrman, Meichen Yu, Tianxin Mao, Yao Deng, Joy Rao, Hui Shi, Peng Quan, Jing Xu, Xiaocui Zhang, Hui Lei, Zhuo Fang, Sihua Xu, Elaine Boland, Jennifer R. Goldschmied, Holly Barilla, Namni Goel, Mathias Basner, Michael E. Thase, Yvette I. Sheline, David F. Dinges, John A. Detre, Xiaochu Zhang, Hengyi Rao

*** Correspondence:**

Hengyi Rao, Ph.D.

Center for Functional Neuroimaging & Department of Neurology

University of Pennsylvania Perelman School of Medicine

Room D502, Richards Medical Research Building

3700 Hamilton Walk, Philadelphia PA, 19104, USA

Phone: 215-746-2470

Email: hengyi@penmedicine.upenn.edu

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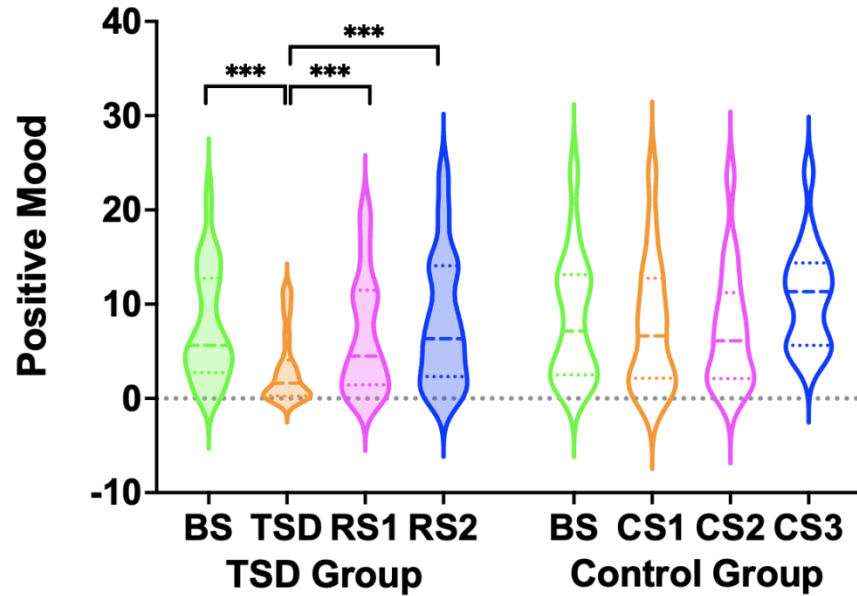


Fig. S1. POMS-positive mood score across the four consecutive days for the TSD group and the control group. Significant differences were found in positive mood across the four consecutive days in the TSD group but not in the control group. Positive mood worsened significantly following one night of TSD compared to BS but significantly improved after one night of RS. The baseline levels of positive mood did not differ between groups. The dashed lines represent the median values, and the dotted lines represent the quartiles. POMS: profile of mood states questionnaire; BS: baseline sleep; TSD: total sleep deprivation; RS: recovery sleep; CS: control sleep. *** $p < 0.001$

