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Sleep quality and adolescent default mode network connectivity

Sarah M. Tashjian,[1] Diane Goldenberg,[1] Martin M. Monti,[1,2] and Adriana Galván[1,2]

[1]Department of Psychology, and [2]Brain Research Institute, University of California, Los Angeles, Los Angeles, CA 90095, USA

Correspondence should be addressed to Adriana Galván, Department of Psychology, University of California, 1285 Franz Hall, Los Angeles, CA 90095-1563, USA. E-mail: agalvan@ucla.edu

Abstract

Sleep suffers during adolescence and is related to academic, emotional and social behaviors. How this normative change relates to ongoing brain development remains unresolved. The default mode network (DMN), a large-scale brain network important for complex cognition and socioemotional processing, undergoes intra-network integration and inter-network segregation during adolescence. Using resting state functional connectivity and actigraphy over 14 days, we examined correlates of naturalistic individual differences in sleep duration and quality in the DMN at rest in 45 human adolescents (ages 14–18). Variation in sleep quality, but not duration, was related to weaker intrinsic DMN connectivity, such that those with worse quality sleep evinced weaker intra-network connectivity at rest. These novel findings suggest sleep quality, a relatively unexplored sleep index, is related to adolescent brain function in a network that contributes to behavioral maturation and undergoes development during adolescence.

Key words: adolescence; actigraphy; fMRI; resting state; sleep quality

Introduction

Sleep is essential for survival and plays an important role in supporting healthy brain development. Growing public and scientific concern has focused on a 'sleep deprivation epidemic' in human adolescents (Leger *et al.*, 2012; NSF, 2014). Research has revealed detrimental consequences of insufficient sleep duration on adolescent health, academics, clinical outcomes and safety (Carskadon, 2011a); however, differences in sleep quality remain relatively unexplored. Further, surprisingly little work has explored the association between adolescent sleep and functional connectivity in large-scale brain networks, which undergo fundamental development throughout adolescence. In this study, we collected objective measures of sleep and functional magnetic resonance imaging (fMRI) scans to identify the association between sleep (duration and quality) and intrinsic connectivity in the default mode network (DMN) in the adolescent brain.

Sleep during adolescence

Adolescent sleep deficiencies are rooted in biological and psychosocial changes (Carskadon, 2011b). Biological alterations during puberty contribute to a sleep phase delay, shifting the body's internal clock and making it more difficult for adolescents to fall asleep before 11 p.m. (Hagenauer *et al.*, 2009). Sleep phase delay pushes bed times later while school start times force early wake times, leading to shorter nighttime sleep durations compared to pre-puberty (Hagenauer and Lee, 2012). Psychosocial factors such as socializing (Arora *et al.*, 2014) and studying (Adam *et al.*, 2007) often exacerbate sleep loss among adolescents. Although these sleep alterations are normative,

persistent sleep deficiency and subsequent sleepiness have negative impacts on adolescent cognition, mood, health and safety (Owens *et al.*, 2014).

Insufficient sleep is also associated with alterations in neural functioning, whereby poorer self-reported sleep quality has been associated with less dorsolateral prefrontal cortex activation during cognitive control (Telzer *et al.*, 2013) and self-reported sleep duration variability has been associated with lower white matter integrity longitudinally (Telzer *et al.*, 2015). In adolescents and adults, shorter self-reported sleep duration interacts with stress and neural activity to result in greater risk-taking under conditions of high stress (Uy and Galván, 2017). Although these studies raised the importance of studying adolescent sleep and neural functioning, they were limited in that they did not use objective measures such as actigraphy, a non-invasive method of monitoring human rest/activity cycles, to assay normative sleep. In two studies using four days of actigraphy, increased weekend sleep duration and quality were associated with greater ventral striatum activation to reward (Holm *et al.*, 2009) and greater shifts between weekend and weekday sleep was associated with reduced striatal and prefrontal activation to reward (Hasler *et al.*, 2012). In a recent study using the current sample of participants, the DMN was functionally coupled to a greater extent with non-DMN regions of the prefrontal cortex during a go/no-go response inhibition task in adolescents, who had worse sleep quality as assessed by actigraphy over a 2-week period (Tashjian *et al.*, 2017). The extent of this coupling buffered against self-reported impulsivity. That study did not probe differences in intrinsic functional connectivity within large-scale brain networks. In the present study, we measured four key facets of nighttime sleep over a 2-week period to address sleep-related functional connectivity within the DMN at rest.

