HHS Public Access

Author manuscript

Depress Anxiety. Author manuscript; available in PMC 2018 July 01.

Published in final edited form as:

Depress Anxiety. 2017 July ; 34(7): 651–660. doi:10.1002/da.22622.

Subjective and Objective Sleep Quality Modulate Emotion Regulatory Brain Function in Anxiety and Depression

Heide Klumpp, PhD, **Julia Roberts, BS**, **Mary C. Kapella, PhD**, **Amy E. Kennedy, MSW**, **Anand Kumar, MD**, and **K. Luan Phan, MD**

Mood and Anxiety Disorders Research Program, Department of Psychiatry (HK, JR, AEK, AK, KLP), University of Illinois at Chicago, Chicago, IL; Departments of Psychology and Psychiatry (HK, KLP), University of Illinois at Chicago, Chicago, IL; Department of Biobehavioral Health Science (MCK), University of Illinois at Chicago; Mental Health Service (AEK, KLP), Jesse Brown VA Medical Center, Chicago, IL

Abstract

Background—Disturbances in emotion regulation and sleep are shared across anxiety and mood disorders. Poor sleep has been shown to impair cognitive processes which may undermine cognitive regulatory function. However, it remains unknown if sleep quality impacts regulatory mechanisms in clinical anxiety and depression.

Methods—During fMRI, 78 patients with social anxiety disorder, generalized anxiety disorder, and/or major depressive disorder completed a validated emotion regulation task, which involved reappraisal (i.e., decrease negative affect) as compared to viewing aversive images. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI) and actigraphy, representing subjective and objective measures of sleep, respectively. Regression analysis was conducted with the PSQI and actigraphy sleep efficiency, duration, and wake-after sleep onset variables.

Results—PSQI and actigraphy measures indicated that the majority of patients experienced problematic sleep, however, subjective and objective sleep measures were uncorrelated. Whole-brain voxel-wise regression analysis, controlling for diagnosis, revealed worse self-reported sleep corresponded with less reappraise-related activation in the dorsal anterior cingulate cortex (DACC). The same analysis performed with actigraphy data showed less sleep efficiency positively corresponded with DACC activation. Post-hoc stepwise regression analysis showed these sleep measures predicted DACC activity whereas anxiety and depression symptoms did not.

Conclusions—Individual differences in self-perceived and objective sleep quality differentially modulated the DACC, which is implicated in cognitive reappraisal. Findings suggest neural correlates of emotion regulation tracks different aspects of the sleep experience. Results also

Corresponding Author: Heide Klumpp, PhD, Department of Psychiatry, University of Illinois at Chicago, 1747 W. Roosevelt Rd, Chicago, IL 60608, hklumpp@psych.uic.edu, Phone: (312) 996-0416, Fax: (312) 413-1703.

Financial Disclosures: This work was supported by NIMH K23MH093679, Brain & Behavior Research Foundation (formerly NARSAD) Award, and University of Illinois at Chicago Campus Research Board Award (HK) and in part by NIMH R01MH101497 (KLP) and the Center for Clinical and Translational Research (CCTS) UL1RR029879.

Competing Interests: Dr. Klumpp, Ms. Roberts, Dr. Kapella, Ms. Kennedy, Dr. Kumar, and Dr. Phan report no competing interests.

Financial Disclosure

Dr. Klumpp, Ms. Roberts, Dr. Kapella, Ms. Kennedy, Dr. Kumar, and Dr. Phan report no competing interests.

indicate sleep disturbance may play a role in the emotion dysregulation observed in anxiety and depressive disorders.

Keywords

fMRI; neuroimaging; insomnia; reappraisal; anterior cingulate cortex; social anxiety disorder; generalized anxiety disorder; major depressive disorder

Introduction

Sleep is crucial to brain function and the adverse cognitive and emotional effects resulting from sleep deficiency are well known (Czeisler, 2011; LeBlanc et al., 2007). A growing body of neuroimaging data signify a frontolimbic network plays a role in sleep-emotion interactions. That is, studies independent of sleep have established that prefrontal and anterior cingulate cortices regulate subcortical emotion processing regions (e.g., amygdala) (Etkin, Egner, & Kalisch, 2011; Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003). Furthermore, investigations of emotion processing as they pertain to sleep mechanisms have shown less sleep alters frontolimbic connections resulting in hyper-limbic reactivity to negative stimuli (Gruber & Cassoff, 2014). For example, sleep deficiency decreases medial prefrontal cortex (PFC)-amygdala connectivity and anterior cingulate cortex-amygdala connectivity in the presence of negative stimuli (Motomura et al., 2013; Yoo, Gujar, Hu, Jolesz, & Walker, 2007). Findings indicate poor sleep disrupts top-down control of amygdala response to salient stimuli. Sleep loss also impairs higher-order performance in specific domains (e.g., attention, working memory) (Lim & Dinges, 2010) integral to executing complex cognitive tasks such as ‘reappraisal’.

Reappraisal is a well-researched adaptive regulation strategy directed at altering (e.g., re-interpreting) a stimulus to change the trajectory of an emotional response or reduce the negative affective state it would otherwise evoke (Gross, 1999). Meta-analytic studies show reappraisal consistently recruits a large-scale cognitive control network (Buhle et al., 2014; Messina, Bianco, Sambin, & Viviani, 2015), therefore, we might expect sleep quality to impact emotion regulation. In support, Minkel and colleagues (Minkel et al., 2012) demonstrated worse sleep, as assessed with the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) corresponded with less reappraise-related activation in the dorsomedial PFC in healthy participants. Results suggest mechanisms of regulation are mediated by individual differences in subjective sleep quality, which has important inferences in clinical populations where sleep problems are frequently observed.

In patients with anxiety and mood disorders such as major depressive disorder, several lines of research point to strong links between these psychiatric illnesses and poor sleep. In studies that tracked sleep patterns over the course of anxiety and depression, the onset of sleep disturbance commonly occurred at the time symptoms manifested (e.g., 80% of cases in anxiety) (Breslau, Roth, Rosenthal, & Andreski, 1996; Ford & Kamerow, 1989; Gregory et al., 2005; Ohayon & Roth, 2003) and frequently preceded relapse (e.g., 56% of mood disorder cases) (Ford & Kamerow, 1989; Gillin, 1998; Gregory et al., 2005; Ohayon & Roth, 2003). Findings are in line with reports that poor sleep is a risk-factor in the development

and maintenance of mood disorders (Ford & Kamerow, 1989; Gillin, 1998; Gregory et al., 2005). Problematic sleep has also been shown to exacerbate symptom severity (Cox & Olatunji, 2016) and may reflect the general influence sleep has on the capacity to regulate emotions (Gruber & Cassoff, 2014). In further support of close ties between mood and sleep, 40–50% of individuals who suffer from sleep difficulties have a concurrent psychiatric disorder (Ford & Kamerow, 1989; Gillin, 1998; Gregory et al., 2005). Collectively, associations between negative mood and sleep are multifaceted and bidirectional yet we know little about the effect of sleep on emotion regulation mechanisms in anxiety and depression (Gruber & Cassoff, 2014).