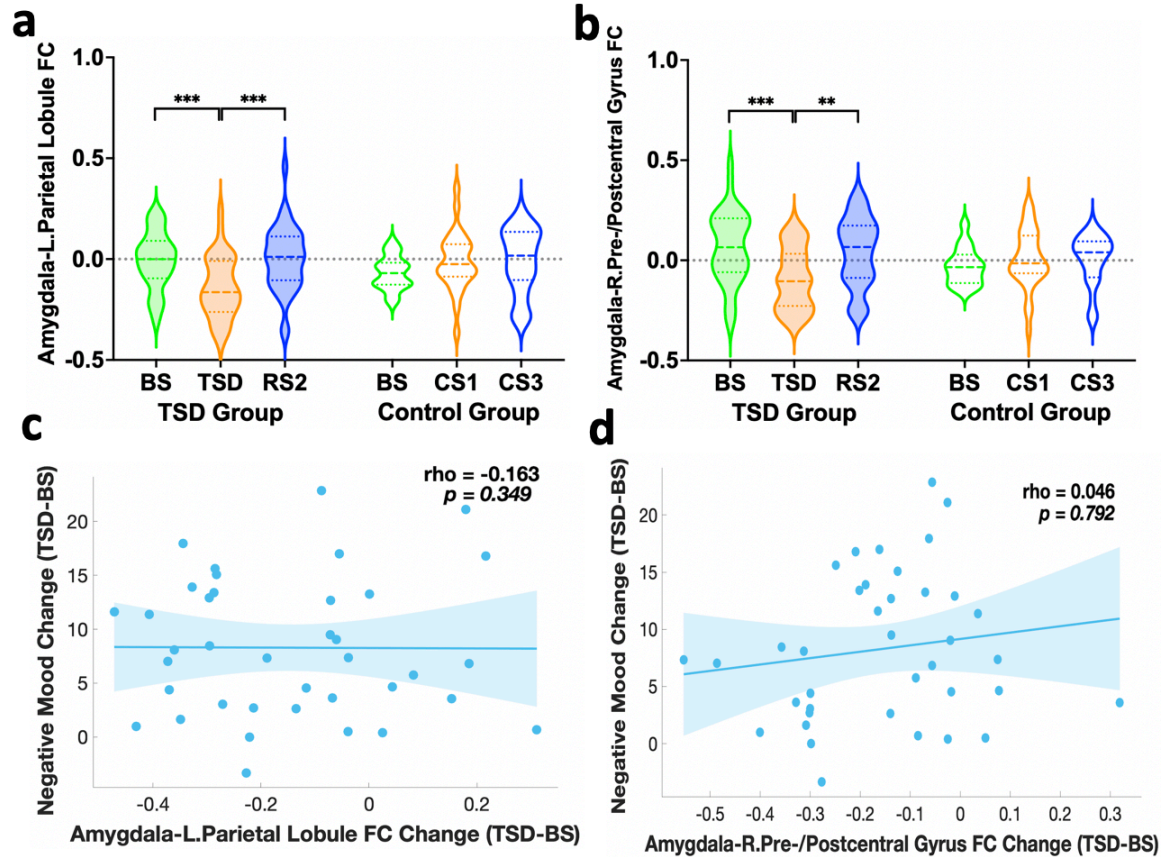


Fig. S2. Comparison of functional connectivity (FC) between bilateral amygdala and left parietal lobule (a), and right pre-/postcentral gyrus (b) among baseline sleep (BS), TSD/control sleep 1 (CS1), and recovery sleep 2 (RS2)/control sleep 3 (CS3) for the TSD group and control group. In the TSD group, amygdala connectivity with left parietal lobule and right pre-/postcentral gyrus decreased significantly after TSD and increased after RS2. There were no significant changes in amygdala connectivity with these two regions among corresponding days in the control group. The dashed lines represent the median values, and the dotted lines represent the quartiles. L: left; R: right. ** $p < 0.01$, *** $p < 0.001$. The scatter plots show non-significant correlations between mood worsening pre- to post-TSD and changes in amygdala FC with brain regions (other than bilateral ACC) showing significant FC decreases with the amygdala in Study 1 [i.e., left parietal lobule (c) and right pre-/postcentral gyrus (d)], controlling for age, gender, head motion, and baseline negative mood.

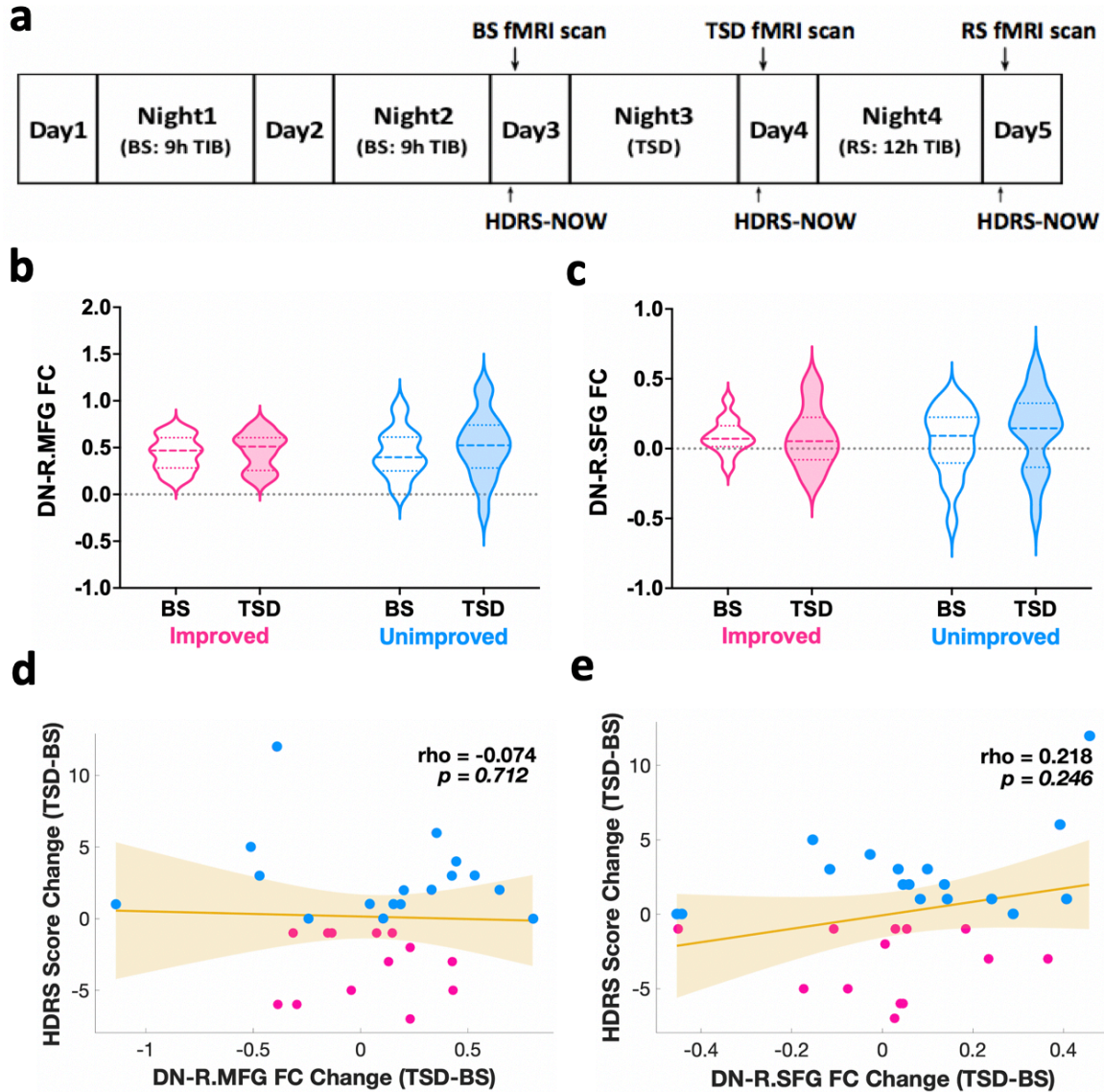


Fig. S3. (a) Protocol of Experiment 2. BS: baseline sleep; TSD: total sleep deprivation; RS: recovery sleep; TIB: time-in-bed. Comparison of DN connectivity with R.MFG (b) and R.SFG (c) between BS and TSD in improved mood group (pink) and unimproved mood group (blue). The increased/decreased DN-R.MFG and DN-R.SFG connectivity after TSD in the two patient groups did not reach statistical significance. The dashed lines represent the median values, and the dotted lines represent the quartiles. After TSD, neither DN-R.MFG (d) nor DN-R.SFG (e) connectivity changes correlated significantly with depressive mood changes, while controlling for age, gender, head motion, and baseline depressive mood. DN: dorsal nexus; MFG: middle frontal gyrus; SFG: superior frontal gyrus; FC: functional connectivity; HDRS: Hamilton Rating Scale for Depression; Pink lines and dots: improved mood; Blue lines and dots: unimproved mood.