Default mode network

The DMN is a large-scale functional brain network anatomically identified as anterior-posterior midline regions of the medial prefrontal cortex (mPFC) (ventromedial PFC, anterior cingulate cortex), the medial parietal cortex (posterior cingulate cortex [PCC], precuneus, retrosplenial cortex) and lateral temporo-parietal cortex (supramarginal gyrus, angular gyrus, superior temporal sulcus) (Fox and Raichle, 2007). The PCC is widely regarded as the central node of the network (Fransson and Marrelec, 2008; Utevsky *et al.*, 2014). In children and adolescents, a similar network has been identified with some reports of additional regions compared to adults (e.g. Fair *et al.*, 2009; Sherman *et al.*, 2014).

The DMN is characterized by a high level of resting metabolic activity, which typically decreases during cognitively demanding tasks (Raichle *et al.*, 2001; Andrews-Hanna *et al.*, 2010; Anticevic *et al.*, 2012). Robust correlations within the DMN at rest suggest that the network is functionally connected (Greicius *et al.*, 2003; Fox and Raichle, 2007; Buckner *et al.*, 2008). Investigating intrinsic connectivity during rest identifies interacting brain regions within the DMN independent of task-induced differences in activation. Disruption of this intrinsic connectivity has been identified as a distinctive feature of numerous psychiatric and neurological diseases (Buckner *et al.*, 2008; Broyd *et al.*, 2009; Schreiner *et al.*, 2014; Zhang and Raichle, 2010). Weaker connectivity within the DMN at rest has also been linked to social deficits in individuals with autism (Yerys *et al.*, 2015) and schizophrenia (Fox *et al.*, 2017). Prior work indicates the strength of intra-network functional connectivity at rest is relevant for the way the DMN behaves during task as well as for task performance. For example, Hampson *et al.* (2006)

found that greater resting state connectivity within the DMN was positively correlated with performance and greater DMN intra-network connectivity during a working memory task. Together, this work highlights the importance of intrinsic functional connectivity within the DMN and calls for investigating potential reasons for differences in DMN connectivity.

Most knowledge of the DMN is based on studies with adults, but emerging evidence suggests the DMN undergoes significant maturation during adolescence. Using longitudinal designs, Sherman *et al.* (2014), found increased resting state connectivity within the DMN in youth from age 10–13 years, and Horowitz-Kraus *et al.* (2017) found increased and more diffuse deactivation of the DMN during a narrative comprehension task at age 18 compared to age 11. From childhood to adulthood, DMN resting-state functional connectivity becomes more integrated as correlations among network nodes strengthen (Fair *et al.*, 2008) and this intra-network integration is accompanied by inter-network segregation, both of which have important implications for the development of complex cognition (Fair *et al.*, 2009). Stevens *et al.* (2009) observed these same developmental changes using independent components analysis to assess resting state networks in a study of 12- to 30-year-olds. Given the broad importance of the DMN (e.g. implications in cognition and social functioning), identifying environmental factors (e.g. sleep) related to DMN connectivity may be a critical step in understanding brain-based contributors to adolescent behavior.

Sleep and the default mode network

Regions of the DMN decouple during deep sleep (Horovitz *et al.*, 2009), signifying connectivity in this network may support certain states of consciousness (Vanhaudenhuyse *et al.*, 2010). In adults, resting state DMN connectivity is reduced following experimental sleep deprivation compared to connectivity after a night of normal sleep, suggesting intrinsic connectivity in the DMN may be vulnerable to extreme alterations in sleep behavior (De Havas *et al.*, 2012). The bulk of prior sleep-brain associations in adults and children have been characterized in clinical populations (Drummond *et al.*, 2013) or with experimental sleep restriction (Beebe *et al.*, 2009), both of which fail to capture the naturalistic pattern of adolescent sleep as related to brain function. In contrast, the current study measured sleep over the course of 2 weeks to capture typical sleep patterns rather than relying on exaggerated differences in sleep imposed by experimental deprivation methods. Studies that explore the relation between naturalistic sleep and the brain have used self-report and focused on specific neural regions activated by a task (e.g. Telzer *et al.*, 2013), leaving intrinsic neural network functioning unexplored. Additionally, although prior adult research is valuable, the association between sleep and adolescent DMN connectivity may differ because the adult DMN is relatively mature (more integrated and more segregated from other networks) compared to children and adolescents. Further, changes in sleep patterns during adolescence can be dramatic, but are normative, and the adolescent brain is plastic (Spear, 2013; Fuhrmann *et al.*, 2015), which may lead to differences in how sleep deficiencies relate to DMN connectivity in adolescents compared to adults. Thus, the association between normative sleep and adolescent DMN connectivity remains unclear.