Adding to the complexity in understanding these relationships is the means by which sleep is evaluated. For example, the Pittsburgh Sleep Quality Index (PSQI) is the most frequently used general measure of sleep in clinical and research settings (Mollayeva et al., 2016), however, as a self-report questionnaire (Buysse et al., 1989), it is subject to bias. In contrast, actigraphy relies on the continuous recording of activity/inactivity 24-hours a day to estimate sleep quality (Ancoli-Israel et al., 2003). As a result, these measures likely capture different aspects of sleep as evinced by reports of discrepancy between such measures (Girschik, Fritschi, Heyworth, & Waters, 2012; Mccall & Mccall, 2012; O'Brien, Hart, & Wing, 2016; Van Den Berg et al., 2008; Van Ravesteyn et al., 2014).

To date, studies of emotion regulatory brain function, independent of sleep, have shown reduced and/or inefficient activity in structures that support cognitive reappraisal (e.g., anterior cingulate cortex, dorsolateral PFC) in anxious or depressed individuals relative to healthy participants (Ball, Ramsawh, Campbell-Sills, Paulus, & Stein, 2013; Dillon & Pizzagalli, 2013; Goldin, Manber, Hakimi, Canli, & Gross, 2009; Goldin, Manber-Ball, Werner, Heimberg, & Gross, 2009; Heller et al., 2013; Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007; Kanske, Heissler, Schönfelder, & Wessa, 2012; New et al., 2009; Rabinak et al., 2014; Smoski, Keng, Schiller, Minkel, & Dichter, 2013). Yet, the extent to which naturalistic sleep impacts such regions in these internalizing conditions is unknown. Therefore, the primary aim of the current study was to examine the relationship between sleep and reappraise-related neurofunctional activity in anxious and depressed patients with the PSQI and actigraphy. We hypothesized greater sleep disturbance would correspond with less engagement in frontal regions critically involved in reappraisal (Buhle et al., 2014; Messina et al., 2015). Behaviorally, we hypothesized a lack of concordance between self-report and actigraphy estimates of sleep quality. Additionally, we explored relationships among subjective and objective sleep measures and symptoms.

Method

Participants

As part of a research study evaluating mechanisms of change associated with standard psychotherapy or pharmacotherapy intervention, treatment-seeking adults ages 18 to 65 years old experiencing generalized anxiety disorder (GAD), generalized social anxiety disorder (gSAD), or major depressive disorder (MDD) were recruited via flyers posted throughout the communities, newspaper, and internet advertisements. Interested participants completed a phone screen followed by a psychiatric evaluation during which time they

reviewed the consent form as approved by the local Institutional Review Board at the University of Illinois at Chicago. After attaining consent, participants met with a Master's-level clinician trained in the Structured Clinical Interview for DSM-IV ("SCID-IV"; First, Spitzer, Gibbon, & Williams, 1995), which determined diagnosis, and completed clinician-administered measures. Comorbidity was permitted, therefore, the Hamilton Depression Rating Scale ["HAM-D"; Hamilton, 1960)] and Hamilton Anxiety Rating Scale ["HAM-A"; Hamilton, 1959)] were used to assess symptom severity across disorders. All measures were collected within a week of the fMRI scan and participants were required to test negative on a urine toxicology screen before the scan.

All participants were free of major medical and neurological illness as confirmed by a Board Certified physician. Exclusion criteria included contraindications to magnetic resonance imaging (e.g., pregnancy, non-removable ferrous objects), current substance dependence (within 6 months of the study), history of other major psychiatric illness (e.g., bipolar disorder, psychotic disorders), or current cognitive dysfunction (e.g., traumatic brain injury, pervasive developmental disorder). All participants were compensated for their time and all procedures complied with the Helsinki Declaration.

Subjective and Objective Sleep Measures

Self-reported sleep quality was evaluated with the PSQI global score, a 19-item questionnaire that assesses sleep over the period of a month (Buysse et al., 1989). Higher scores indicate worse sleep and a PSQI global score >5 denotes problematic sleep (sensitivity 89.6%, specificity 86.5%) (Buysse et al., 1989). For an objective estimate of sleep quality actigraphy was used. Actigraphy variables were sleep efficiency (average percentage of time asleep), duration (average number of minutes slept), wake after sleep onset ("WASO"; average number of minutes awake after initial onset of sleep), and latency (average number of minutes between going to bed and falling asleep). All variables were used in analysis except latency due to its reduced reliability (Martin & Hakim, 2011).

In the Statistical Package for the Social Sciences ("SPSS") (Chicago, IL version 22), sleep measures were examined to determine if assumptions of normality were met (i.e., Shapiro-Wilk test, skewness between −1 and 1) (Leech, Barrett, & Moran, 2005; Peat & Barton, 2005). Tests for normality revealed the PSQI global score and actigraphy efficiency, duration, and WASO variables were not normally distributed (e.g., all p's<0.05 for Shapiro-Wilk). Additionally, sleep efficiency and WASO variables exceeded skewness limits. Consequently, all measures were log-transformed though normalization of sleep duration was achieved with Box Cox transformation. Accordingly, transformed data were used in all neuroimaging regression analysis. Subsequently, these data were back-transformed to their original scale for ease of interpretation.

Pearson's correlations were conducted to examine relationships between subjective/PSQI and objective/actigraph measures, associations between sleep measures and symptom severity, and to illustrate significant neuroimaging findings. All Pearson's correlations were two-tailed with alpha level 0.05.