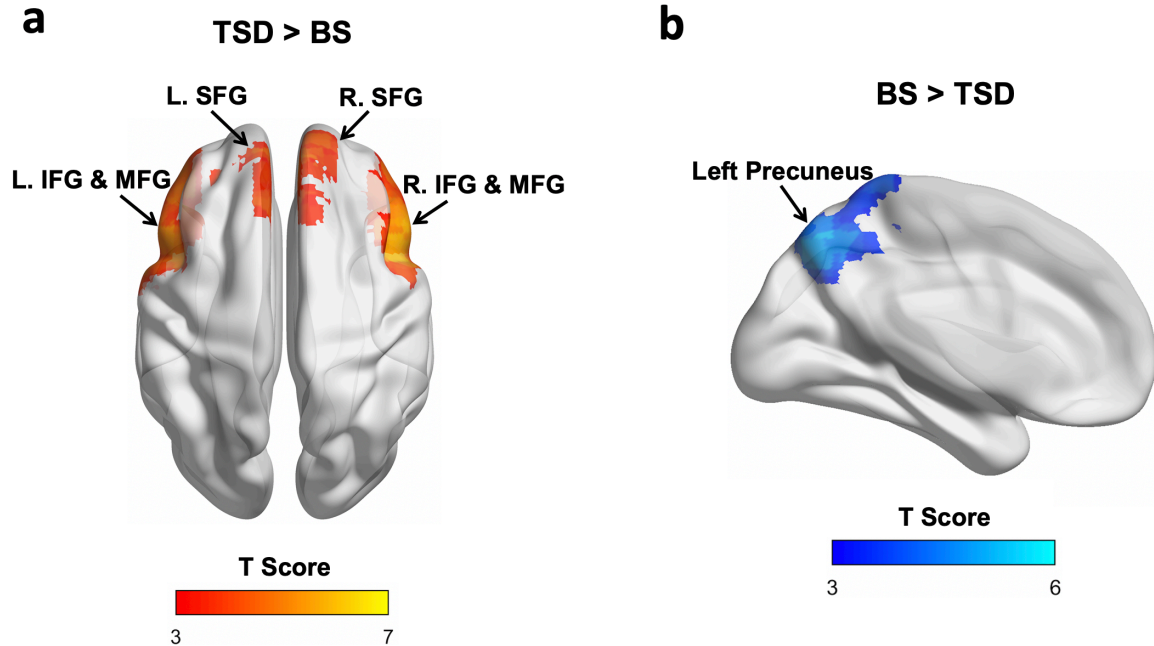


Fig. S4. Whole-brain analysis for functional connectivity (FC) with bilateral dorsal nexus (DN). Increased FC of the DN with bilateral superior, inferior, and middle frontal gyrus (a), while decreased DN connectivity with left precuneus (b) following total sleep deprivation (TSD) relative to baseline sleep (BS) in the healthy TSD group. Paired samples t-tests were performed to examine the differences in FC of DN with all other voxels in the brain between BS and TSD, with age, gender, and head motion as covariates. The threshold was set at whole-brain FWE corrected $p < 0.001$ at a cluster level, with cluster size larger than 30 voxels.