Current study

The present study combines actigraphy measures of normative sleep duration and quality with fMRI resting state functional

connectivity analyses to investigate links between sleep and DMN connectivity in a sample of 55 adolescents ages 14–18. Insufficient nighttime sleep has been documented as more pervasive during the transition to high school (NSF, 2014; Winsler *et al.*, 2015), and, thus, we focused on high-school individuals. Based on prior literature indicating DMN connectivity is weaker after experimental sleep restriction, we hypothesized that shorter sleep durations and worse sleep quality (i.e. less efficiency, greater nighttime awakenings, and longer duration of nighttime awakenings) would relate to weaker intra-network resting state connectivity between the PCC and other central regions of the DMN. Given that objective measures of sleep quality are lacking in literature exploring adolescent sleep and brain function, we did not have hypotheses as to whether sleep duration or sleep quality would be a better predictor of DMN connectivity.

Materials and methods

Participants

Data were collected for 59 adolescents (29 female, M_{Age} = 16.31 years, s.d. = 1.12, range = 14–18 years). Two adolescents were excluded from the fMRI scan due to a metal implant and self-reported attention-deficit hyperactivity disorder (ADHD) diagnosis, respectively. One adolescent taking psychotropic medications and one adolescent whose motion parameters exceeded 2.0 mm based on absolute displacement for any frame were excluded from analyses. Data are presented for 55 adolescents (28 female, M_{Age}=16.22 years, s.d. = 1.12, range = 14–18 years). Males and females did not differ on age (females M_{Age} = 16.25, s.d. = 1.00, range = 14–18 years; males M_{Age} = 16.20 years, s.d. = 1.24, range = 14–18 years).

Procedures

Inclusion criteria required all participants be right handed, free of metal and speak fluent English. Exclusion criteria included having no previously diagnosed sleep, psychiatric, neurological or developmental disorders, as determined by parent self-report. Participants' eligibility was determined by a phone screening with a parent. Participants completed written consent and assent in accordance with the university's Institutional Review Board and were compensated for their participation.

Initial study visits took place in the participants' homes during which participants were trained on use of the actigraph watch and completed questionnaires. Approximately 3 weeks following the home visit, participants underwent an MRI scan at the laboratory.

Participant sleep data included in this sample have been published elsewhere, in a study addressing a separate research question (Tashjian *et al.*, 2017). The resting state functional connectivity data presented here have not been previously published.

Sleep

Sleep indices were tracked using a Micro Motionlogger® Sleep Watch actigraph by Ambulatory Monitoring, Incorporated (AMI). Each participant was instructed to wear the actigraph device on their non-dominant wrist at night for 14 days. Adolescents' body movement during nighttime sleep was monitored in 1 min epochs using zero crossing mode. Adolescents were asked to push the event marker button when they turned off the lights to go to sleep and again when they got out of bed in the morning. Adolescent reports of sleep and wake times were collected via daily text messages. The in-bed period began at the time of the first event marker indicating when participants turned off the lights to go to sleep and ended at the time when the participant awoke in the morning. If event markers were not available for a particular night, adolescent report was used. Sleep onset time was not recorded until the first of at least three consecutive minutes of sleep and sleep offset time was recorded at last five or more consecutive minutes of sleep. Significant discrepancies in adolescent report and the actigraph record were reconciled by discussion between two trained coders using additional indices of sleep onset and offset (e.g. light monitoring, time stamps). Each nightly record was scored using validated AMI algorithms (Sadeh, Action4 software package) for the portion indicated as nighttime sleep (sleep onset to offset). Actigraphy has been validated for use in adolescent populations (Sadeh *et al.*, 1994; Acebo *et al.*, 1999) and as a reliable assessment of sleep disruption when compared with polysomnography (Sadeh *et al.*, 1994; Marino *et al.*, 2013).

Actigraphy data was used to calculate four sleep indices of interest: *sleep duration*, *sleep efficiency, number of awakenings*, and *duration of awakenings*. Sleep duration was calculated by averaging across the 14 days the number minutes of sleep attained each night from the time adolescents fell asleep to the time they awoke the next morning (average number of days collected per participant M = 13.69 days, s.d. = 2.43). Consistent with standard use of sleep duration, this measurement included times when participants experienced nighttime awakenings. Sleep efficiency was calculated as the percentage of time spent asleep each night (time asleep/sleep duration), with larger percentages reflecting greater sleep efficiency. Number of awakenings experienced each night were averaged across the 14-day duration of the study. For each night, average duration of the awakenings was multiplied by the number of awakenings and then these durations were averaged across the study to calculate a single average of duration of awakenings for each participant.