Actigraphy Methods

A wrist-worn accelerometer, the Actiwatch 2™ (Minimitter, Philips Respironics, Andover MA), was placed on the participant's non-dominant wrist and participants were instructed to maintain a sleep diary and record habitual sleep times. The omni-directional accelerometer uses a piezoelectric sensor to monitor the occurrence and degree of motion. The motion sensor integrates degree and speed of motion, and this information is stored in the Actiwatch 2 memory as activity counts; the data were stored in 15-second epochs. The Actiwatch was programmed for start time and data collection interval and data were retrieved for analysis via a PC interface scoring software (Actiware 5.70) provided with the accelerometer. Activity counts were scored as sleep or wake epochs using the software, and the software automatically assigned rest, sleep, and active intervals based on activity counts. An automated analysis was used to determine sleep start by searching for the first 10 minutes during which no more than one epoch was scored as "wake." The default software settings were used for the analysis (10 immobile or mobile minutes for sleep onset or end and a wake activity count threshold of 40). All actigraphy data was evaluated by a trained scorer who used a standardized approach to check the periods when the subject was trying to sleep (rest interval) based on event markers, sleep diary, light intensity, and activity. One main rest interval at night was identified as the period for sleep. Sleep variables (e.g., efficiency, duration) were scored for each 24-hour period and a mean was computed.

fMRI Task

The fMRI Emotion Regulation Task (ERT) is based on paradigms previously validated in other labs (Ochsner, Bunge, Gross, & Gabrieli, 2002) and in our lab in healthy participants (Phan et al., 2005) and patient cohorts (MacNamara et al., 2016; Rabinak et al., 2014). Consistent with these studies, participants were instructed to: 1) use a cognitive strategy to reduce negative affect to aversive images ("Reappraise"); 2) attend to the emotional state elicited by aversive images ("Maintain"); or 3) view neutral images ("Look"). Prior to the scan, participants were instructed on the strategy of reappraisal (Ochsner et al., 2002; Phan et al., 2005); all conditions were practiced with images not used in the experiment.

The task comprised 64 unpleasant and 32 neutral International Affective Picture System images (Lang, Bradley, & Cuthbert, 2008). There were eight 20-s blocks of each condition (four images presented for 5 s each), which were interspersed with 20-s baseline blocks (i.e., fixation cross). At the beginning of each block, the instruction to 'Reappraise,' 'Maintain,' or 'Look' appeared on a screen for 5 s. Immediately following each task block, participants were asked to rate "How negative do you feel?" on a 5-point scale (1=not at all, 5=extremely) via button response. The order of blocks was pseudo-randomized over 2 separate runs of 5 minutes each.

fMRI Data Acquisition and Preprocessing

Scanning was conducted on a 3 Tesla GE Signa System (General Electric; Milwaukee, WI) and performed with blood oxygen-level dependent (BOLD)-sensitive whole-brain fMRI. Images were acquired using a gradient-echo echo-planar imaging sequence with the following parameters: TR = 2s, TE = 25 ms, flip angle = 90°, field of view = 22 x 22 cm^2,

acquisition matrix 64 x 64; 44 axial, 3-mm-thick slices with no gap. For anatomical localization, a high-resolution, T1-weighted volumetric anatomical scan was acquired.

Data from all participants met criteria for quality with minimal motion correction (movements were <3 mm and <3 degrees rotation in any one direction) and the first 4 volumes from each run were discarded to allow for T1 equilibration effects. Conventional preprocessing steps were used in the Statistical Parametric Mapping (SPM8) software package (Wellcome Trust Centre for Neuroimaging, London www.fil.ion.ucl.ac.uk/spm). Briefly, images were temporally corrected to account for differences in slice time collection, spatially realigned to the first image of the first run, normalized to a Montreal Neurological Institute (MNI) template, resampled to 2 x 2 x 2 mm voxels, and smoothed with an 8mm isotropic Gaussian kernel.

fMRI Analyses

A general linear model was applied to the time series, convolved with the canonical hemodynamic response function and with a 128s high-pass filter. Nuisance regressors comprising 6 motion parameters were included to correct for motion artifacts. Blocks of Reappraise, Maintain, and Look were modeled separately, the effects of which were estimated for each voxel for each participant and taken to the second level for random effects analysis.

Reappraise vs. Maintain was the contrast of interest as both conditions comprised negative stimuli, therefore, the effects of regulating emotional state was contrasted with experiencing naturally (i.e., not trying to change or alter) the affective state elicited by negative images. To examine the relationship between sleep quality and regulation, we performed a regression analysis where Reappraise (>Maintain) was entered into a whole-brain analysis of covariance and each sleep measure was entered as a covariate of interest. To control for primary diagnosis gSAD, GAD, and MDD were dummy coded and entered as a covariate of no interest in all regression models.

Given *a priori* hypotheses involving frontal regions and evidence regions outside frontal areas are involved in reappraisal, significance was based on a large search volume (466,624 mm) comprising an MNI atlas-based emotion regulation mask (Tzourio-Mazoyer et al., 2002) consisting of bilateral dorsolateral PFC, dorsomedial PFC, dorsal anterior cingulate cortex, inferior frontal gyrus, ventrolateral PFC, limbic/paralimbic regions (e.g., amygdala, anterior insula), middle and superior temporal gyrus, parietal regions including angular gyrus, and inferior and superior occipital gyrus in light of recent meta-analyses (Buhle et al., 2014; Messina et al., 2015). To correct for multiple comparisons within this search volume, 3dClustSim (updated December 2015 [https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html], AFNI; Cox, 1996) was conducted via Monte Carlo simulations (10,000 iterations) and applied to second-level statistical results for a corrected $p<0.05$ alpha level with a height threshold of $p<0.005$. Results revealed the minimum cluster size for significant effects in Reappraise (>Maintain) was 75 voxels.

To illustrate the magnitude and direction of activation effects, and its associations with symptom severity, parameter estimates of peak activation for significant *a priori* findings (β

weights, arbitrary units [a.u.]) were extracted from spherical (10-mm diameter) regions of interest (ROI) from each participant and submitted to Pearson's correlations and scatter plots in SPSS. Of note, these correlations and scatter plots were performed for illustrative purposes as significance at the whole-brain level was already established.

To explore whether anxiety and/or depression symptoms influenced significant neural correlates of sleep quality in Reappraise (>Maintain), post-hoc stepwise linear regression analysis was performed in SPSS. The dependent variable consisted of neural activity extracted with a spherical ROI and independent variables comprised anxiety symptoms (HAM-A), depression symptoms (HAM-D), and the relevant sleep measure.

Results

Participants

Seventy-eight patients (70.5% [n=55] female) had mean ± S.D. age of 26.3±7.0 and educational level of 15.9±2.9. Regarding primary diagnosis 38 patients (48.7%) met criteria for gSAD, 19 (24.4%) had MDD, and 21 (26.9%) presented with GAD. Comorbid diagnoses included gSAD (25.6%), GAD (21.8%), MDD (19.2%), posttraumatic stress disorder (12.8%), and dysthymia (12.8%). Twenty-seven patients (34.6%) had two or more comorbid disorders. See Table 1 for all concurrent disorders and clinical and demographic characteristics. All but three patients were free of psychotropic medications and none were receiving concurrent psychotherapy.