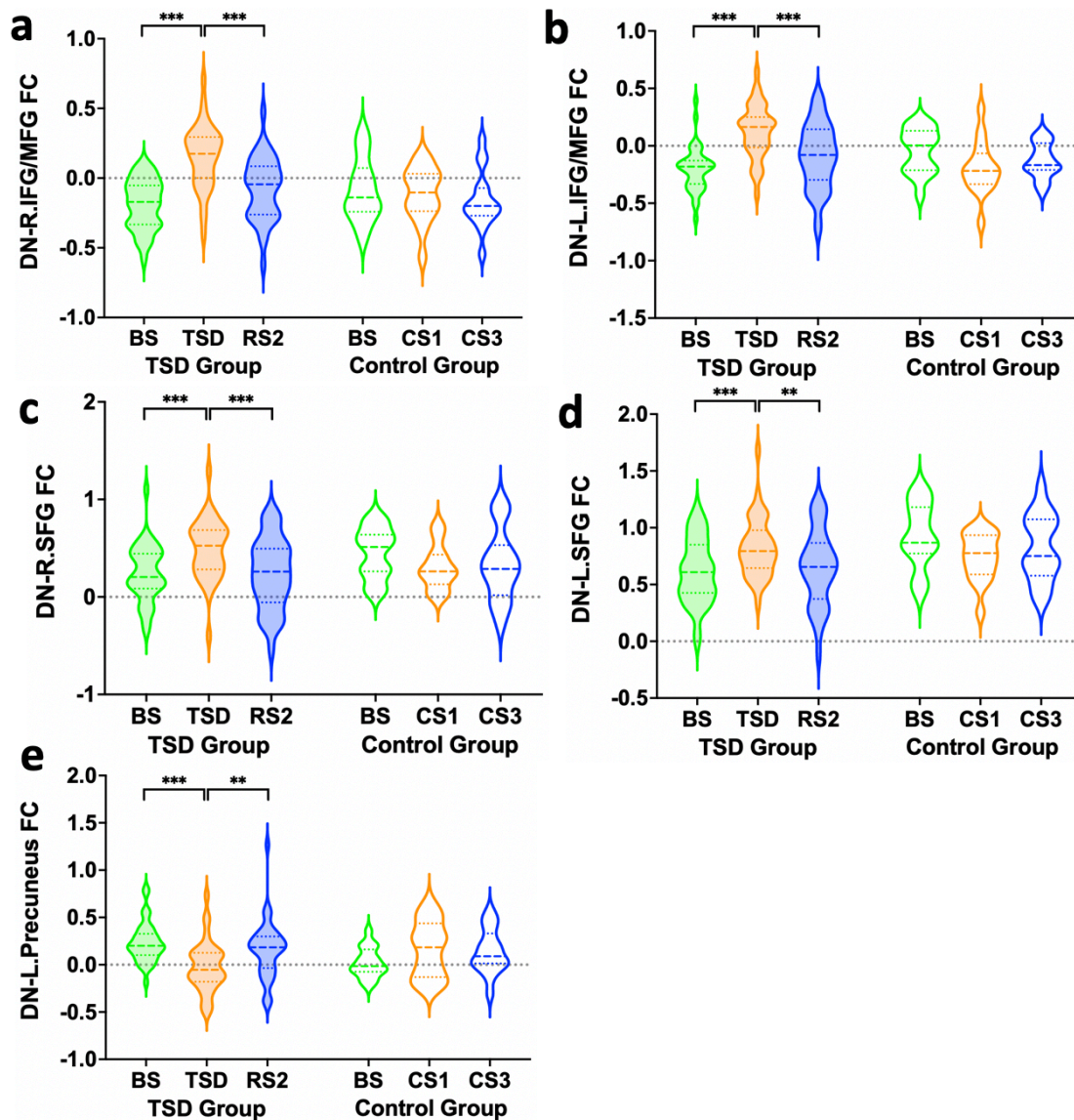


Fig. S5. Comparison of functional connectivity (FC) of bilateral dorsal nexus (DN) with bilateral inferior frontal gyrus/middle frontal gyrus (IFG/MFG; a & b), bilateral superior frontal gyrus (SFG; c & d), and left precuneus (e) among baseline sleep (BS), total sleep deprivation (TSD)/control sleep 1 (CS1), and recovery sleep 2 (RS2)/control sleep 3 (CS3) for the TSD group and control group. In the TSD group, DN connectivity with bilateral IFG/MFG and SFG increased significantly after TSD and decreased after RS2, whereas DN connectivity with left precuneus exhibited the inverted pattern. There were no significant changes in DN connectivity with any of the above regions among corresponding days in the control group. The dashed lines represent the median values, and the dotted lines represent the quartiles. L: left; R: right. ** $p < 0.01$, *** $p < 0.001$