Principal component analysis

To limit concerns related to multiple comparisons, three of the four sleep items were reduced using principal component analysis (PCA). Sleep duration was not correlated with the other variables of interest (Table 1), and thus was considered separately using the raw, demeaned sleep duration values for each participant. For sleep efficiency, number of awakenings, and duration of awakenings, several well-recognized criteria for using PCA were assessed. First, the items were highly correlated (Table 1). The Kaiser-Meyer-Olkin measure of sampling adequacy was .57, above the commonly recommended value of .50, and Bartlett's

Table 1. Correlations among variables of interest

Variable	1	2	3	4	5	6
1. Age	—					
2. Sex[a]	.03	—				
3. 14-day sleep duration	−.28*	.38**	—			
4. 14-day sleep efficiency	.17	.33*	.22	—		
5. 14-day number of awakenings	−.01	−.28*	−.02	−.51***	—	
6. 14-day duration of awakenings	−.18	−.26	−.02	−.89***	.68***	—

Note: N = 55.
[a]Sex scored as 0 = male, 1 = female.
*P < .05, **P < .01, ***P < .001.

test of sphericity was significant ($\chi^2(3) = 118.19$, P < .001). The diagonals of the anti-image correlation matrix were all over .5. Given these indicators, PCA was deemed to be suitable. PCA with variance maximizing (varimax) rotation was used to identify and compute composite scores for the components underlying these three sleep metrics. Components were extracted with eigenvalues greater than 1. Component scores ranged from −1.28 to 3.14, skew = 1.60 (SE = .32), kurtosis = 2.48 (SE = .63).

One component emerged explaining 79.97% of the variance. All items met a minimum criterion of having a primary loading of .5 or above and no item had a cross loading of .3 or above. These analyses indicated that one distinct component was underlying adolescent sleep efficiency, number of awakenings and duration of awakenings. Given the component loadings, sleep efficiency (−.91), number of awakenings (.80), and duration of awakenings (.97), we interpreted this component as poor sleep quality (higher scores = worse quality). Regression scores for this component were calculated and used as demeaned explanatory variables in fMRI analyses.

To assess intra-individual variability in sleep quality across the 14 days, we conducted a separate PCA using standard deviation (s.d.) of sleep efficiency, s.d. of number of awakenings and s.d. of duration of awakenings. The Kaiser-Meyer-Olkin measure of sampling adequacy, Bartlett's test of sphericity and diagonals of the anti-image correlation matrix indicated that PCA was suitable. One component emerged explaining 68.20% of the variance (loadings: s.d. sleep efficiency [.97], s.d. number of awakenings [.42] and s.d. duration of awakenings [.97]). Regression scores for this component were calculated and used as demeaned explanatory variables in fMRI analyses.

Resting state fMRI paradigm

At the conclusion of actigraphy data collection, participants completed a resting state scan. They were instructed to lie still and relax in the scanner with their eyes open and focused on a white fixation cross presented in the center of a black screen. Resting state fMRI data were collected for 5 min and 6 s.

Resting state fMRI data acquisition and analysis

Resting state fMRI data acquisition. The scan was conducted on a Siemens 3T TIM Trio MRI scanner with a 32-channel head coil. Parameters for image acquisition were voxel size = 3.8 × 3.8 × 3.8 mm, slices = 33, slice thickness = 3.8 mm, repetition time = 2000 ms, echo time = 30 ms, flip angle = 90°, interleaved slice geometry, field of view = 240 mm, 146 volumes.

Resting state fMRI data analysis. The first 7 volumes were discarded to ensure magnet stabilization. Preprocessing was conducted using FEAT (FMRI Expert Analysis Tool) version 6.00, part of FSL (FMRIB Software Library, www.fmrib.ox.ac.uk/fsl). Preprocessing consisted of slice timing correction, non-brain removal using BET, high-pass filtering below 0.008 Hz and spatial smoothing using a Gaussian kernel of FWHM 5 mm. Rigid body motion correction with six degrees of freedom (df), the six backward temporal derivatives of those regressors and the squares of the 12 resulting regressors was performed using MCFLIRT for a total of 24 nuisance regressors and additional individual spike regressors created using FSL Motion Outliers. The threshold used to define an outlier in FSL Motion Outliers is the upper one used when creating boxplots (75th percentile + 1.5 times InterQuartile Range). Of 146 volumes, participants had on average 8.31 (5.69%) spike regressors (s.d. =

4.34 [2.97%], range 3–20 [2.05%–13.70%]). In order to address whether motion was related to connectivity after processing, we correlated the average beta weights from the negative connectivity analysis with average absolute motion, $r(55) = −.14$, P = .30, and number of spike regressors, $r(55) = −.12$, P = .38, and neither were significant.