Sleep Quality Characteristics

PSQI results revealed patients had a mean ± S.D. global score of 8.6±3.7 and that the majority of patients met criteria for problematic sleep as 74% (n=58) had a PSQI global score >5 (Buysse et al., 1989). Regarding objective sleep, the actigraph device was worn for an average of six consecutive days and nights and the rate of rejection of actigraph nights due to ambiguity or artifact was 6% on average (SD=10.7). Concerning simultaneous sleep diaries, 62 out of 78 participants were compliant. Actigraphy values showed average sleep efficiency was 83.1%±9.2%, duration was 6.6±0.95 hours, and WASO was 32.8±17.0 minutes. Findings are generally consistent with insomnia, which is commonly associated with sleep efficiency < 85%, duration < 6.5 hrs, and/or WASO >30 minutes (Schutte-Rodin, Broch, Buysse, Dorsey, & Sateia, 2008). While both subjective and objective measures of sleep signified poor sleep quality across patients, the PSQI global score did not correlate with actigraphy estimates of sleep efficiency (r=−0.11, p=0.34), duration (r=0.04, p=0.76), or WASO (r=0.07, p=0.54).

Sleep Measures and Symptom Relationships

Subjective—Evaluation of associations between the PSQI and symptom severity revealed the PSQI global score positively correlated with HAM-D (r=0.44, p<0.001) and HAM-A total scores (r=0.39, p<0.001).

Objective—Regarding actigraphy, HAM-D total scores were negatively associated with sleep efficiency (r=−0.26, p<0.02) and positively correlated with WASO (r=0.25, p<0.03).

There was no relationship between HAM-D and sleep duration (r=0.02, p=0.85). Also, no relationships were observed between HAM-A total scores and sleep efficiency (r=−0.04, p=0.76), WASO (r=−0.02, p=0.87) or sleep duration (r=0.04, p=0.75).

Subjective Affective Ratings in fMRI

Affective ratings for Reappraise, Maintain, and Look were submitted to a repeated measures ANOVA and the result was significant [F(2, 154)=200.24, p<0.001]. Follow-up two-tailed paired t-tests revealed more negative affect in Maintain (2.96±0.71) relative to Reappraise (2.58±0.69) [t(77)=4.71, p<0.001] and Look (1.38±0.51) [t(77)=16.84, p<0.001] conditions. Negative affect was also reported as greater in Reappraise when contrasted with looking at neutral images [t(77)=16.76, p<0.001].

Sleep Measures and Subjective Affective Ratings in fMRI

Pearson's correlations failed to show significant relationships between subjective and objective measures of sleep quality and 'on-line' affective state ratings in Reappraise (>Maintain); lowest p=0.18.

fMRI Results

Subjective/PSQI—Controlling for primary diagnosis in Reappraise (>Maintain), the log-transformed PSQI global score negatively corresponded with left dorsal ACC [(−10, 16, 30) z=3.28, k=146 volume=1168 mm^3] (r=−0.30, p<0.01) (Fig. 1). No positive relationships were observed. In SPSS, post-hoc stepwise regression analysis showed transformed PSQI global scores predicted DACC activity [R^2=0.10, F(1,76)=8.48, p<0.005] (B= −0.64; p<0.005) whereas HAM-D (B=−0.18, t=1.48, p=0.14) and HAM-A (B=−0.12, t=0.98, p=0.33) were excluded in the model.

Objective/Actigraphy Sleep Efficiency—Controlling for primary diagnosis in Reappraise (>Maintain), log-transformed sleep efficiency was negatively associated with right dorsal ACC activation [(6, 4, 28) z=3.37, k=76 volume=608 mm^3] (r=−0.29, p<0.01) (Fig. 2). No positive associations were detected. In SPSS, post-hoc stepwise regression analysis showed transformed sleep efficiency values significantly influenced DACC activity [R^2=0.12, F(1,76)=10.60, p<0.002] (B= −0.61; p<0.002). Again, HAM-D (B=−0.18, t=1.59, p=0.12) and HAM-A measures (B=−0.13, t=1.24, p=0.22) were excluded in the model.

Since DACC activity corresponded to both the PSQI global score and sleep efficiency, we conducted a two-tailed Fisher r-to-z transformation to test if correlation coefficients between the PSQI global score and corresponding DACC activity differed from that of sleep efficiency and DACC activity. Results indicated coefficients were analogous (z=0.11, p=0.91).

Regression analysis for actigraphy estimates of WASO and sleep duration revealed no significant effects in Reappraise (>Maintain) when controlling for diagnosis.

Discussion

To our knowledge this is the first study to examine the impact of naturalistic sleep on reappraise-related neurofunctional activity in a transdiagnostic sample of depressed and anxious patients. Regarding sleep quality both subjective sleep as indexed with the PSQI global score and objective sleep as assessed with actigraph indicated the majority of patients experienced clinically problematic sleep. Specifically, 74% of patients met criteria for sleep disturbance according to a conventional PSQI global score cutoff (Buysse et al., 1989) and actigraphy estimates of sleep efficiency, duration, and wake after sleep onset were generally consistent with insomnia (Schutte-Rodin et al., 2008).

However, despite evidence these measurements yielded comparable results insofar as discerning sleep disturbance was concerned, no significant relationships between the PSQI global score and objective/actigraphy measures were found. Therefore, it is reasonable to expect that differences between the PSQI global score and actigraphy indices of sleep would occur at the neural level. A validated emotion regulation paradigm was used to examine the influence of sleep quality on brain activity when reappraising aversive images relative to experiencing naturally the emotional state evoked by negative images (i.e., ‘Maintain’ condition). Affective ratings during fMRI confirmed patients were able to reduce negative affective state when instructed to reappraise. No significant correlations between affective state and sleep measures were observed suggesting sleep quality did not factor into self-reported regulation ability.

In support of our hypothesis, regression analysis with the PSQI global score revealed worse sleep was linked with less reappraise-related frontal activation. Specifically, dorsal anterior cingulate cortex (DACC) activity negatively corresponded with the PSQI global score when controlling for primary diagnosis. Notably, a similar PSQI-frontal relationship was reported in a previous emotion regulation study in healthy participants (Minkel et al., 2012). Thus, problematic sleep-regulation effects may occur in clinical and non-clinical populations potentially vulnerable to experiencing excessive/inappropriate negative mood given ties between poor sleep and risk of affective conditions (Ford & Kamerow, 1989; Gillin, 1998; Gregory et al., 2005).

Regarding actigraphy, sleep efficiency was the only measure to yield significant whole-brain regression findings, controlling for primary diagnosis. Sleep efficiency, commonly defined as the ratio of sleep duration to time spent in bed, plays a central role in insomnia (Reed & Sacco, 2016), which is consistent with the type of sleep difficulty observed in our patient sample. In contrast to the PSQI global score where high scores denote worse sleep, high sleep efficiency values signify better sleep. Although the negative relationship between sleep efficiency and anterior cingulate activity was not expected, varied DACC functions would appear to explain results.