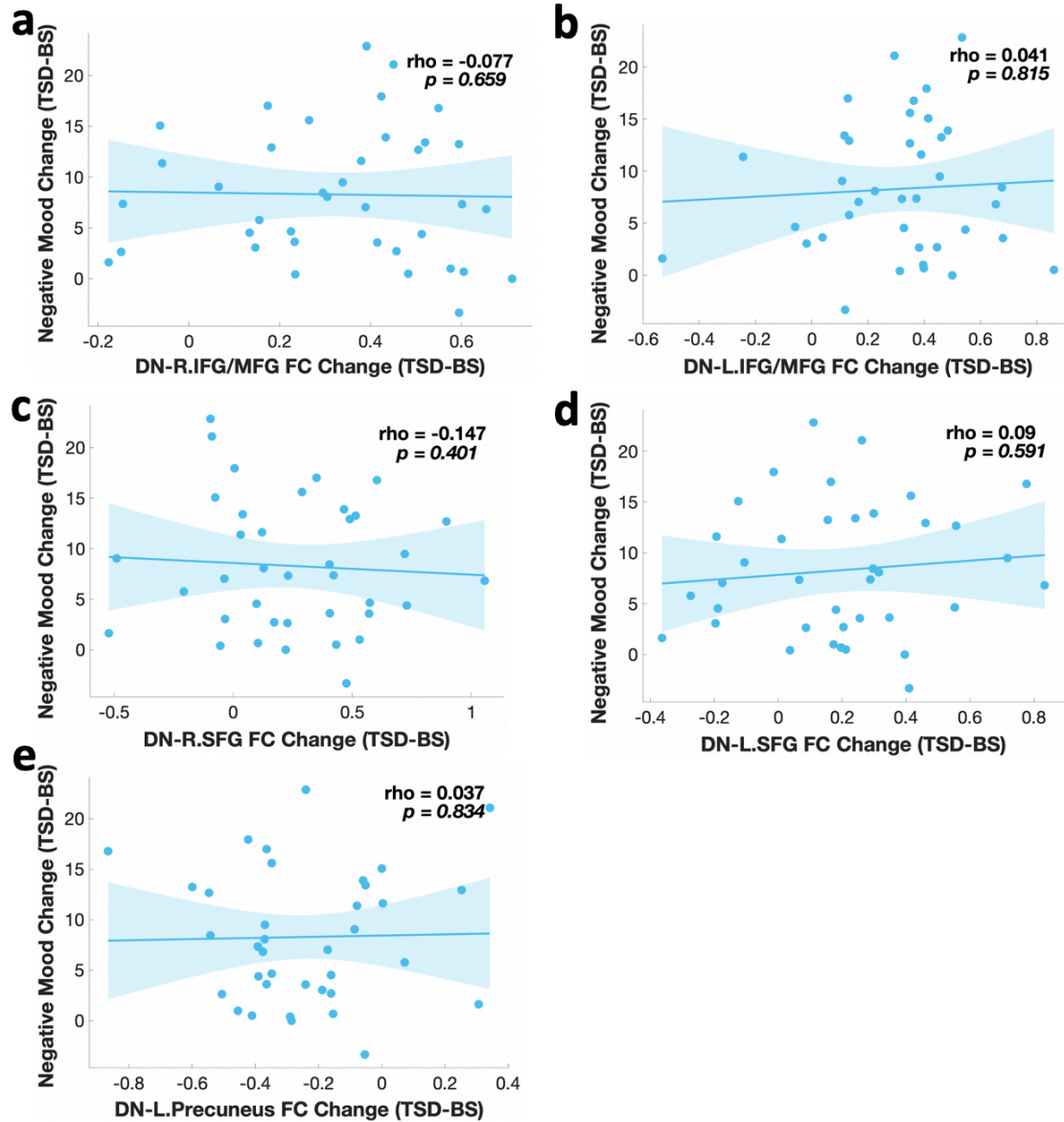


Fig. S6. These scatter plots show non-significant correlations between mood worsening pre- to post-TSD and increases/decreases in DN FC with brain regions showing significant FC changes with the DN after TSD relative to BS in Study 1 [i.e., left and right IFG/MFG (a & b), left and right SFG (c & d), and left precuneus (e)], controlling for age, gender, head motion, and baseline negative mood. BS: baseline sleep; TSD: total sleep deprivation; DN: dorsal nexus; IFG: inferior frontal gyrus; MFG: middle frontal gyrus; SFG: superior frontal gyrus; L: left; R: right; FC: functional connectivity.

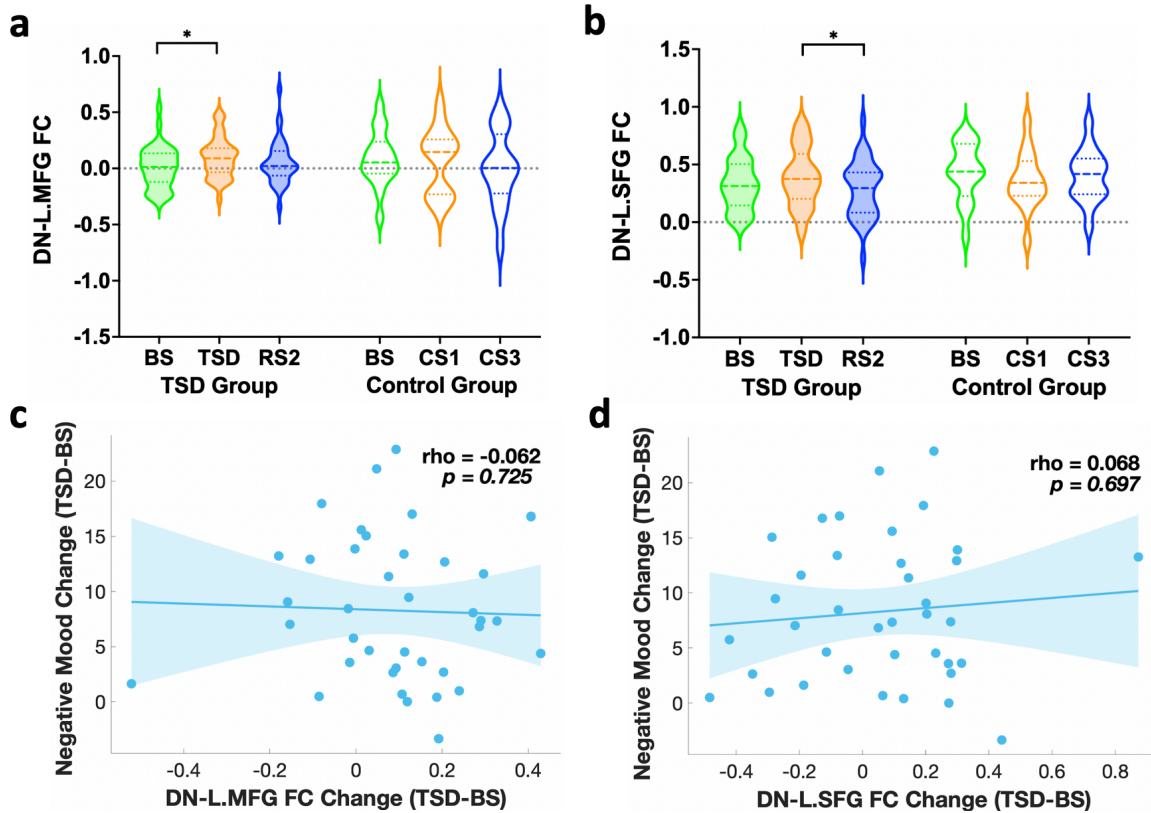


Fig. S7. Comparison of FC of bilateral DN with left MFG (a) and SFG (b) among BS, TSD/CS1, and RS2/CS3 for the TSD group and control group. In the TSD group, DN connectivity with left MFG and SFG increased after TSD and decreased after RS2. There were no significant changes in DN connectivity with these two regions among corresponding days in the control group. The dashed lines represent the median values, and the dotted lines represent the quartiles. $*p < 0.05$. The scatter plots show non-significant correlations between worsened mood and increased DN connectivity with left MFG (c) or SFG (d) pre- to post-TSD, while controlling for age, gender, head motion, and baseline negative mood. BS: baseline sleep; TSD: total sleep deprivation; RS: recovery sleep; CS: control sleep; DN: dorsal nexus; MFG: middle frontal gyrus; SFG: superior frontal gyrus; L: left; FC: functional connectivity.