The time series from white matter and cerebrospinal fluid voxels were also regressed. Each participant's functional data were registered to their anatomical scans using linear registration with seven df and further registered to MNI (Montreal Neurological Institute) stereotaxic space with 12 df using FSL's registration method FLIRT. Alignment was visually confirmed for all participants.

Resting state fMRI data analysis. To target the DMN, we employed a seed-based functional connectivity analysis selecting a precuneus/PCC seed based on prior work identifying this region as the central node of the DMN (Fransson and Marrelec, 2008; Utevsky *et al.*, 2014). Following the recommendations of Kriegeskorte *et al.* (2009), the DMN region of interest (ROI) used in this study was defined independently from the current fMRI data and created in MNI space (8 mm^3; $x = 0$, $y = −52$, $z = 22$; Figure 1) based on findings from Allen *et al.* (2011). We chose this seed because the wide age range of participants in that study was inclusive of older adolescents (12–71 years, $M_{age} = 23.4$ years). This standard-space ROI was transformed to individual functional space using FLIRT, and the average time course of all voxels within the individual's ROI were extracted using *fslmeans* and then correlated with every other voxel in the brain to generate individual connectivity maps of the DMN. This whole-brain analysis was restricted to only voxels within the adolescent-specific DMN mask from Sherman *et al.* (2014). To generate a single group connectivity map, voxelwise statistics were carried out using FSL Randomise with 5000 permutations. To examine the possible association between sleep and individual differences in intrinsic DMN connectivity, we used Randomise to perform a single-group average with additional covariate design relating the two sleep variables of interest (sleep duration and the poor sleep quality PCA component) to connectivity between the PCC and other brain regions of the DMN as constrained by the DMN mask from Sherman *et al.* (2014). Sleep variables were demeaned and individually entered as regressors in two separate GLM models in FSL. Randomise uses a permutation-based statistical inference that does not rely on a Gaussian distribution (Nichols and Holmes, 2002). A statistical threshold of P < .05, corrected for multiple comparisons with familywise error correction (FWE) and threshold-free cluster enhancement (TFCE), was used for all analyses. TFCE
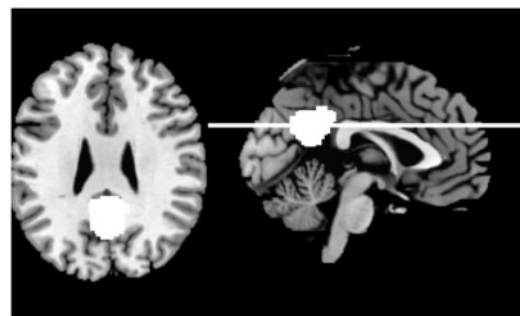

Fig. 1. PCC/precuneus seed (white) created in MNI space (8 mm^3; $x = 0$, $y = −52$, $z = 22$) based on findings from Allen *et al.* (2011).

helps identify significant clusters without defining an initial cluster-forming threshold or carrying out a large amount of data smoothing (Smith and Nichols, 2009). MRIcron software was used for visualization.

Results

Descriptives

On weekdays, adolescents went to bed at 11:49 p.m. on average (range 9:30 p.m.–3:42 a.m.) and woke up at 7:14 a.m. (range 5:15 a.m.–10:00 a.m.). On weekends, adolescents went to bed at 12:34 a.m. on average (range 11:10 p.m.–3:38 a.m.) and woke up at 8:44 a.m. (range 6:25 a.m.– 11:38 a.m.). Adolescents attained an average of 418.98 min (6.98 h) of sleep per night, including both weekdays and weekends (Table 2). Only six participants achieved the recommended sleep duration of 8+ hours on average, with only four participants achieving this duration on weekdays and 15 on weekends. On average, participants slept 37.39 min longer (s.d. 67.41) on weekends than on weekdays, had 1.15 (s.d. 3.76) more awakenings, and duration of awakenings were 2.20 min (s.d. 19.70) longer. We did not obtain any weekend information from two participants.