Broadly, the DACC is part of a network encompassing cognitive, motor (i.e., action) execution, and related functional systems (Bush et al., 2000; Etkin et al., 2011). Relevant to our findings is the role DACC plays in automatic and controlled processes that underlie cognitive control (Shenhav et al., 2013). Regarding automaticity, the DACC engages

multiple sub-processes (e.g., attention, planning, working memory) to carry out goal-directed activities (Niendam et al., 2012) and these sub-processes are vulnerable to sleep-related decrements. For example, in studies of sleep restriction, impairment resulting from sleep loss has been shown to fall on a continuum where basic tasks (e.g., simple attention) are more negatively affected by less sleep than complex ones (Lim & Dinges, 2010). Even moderate levels of sleep deficiency, when chronic, impairs neurobehavioral functions in a dose-dependent manner (Van Dongen, Maislin, Mullington, & Dinges, 2003). Consequently, self-perceived poor sleep may relate to disruptions or lapses in the performance of certain sub-processes or in the mobilization of elementary functions that underlie cognitive control (Niendam et al., 2012). Put another way, the subjective sleep-DACC relationship suggests a deficient or inefficient response.

Conversely, evidence more DACC activity was predicted by less sleep efficiency implies a compensatory response that may pertain to controlled functions. For example, demanding situations (e.g., inhibiting response bias, set-shifting) recruit the DACC (Petersen & Posner, 2012; Shackman et al., 2011; Venkatraman & Huettel, 2012). Anxious and/or depressed individuals are characterized by emotion dysregulation (Zilverstand, Parvaz, & Goldstein, 2016) and problematic sleep as observed in our cohort. Therefore, reappraisal would present as an effortful task. As a result, enhanced DACC recruitment may be motivated by the taxing nature of reappraising mood-congruent (i.e., negative) stimuli to reduce negative affective state. Certainly, further study is necessary to understand interactions between subjective and objective sleep measures and DACC activity during emotion regulation.

Discrepancy between self-reported sleep and actigraphically recorded sleep were also evident in relation to symptom severity. Whereas, the PSQI global score positively correlated with depression and anxiety symptoms, relationships with actigraphy were circumscribed. Namely, depression symptoms negatively corresponded with sleep efficiency and was positively associated with wake after sleep onset. However, no relationships between actigraphy estimates of sleep and anxiety symptoms emerged and sleep duration was uncorrelated with symptom severity. Potentially, the PSQI more closely relates to the psychological component of sleep symptoms, hence, its robust associations with depression and anxiety symptoms.

In summary, findings have important implications in our understanding of sleep-emotion regulation interactions in clinical depression and anxiety disorders. First, at the behavioral level no significant relationships between self-report and actigraphy sleep measures were detected. Results are consistent with previous reports of disagreement between subjective and objective sleep measurements (Girschik et al., 2012; Mccall & Mccall, 2012; O'Brien et al., 2016; Van Den Berg et al., 2008; Van Ravesteyn et al., 2014) and suggest these approaches capture different aspects of the sleep experience. For example, the PSQI global score is frequently associated with psychological symptoms (e.g., depression, anxiety) suggesting a form of 'hyperarousal' may contribute to both problematic sleep and distress/misery (Buysse et al., 2008; Perlis, Smith, & Pigeon, 2005).

Extending this conceptualization to our neuroimaging data, it is plausible that the divergent reappraise-related DACC findings where worse self-perceived sleep and better objective

sleep efficiency both negatively corresponded with DACC activation reflect orthogonal dimensions of sleep symptoms. Variation in DACC activity, a region strongly involved in cognitive reappraisal (Buhle et al., 2014; Messina et al., 2015), may be explained by individual differences related to psychological factors and objective sleep-wake patterns when engaging in a cognitive approach to downregulate emotional reactivity to negative cues.

Furthermore, findings support the notion that sleep dysfunction is transdiagnostic and etiologically linked to various forms of psychopathology due in part to shared neurobiology between sleep systems and emotion regulation (Cox & Olatunji, 2016; Harvey, Murray, Chandler, & Soehner, 2011). That said, there was no comparative healthy control group or cohort comprising participants with sleep dysfunction but not psychopathology. Thus, further study is needed to disambiguate sleep-emotion regulation neurofunctional activity from psychopathology.

Other important limitations include the cross-sectional and correlational nature of our study, which does not permit inference that sleep disturbance led to altered regulatory brain function or vice versa. Second, we did not screen for sleep disorders. Third, 21% did not complete a sleep diary when actigraphy data was collected, therefore, sleep onset/offset could not be confirmed in these participants. Fourth, actigraphy involved 15-second epochs. Though limited research suggests this time window is consistent with ‘gold standard’ polysomnography sleep measures (Mantua, Gravel, & Spencer, 2016), earlier studies were validated with 30-second epochs (Marino et al., 2013). Lastly, there was no direct manipulation of sleep, therefore, results rely on indirect estimates of sleep quality.

Conclusions

Results suggest perceived sleep quality differs from objective parameters of sleep at the brain and behavioral level. Additionally, shared neurobiological substrates in sleep and cognitive reappraisal may explain disturbances in emotion regulation across anxiety and depression and thus could serve as a transdiagnostic target for therapeutic strategies (Harvey et al., 2011).

Acknowledgments

This work was supported by NIMH K23MH093679, Brain & Behavior Research Foundation (formerly NARSAD) Award, and University of Illinois at Chicago Campus Research Board Award (HK) and in part by NIMH R01MH101497 (KLP) and the Center for Clinical and Translational Research (CCTS) UL1RR029879. We would like to thank Dr. Runa Bhaumik who provided biostatistical consultation.

References

Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. Sleep. 2003; 26(3):342–392. [PubMed: 12749557]

Ball TM, Ramsawh HJ, Campbell-Sills L, Paulus MP, Stein MB. Prefrontal dysfunction during emotion regulation in generalized anxiety and panic disorders. Psychological Medicine. 2013; 43(7):1475–1486. https://doi.org/10.1017/S0033291712002383. [PubMed: 23111120]

Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. Biological Psychiatry. 1996; 39(6):411–418. https://doi.org/http://dx.doi.org/10.1016/0006-3223(95)00188-3. [PubMed: 8679786]

Buhle JT, Silvers JA, Wager TD, Lopez R, Onyemekwu C, Kober H, … Ochsner KN. Cognitive reappraisal of emotion: A meta-analysis of human neuroimaging studies. Cerebral Cortex (New York, NY: 1991). 2014; 24(11):2981–2990. https://doi.org/10.1093/cercor/bht154.

Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. Trends in Cognitive Sciences. 2000; 4(6):215–222. [PubMed: 10827444]

Buysse DJ, Hall ML, Strollo PJ, Kamarck TW, Owens J, Lee L, … Matthews KA. Relationships between the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and clinical/polysomnographic measures in a community sample. Journal of Clinical Sleep Medicine. 2008; 4(6):563–571. [PubMed: 19110886]

Buysse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Research. 1989; 28(2):193–213. https://doi.org/10.1016/0165-1781(89)90047-4. [PubMed: 2748771]

Cox RC, Olatunji BO. A systematic review of sleep disturbance in anxiety and related disorders. Journal of Anxiety Disorders. 2016; 37:104–129. https://doi.org/10.1016/j.janxdis.2015.12.001. [PubMed: 26745517]

Czeisler CA. Impact of sleepiness and sleep deficiency on public health--utility of biomarkers. Journal of Clinical Sleep Medicine. 2011; 7(5 Suppl):S6–8. https://doi.org/10.5664/JCSM.1340. [PubMed: 22003334]

Dillon DG, Pizzagalli DA. Evidence of successful modulation of brain activation and subjective experience during reappraisal of negative emotion in unmedicated depression. Psychiatry Research. 2013; 212(2):99–107. https://doi.org/10.1016/j.pscychresns.2013.01.001. [PubMed: 23570916]

Etkin A, Egner T, Kalisch R. Emotional processing in anterior cingulate and medial prefrontal cortex. Trends in Cognitive Sciences. 2011; 15(2):85–93. https://doi.org/10.1016/j.tics.2010.11.004. [PubMed: 21167765]

First, M., Spitzer, R., Gibbon, M., Williams, J. Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Edition (SCID-P), version 2. New York, NY: Biometrics Research; 1995.

Ford D, Kamerow D. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA Psychiatry. 1989; 262(11):1479–1484.

Gillin JC. Are sleep disturbances risk factors for anxiety, depressive and addictive disorders? Acta Psychiatrica Scandinavica Supplementum. 1998; 393:39–43. [PubMed: 9777046]

Girschik J, Fritschi L, Heyworth J, Waters F. Validation of self-reported sleep against actigraphy. Journal of Epidemiology. 2012; 22(5):462–468. [PubMed: 22850546]

Goldin P, Manber T, Hakimi S, Canli T, Gross JJ. Neural bases of social anxiety disorder: Emotional reactivity and cognitive regulation during social and physical threat. Archives of General Psychiatry. 2009; 66(2):170–180. https://doi.org/10.1001/archgenpsychiatry.2008.525. [PubMed: 19188539]

Goldin PR, Manber-Ball T, Werner K, Heimberg R, Gross JJ. Neural mechanisms of cognitive reappraisal of negative self-beliefs in social anxiety disorder. Biological Psychiatry. 2009; 66(12):1091–1099. https://doi.org/http://dx.doi.org/10.1016/j.biopsych.2009.07.014. [PubMed: 19717138]

Gregory AM, Caspi A, Eley TC, Moffitt TE, Oconnor TG, Poulton R. Prospective longitudinal associations between persistent sleep problems in childhood and anxiety and depression disorders in adulthood. Journal of Abnormal Child Psychology. 2005; 33(2):157–163. [PubMed: 15839494]

Gross JJ. Emotion regulation: Past, present, future. Cognition & Emotion. 1999; 13(5):551–573. https://doi.org/10.1080/026999399379186.

Gruber R, Cassoff J. The interplay between sleep and emotion regulation: Conceptual framework empirical evidence and future directions. Current Psychiatry Reports. 2014; 16(11):500. https://doi.org/10.1007/s11920-014-0500-x. [PubMed: 25200984]

Hamilton M. A rating scale for depression. Journal of Neurology, Neurosurgery, and Psychiatry. 1960; 23:56–62.

Hamilton M. The assessment of anxiety states by rating. British Journal of Medical Psychology. 1959; 32(1):50–55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x. [PubMed: 13638508]

Hariri AR, Mattay VS, Tessitore A, Fera F, Weinberger DR. Neocortical modulation of the amygdala response to fearful stimuli. Biological Psychiatry. 2003; 53(6):494–501. https://doi.org/10.1016/S0006-3223(02)01786-9. [PubMed: 12644354]

Harvey AG, Murray G, Chandler RA, Soehner A. Sleep disturbance as transdiagnostic: Consideration of neurobiological mechanisms. Clinical Psychology Review. 2011; 31(2):225–235. https://doi.org/10.1016/j.cpr.2010.04.003. [PubMed: 20471738]

Heller AS, Johnstone T, Peterson MJ, Kolden GG, Kalin NH, Davidson RJ. Increased prefrontal cortex activity during negative emotion regulation as a predictor of depression symptom severity trajectory over 6 months. JAMA Psychiatry. 2013; 70(11):1181–1189. https://doi.org/10.1001/jamapsychiatry.2013.2430. [PubMed: 24173657]

Johnstone T, van Reekum CM, Urry HL, Kalin NH, Davidson RJ. Failure to regulate: Counterproductive recruitment of top-down prefrontal-subcortical circuitry in major depression. The Journal of Neuroscience. 2007; 27(33):8877–8884. https://doi.org/10.1523/JNEUROSCI.2063-07.2007. [PubMed: 17699669]

Kanske P, Heissler J, Schönfelder S, Wessa M. Neural correlates of emotion regulation deficits in remitted depression: The influence of regulation strategy, habitual regulation use, and emotional valence. NeuroImage. 2012; 61(3):686–693. https://doi.org/10.1016/j.neuroimage.2012.03.089. [PubMed: 22613776]

Lang, PJ., Bradley, MM., Cuthbert, BN. International affective picture system (IAPS): affective ratings of pictures and instruction manual. Gainesville, FL: University of Florida; 2008. (Technical Report A-8)

LeBlanc M, Beaulieu-Bonneau S, Mérette C, Savard J, Ivers H, Morin CM. Psychological and health-related quality of life factors associated with insomnia in a population-based sample. Journal of Psychosomatic Research. 2007; 63(2):157–166. https://doi.org/10.1016/j.jpsychores.2007.03.004. [PubMed: 17662752]

Leech, L., Barrett, K., Moran, A. SPSS for intermediate statistics: use and interpretation. 2. Mahwah, N.J: Lawrence Erlbaum Associates; 2005.

Lim J, Dinges DF. A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. Psychological Bulletin. 2010; 136(3):375–389. https://doi.org/10.1037/a0018883. [PubMed: 20438143]

MacNamara A, Rabinak CA, Kennedy AE, Fitzgerald DA, Liberzon I, Stein MB, Phan KL. Emotion regulatory brain function and SSRI treatment in PTSD: Neural correlates and predictors of change. Neuropsychopharmacology. 2016; 41(2):611–618. https://doi.org/http://dx.doi.org/10.1038/npp.2015.190. [PubMed: 26111649]

Mantua J, Gravel N, Spencer R. Reliability of sleep measures from four personal health monitoring devices compared to research-based actigraphy and polysomnography. Sensors. 2016; 16(5):646. https://doi.org/10.3390/s16050646.