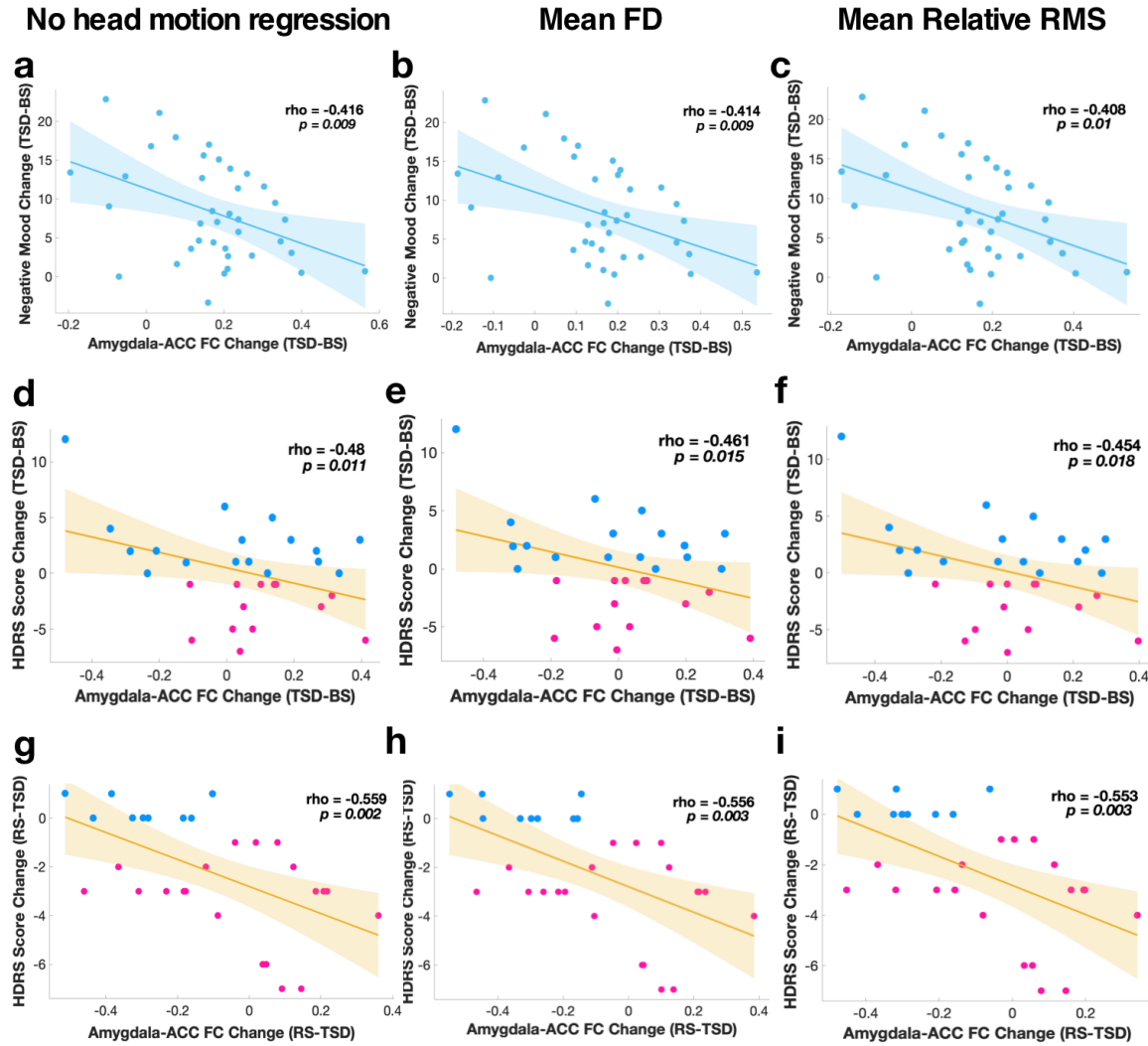


Fig. S8. The correlations between amygdala-ACC FC increases and mood improvement from BS to TSD remain significant when including head motion (i.e., mean FD and mean relative RMS displacement) as another covariate in addition to age, gender, and baseline negative mood score in both controls (a-c) and patients (d-f). Similarly, the correlations between amygdala-ACC FC increases and mood improvement from TSD to RS remain significant when including head motion as another covariate in addition to age and gender in patients (g-i). BS: baseline sleep; TSD: total sleep deprivation; RS: recovery sleep; ACC: anterior cingulate cortex; FC: functional connectivity; HDRS: Hamilton Rating Scale for Depression; FD: framewise displacement; RMS: root mean squared. Pink dots in d-i: improved mood; Blue dots in d-i: unimproved mood.

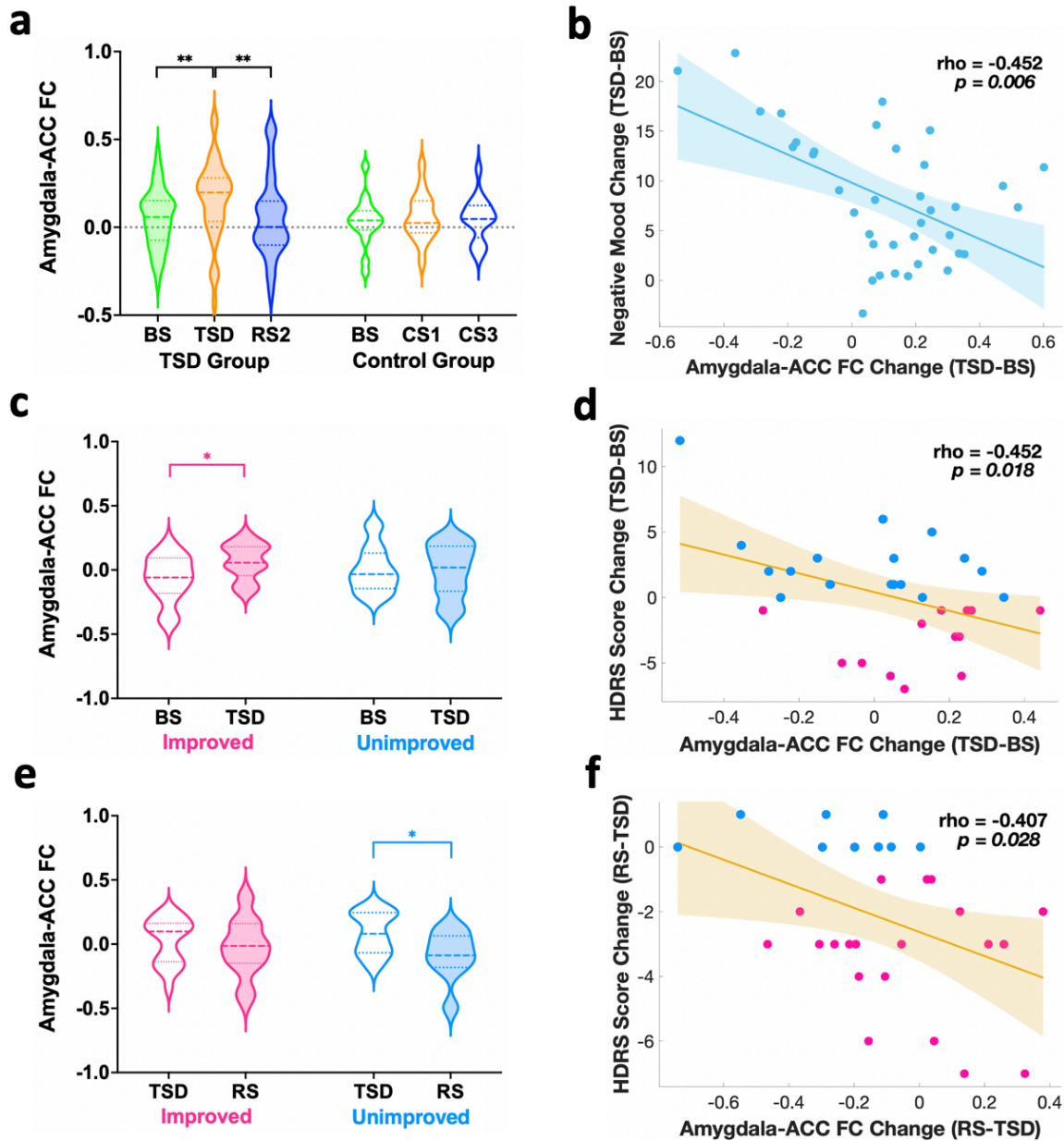


Fig. S9. Replication of findings of amygdala-ACC connectivity and connectivity-mood correlation in individual subject space. (a) Amygdala-ACC connectivity increased significantly after TSD, while it decreased significantly after RS2 in the healthy TSD group. There were no significant amygdala-ACC connectivity changes among corresponding days in the healthy control group. The dashed lines represent the median values, and the dotted lines represent the quartiles. (b) The scatter plot shows a significant correlation between increased amygdala-ACC connectivity and improved mood from BS to TSD, controlling for age, gender, head motion, and baseline negative mood ($\rho = -0.452$, $p < 0.01$). (c) Comparison of amygdala-ACC connectivity between BS and TSD in improved mood group (pink) and unimproved mood group (blue). Amygdala-ACC connectivity increases after TSD were evident in patients with improved mood ($p < 0.05$), while the increases in patients with unimproved mood did not reach statistical significance. The

dashed lines represent the median values, and the dotted lines represent the quartiles. (d) The scatter plot shows a significant correlation between increased amygdala-ACC connectivity and improved depressive mood from BS to TSD, controlling for age, gender, head motion, and baseline depressive mood ($\rho = -0.452$, $p < 0.05$). (e) Comparison of amygdala-ACC connectivity between TSD and RS in improved mood group (pink) and unimproved mood group (blue). Amygdala-ACC connectivity decreases after RS were evident in patients with unimproved mood ($p < 0.05$), while the decreases in patients with improved mood did not reach statistical significance. The dashed lines represent the median values, and the dotted lines represent the quartiles. (f) The scatter plot shows a significant correlation between decreased amygdala-ACC connectivity and mood worsening from TSD to RS, controlling for age, gender, and head motion ($\rho = -0.407$, $p < 0.05$). BS: baseline sleep; TSD: total sleep deprivation; RS: recovery sleep; CS: control sleep; ACC: anterior cingulate cortex; FC: functional connectivity; HDRS: Hamilton Rating Scale for Depression; Pink lines and dots: improved mood; Blue lines and dots: unimproved mood. $*p < 0.05$, $**p < 0.01$