Marino M, Li Y, Rueschman MN, Winkelman JW, Ellenbogen JM, Solet JM, … Buxton OM. Measuring sleep: Accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. Sleep. 2013; 36(11):1747–1755. https://doi.org/10.5665/sleep.3142. [PubMed: 24179309]

Martin JL, Hakim AD. Wrist actigraphy. Chest. 2011; 139(6):1514–1527. https://doi.org/10.1378/chest.10-1872. [PubMed: 21652563]

Mccall C, Mccall WV. Comparison of actigraphy with polysomnography and sleep logs in depressed insomniacs: Actigraphy, PSG and sleep logs in depressed insomniacs. Journal of Sleep Research. 2012; 21(1):122–127. https://doi.org/10.1111/j.1365-2869.2011.00917.x. [PubMed: 21447050]

Messina I, Bianco S, Sambin M, Viviani R. Executive and semantic processes in reappraisal of negative stimuli: Insights from a meta-analysis of neuroimaging studies. Frontiers in Psychology. 2015; 6:956. https://doi.org/10.3389/fpsyg.2015.00956. [PubMed: 26217277]

Minkel JD, McNealy K, Gianaros PJ, Drabant EM, Gross JJ, Manuck SB, Hariri AR. Sleep quality and neural circuit function supporting emotion regulation. Biology of Mood & Anxiety Disorders. 2012; 2:22. https://doi.org/10.1186/2045-5380-2-22. [PubMed: 23216889]

Mollayeva T, Thurairajah P, Burton K, Mollayeva S, Shapiro CM, Colantonio A. The Pittsburgh sleep quality index as a screening tool for sleep dysfunction in clinical and non-clinical samples: A systematic review and meta-analysis. Sleep Medicine Reviews. 2016; 25:52–73. https://doi.org/10.1016/j.smrv.2015.01.009. [PubMed: 26163057]

Motomura Y, Kitamura S, Oba K, Terasawa Y, Enomoto M, Katayose Y, … Mishima K. Sleep debt elicits negative emotional reaction through diminished amygdala-anterior cingulate functional connectivity. PloS One. 2013; 8(2):e56578. https://doi.org/10.1371/journal.pone.0056578. [PubMed: 23418586]

New AS, Fan J, Murrough JW, Liu X, Liebman RE, Guise KG, … Charney DS. A functional magnetic resonance imaging study of deliberate emotion regulation in resilience and posttraumatic stress disorder. Biological Psychiatry. 2009; 66(7):656–664. https://doi.org/10.1016/j.biopsych.2009.05.020. [PubMed: 19589502]

Niendam TA, Laird AR, Ray KL, Dean YM, Glahn DC, Carter CS. Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. Cognitive, Affective & Behavioral Neuroscience. 2012; 12(2):241–268. https://doi.org/10.3758/s13415-011-0083-5.

O'Brien E, Hart C, Wing RR. Discrepancies between self-reported usual sleep duration and objective measures of total sleep time in treatment-seeking overweight and obese individuals. Behavioral Sleep Medicine. 2016; 14(5):539–549. https://doi.org/10.1080/15402002.2015.1048447. [PubMed: 26503348]

Ochsner KN, Bunge SA, Gross JJ, Gabrieli JDE. Rethinking feelings: An fMRI study of the cognitive regulation of emotion. Journal of Cognitive Neuroscience. 2002; 14(8):1215–1229. https://doi.org/10.1162/089892902760807212. [PubMed: 12495527]

Ohayon MM, Roth T. Place of chronic insomnia in the course of depressive and anxiety disorders. Journal of Psychiatric Research. 2003; 37(1):9–15. [PubMed: 12482465]

Peat, J., Barton, B. Medical Statistics: A guide to data analysis and critical appraisal. Blackwell Publishing; 2005.

Perlis, ML., Smith, MT., Pigeon, WR. Etiology and pathophysiology of insomnia. In: Kryger, MH.Roth, T., Dement, WC., editors. Principles and practice of sleep medicine. 4. Philadelphia: Elsevier Saunders; 2005. p. 714-725.

Petersen SE, Posner MI. The attention system of the human brain: 20 years after. Annual Review of Neuroscience. 2012; 35:73–89. https://doi.org/10.1146/annurev-neuro-062111-150525.

Phan KL, Fitzgerald DA, Nathan PJ, Moore GJ, Uhde TW, Tancer ME. Neural substrates for voluntary suppression of negative affect: A functional magnetic resonance imaging study. Biological Psychiatry. 2005; 57(3):210–219. https://doi.org/10.1016/j.biopsych.2004.10.030. [PubMed: 15691521]

Rabinak CA, MacNamara A, Kennedy AE, Angstadt M, Stein MB, Liberzon I, Phan KL. Focal and aberrant prefrontal engagement during emotion regulation in veterans with posttraumatic stress disorder. Depression and Anxiety. 2014; 31(10):851–861. https://doi.org/10.1002/da.22243. [PubMed: 24677490]

Reed DL, Sacco WP. Measuring sleep efficiency: What should the denominator be? Journal of Clinical Sleep Medicine. 2016; 12(2):263–266. https://doi.org/10.5664/jcsm.5498. [PubMed: 26194727]

Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. Journal of Clinical Sleep Medicine. 2008; 4(5):487–504. [PubMed: 18853708]

Shackman AJ, Salomons TV, Slagter HA, Fox AS, Winter JJ, Davidson RJ. The integration of negative affect, pain and cognitive control in the cingulate cortex. Nature Reviews Neuroscience. 2011; 12(3):154–167. https://doi.org/10.1038/nrn2994. [PubMed: 21331082]

Shenhav A, Botvinick MM, Cohen JD. The expected value of control: An integrative theory of anterior cingulate cortex function. Neuron. 2013; 79(2):217–240. https://doi.org/10.1016/j.neuron.2013.07.007. [PubMed: 23889930]

Smoski MJ, Keng SL, Schiller CE, Minkel J, Dichter GS. Neural mechanisms of cognitive reappraisal in remitted major depressive disorder. Journal of Affective Disorders. 2013; 151(1):171–177. https://doi.org/10.1016/j.jad.2013.05.073. [PubMed: 23796796]

Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, … Joliot M. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage. 2002; 15(1):273–289. https://doi.org/10.1006/nimg.2001.0978. [PubMed: 11771995]