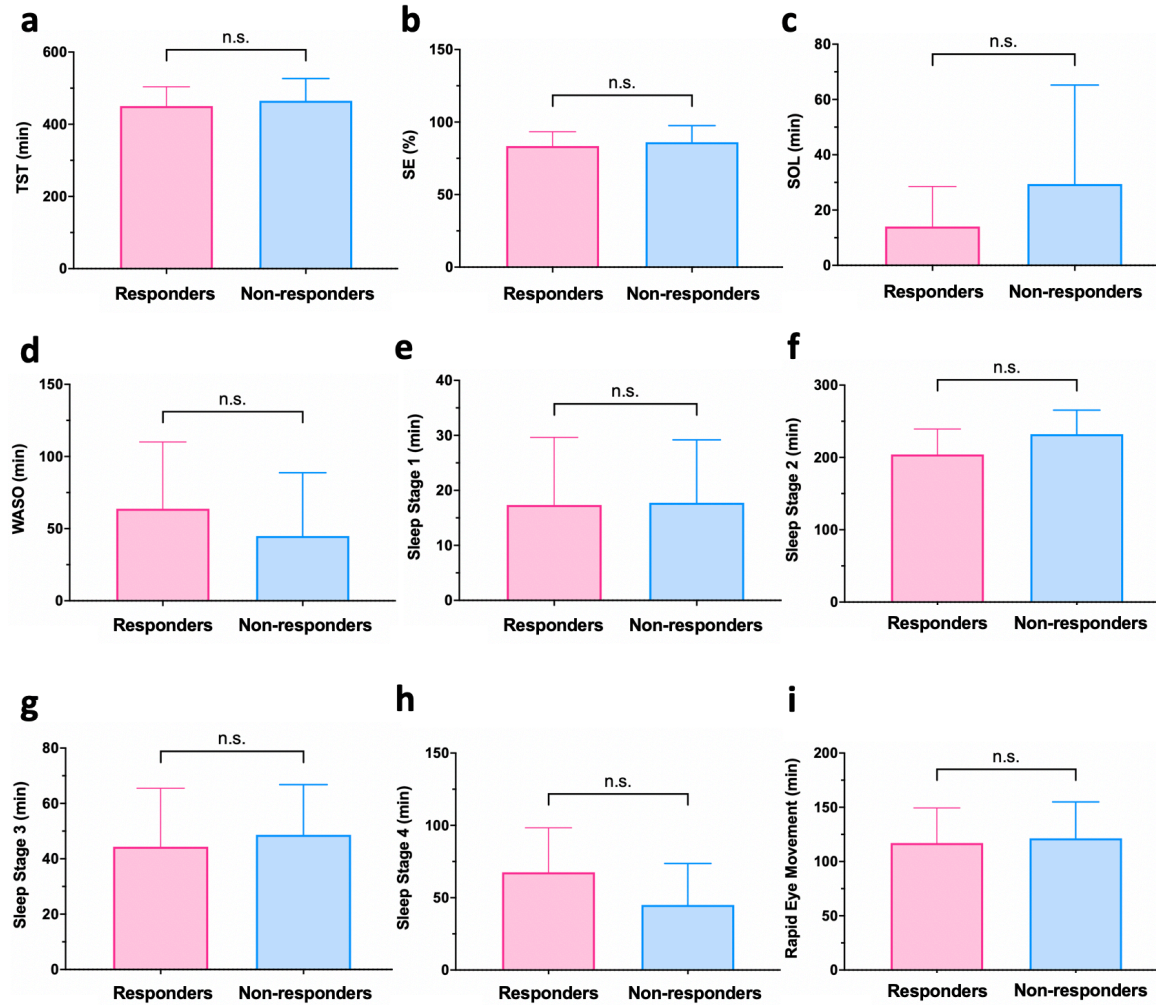


Fig. S10. Non-significant (n.s.) differences between responders (n = 10) and non-responders (n = 14) in baseline sleep parameters at Night2 ($p > 0.05$). These parameters involved total sleep time (TST; a), sleep efficiency (SE, TST/TIB; b), latency to sleep onset (SOL; c), wake after sleep onset (WASO; d), and amount of each stage of sleep (e-i).

Table S1. Demographic information. SD: standard deviation; TSD: total sleep deprivation; BMI: body mass index.

Characteristics	TSD group (n = 38)	Control group (n = 16)
Age (Mean \pm SD years)	33.5 \pm 8.6	35.4 \pm 9.5
% Female (n)	45 (17)	50 (8)
% African American (n)	58 (22)	68.75 (11)
Education (Mean \pm SD years)	14.3 \pm 1.6	15.3 \pm 2.3
BMI (Mean \pm SD)	24.3 \pm 2.8	24.9 \pm 4.2

Table S2. Brain regions showing significantly different amygdala-based functional connectivity during total sleep deprivation (TSD) compared to baseline sleep (BS). *Clusters survived whole-brain FWE corrected $p < 0.001$ and voxel-level FWE corrected $p < 0.05$, with cluster size > 30 voxels. ACC: anterior cingulate cortex.

Brain Regions	x, y, z	p value (FWE corrected)	Cluster Size	Peak T
TSD > BS				
Bilateral ACC *	0, 21, 36	0.000	347	5.97
BS > TSD				
Left Parietal Lobule	-42, -30, 30	0.017	103	4.50
Right Pre-/Postcentral Gyrus	27, -12, 57	0.013	109	4.48

Table S3. Brain regions showing significantly different DN-based functional connectivity during total sleep deprivation (TSD) as compared to baseline sleep (BS). All clusters survived whole brain FWE corrected $p < 0.001$, with cluster size > 30 voxels. *Clusters survived voxel-level FWE corrected $p < 0.05$. IFG: inferior frontal gyrus; MFG: middle frontal gyrus; SFG: superior frontal gyrus.

Brain Regions	x, y, z	p value (FWE corrected)	Cluster Size	Peak T
TSD > BS				
Right IFG/MFG*	54, 15, 27	< 0.001	787	6.61
Left IFG/MFG*	-51, 18, 24	< 0.001	757	5.61
Right SFG*	9, 45, 33	< 0.001	208	5.28
Left SFG	-9, 51, 30	< 0.001	63	4.52
BS > TSD				
Left Precuneus*	-3, -66, 54	< 0.001	332	5.24