Van Den Berg JF, Van Rooij FJA, Vos H, Tulen JHM, Hofman A, Miedema HME, … Tiemeier H. Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. Journal of Sleep Research. 2008; 17(3):295–302. https://doi.org/10.1111/j.1365-2869.2008.00638.x. [PubMed: 18321246]

Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: Dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. SLEEP. 2003; 26(2):117–126. [PubMed: 12683469]

Van Ravesteyn, LM., Tulen, JHM., Kamperman, AM., Raats, ME., Schneider (Tom), AJ., Birnie, E., … Lambregtse–van den Berg, MP. Perceived sleep quality is worse than objective parameters of sleep in pregnant women with a mental disorder. Journal of Clinical Sleep Medicine. 2014. https://doi.org/10.5664/jcsm.4118

Venkatraman V, Huettel SA. Strategic control in decision-making under uncertainty. The European Journal of Neuroscience. 2012; 35(7):1075–1082. https://doi.org/10.1111/j.1460-9568.2012.08009.x. [PubMed: 22487037]

Yoo SS, Gujar N, Hu P, Jolesz FA, Walker MP. The human emotional brain without sleep--a prefrontal amygdala disconnect. Current Biology: CB. 2007; 17(20):R877–878. https://doi.org/10.1016/j.cub.2007.08.007. [PubMed: 17956744]

Zilverstand, A., Parvaz, MA., Goldstein, RZ. Neuroimaging cognitive reappraisal in clinical populations to define neural targets for enhancing emotion regulation. A systematic review. NeuroImage. 2016. https://doi.org/10.1016/j.neuroimage.2016.06.009

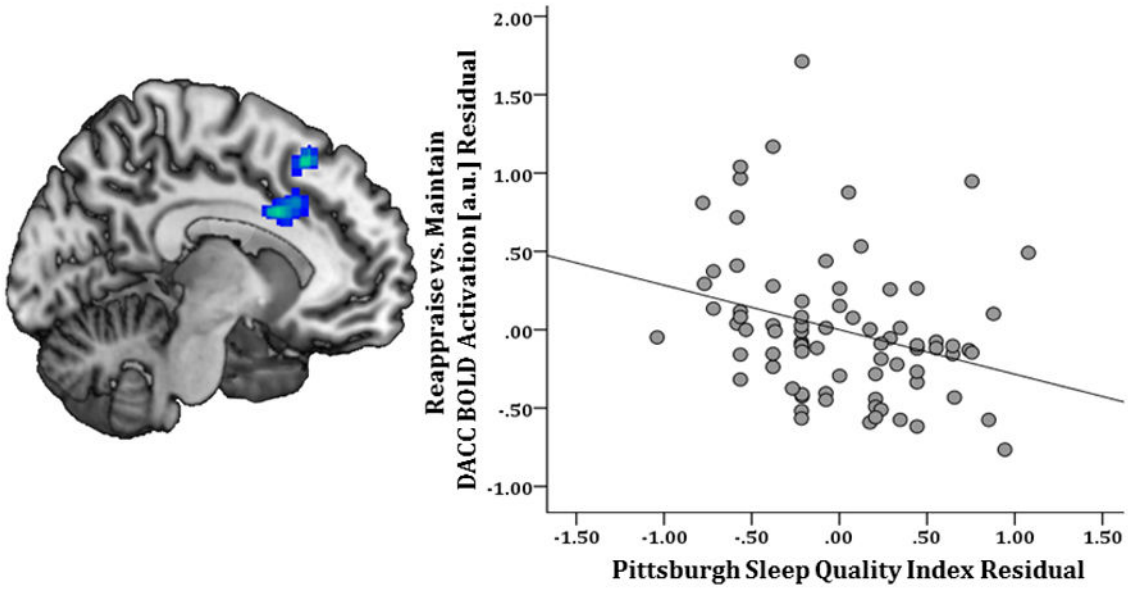

Figure 1.

Regressing global PSQI global scores (log-transformed) while controlling for diagnosis as a regressor of no interest. Brain map depicts whole-brain analysis of covariance ($p<0.005$ uncorrected) showing dorsal anterior cingulate cortex (DACC) in patients as denoted by negative parameter estimates of activation based on Reappraise (>Maintain). B) Scatter plot of the regression analysis in Reappraise (>Maintain) depicting extracted parameter estimates of activation from DACC showing higher raw PSQI global scores corresponded with less DACC activation.

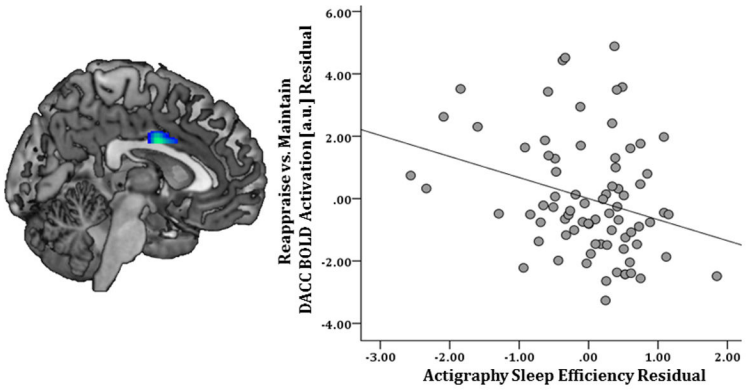

Figure 2.

Regressing actigraphy sleep efficiency scores (log-transformed) while controlling for diagnosis as a regressor of no interest. Brain map depicts whole-brain analysis of covariance ($p<0.005$ uncorrected) showing dorsal anterior cingulate cortex (DACC) in patients as indicated by negative parameter estimates of activation based on Reappraise (>Maintain). B) Scatter plot of the regression analysis in Reappraise (>Maintain) illustrating extracted parameter estimates of activation from DACC showing lower raw sleep efficiency scores corresponded with more DACC activation.

PSQI, Pittsburg Sleep Quality Index

Table 1

Demographic and clinical characteristics

Comorbidity	**N**	**%**
gSAD	20	25.6%
GAD	17	21.8%
MDD	15	19.2%
Posttraumatic Stress Disorder	10	12.8%
Specific Phobia	7	9.0%
Panic Disorder	7	9.0%
Dysthymia	10	12.8%
Binge Eating Disorder	2	2.6%
Obsessive Compulsive Disorder	2	2.6%
Alcohol Abuse	1	1.3%
Acute Adjustment Disorder	1	1.3%
Two or more concurrent diagnoses	27	34.6%
Handedness	**N**	**%**
Right	69	88.5%
Left	9	11.5%
Race/Ethnicity	**N=78**	**%**
Caucasian	54	69.2%
Asian	12	15.4%
African American	5	6.4%
More than one race	6	7.7%
Hispanic	19	24%
Unknown or other than Caucasian, Asian, African American, or Hispanic	1	1.3%