Independent samples t-tests revealed significant sex differences for all sleep variables (average sleep duration, $t(53) = -3.01$, $P = .004$, $d = .81$; average sleep efficiency, $t(53) = -2.55$, $P = .01$, $d = .69$; average number of awakenings, $t(53) = 2.09$, $P = .04$, $d = .56$) except average duration of awakenings ($t(53) = 1.93$, $P = .06$, $d = .52$), such that females attained better sleep (e.g. longer duration, less awakenings) than males. Only sleep duration and sleep efficiency remained significant after controlling for multiple comparisons $P = .05/4$, $P = .0125$.

Age only correlated with sleep duration, such that older adolescents achieved significantly shorter sleep durations, $r(55) = -.28$, $P = .04$, although this correlation was not significant after controlling for multiple comparisons $P = .05/4$ sleep metrics, $P = .0125$.

Association between sleep and DMN connectivity

To test the hypothesis that adolescent sleep activity is related to DMN connectivity, we performed a functional connectivity analysis using an *a priori* seed region from the precuneus/PCC (Allen *et al.*, 2011). Average group connectivity was consistent with prior work on adolescent DMN connectivity (Figure 2;

Stevens *et al.*, 2009; Sherman *et al.*, 2014). There were significant differences in the connectivity of the DMN associated with the PCA component (poor sleep quality), such that individuals with poorer sleep quality demonstrated weaker connectivity between the precuneus/PCC hub and other key regions of the DMN (Table 3; Figure 3). For visualization, we plotted the association between poor sleep quality and regions of the DMN whose connectivity to the PCC varied as a function of sleep quality (Figure 4).

We included sex as a covariate because of significant sex differences in sleep duration, sleep efficiency, and number of awakenings. Age only correlated with sleep duration, but given prior work indicating age as an important factor in sleep patterns for adolescents (Winsler *et al.*, 2015), we included age as a covariate. To determine whether sleep quality related to DMN connectivity over and above sleep duration, we controlled for sleep duration. After including each of these covariates separately and also including the three covariates in the same analysis, poor sleep quality remained significantly related to weaker DMN connectivity (Supplementary Figure S1). Age and sex did not independently relate to differential DMN connectivity. Average sleep duration did not significantly relate to differences in DMN connectivity.

Sleep quality variability (PCA of standard deviation scores) was not significantly related to DMN connectivity. Intra-individual variability in sleep duration, assessed using standard deviation in sleep duration over the 14-day period, was also not related to differential DMN connectivity.

Discussion

In this study poorer sleep quality was significantly associated with weaker intra-network DMN connectivity at rest. The novelty of these findings (i) highlight the importance of considering sleep quality in addition to sleep duration, the most commonly examined measure in sleep research; and (ii) demonstrate that sleep may be associated with functioning of an important neural network during a period of extensive brain development.

This study identified individual differences in intrinsic DMN connectivity related to sleep quality. DMN connectivity is implicated in a wide-range of cognitive, emotional and social functioning (Andrews-Hanna *et al.*, 2010; Spreng and Grady, 2010; Li *et al.*, 2014; Hyatt *et al.*, 2015). Similarly, sleep deficiencies have been linked to poorer cognition, emotion regulation and social

Table 2. Descriptives for sleep variables of interest

	Sleep duration (min)	Sleep efficiency (%)	Number of awakenings	Duration of awakenings (min)
14-day M	418.98 (6.98 h)	92.06	5.56	21.03
14-day s.d.	43.89	5.72	3.85	20.03
14-day range	335.05–518.00	72.52–98.81	0.62–22.93	0.69–96.70
Weekday M	408.52 (6.81 h)	92.14	5.35	20.46
Weekday s.d.	48.87	6.21	3.93	22.42
Weekday range	307.87–507.50	67.85–98.75	0.80–22.50	0.90–109.43
Weekend M	446.75 (7.45 h)	91.70	6.49	22.90
Weekend s.d.	65.25	5.88	5.05	20.89
Weekend range	280.50–632.00	76.61–99.23	0.00–24.67	0.00–91.50
Variability M[a]	77.29 (1.29 h)	4.52	3.52	21.31
Variability s.d.	27.99	4.07	1.46	20.24
Variability range	27.91–135.09	0.83–22.53	0.87–6.97	1.11–105.33

Note: N = 55 for 14-day and weekday values, N = 53 for weekend values.
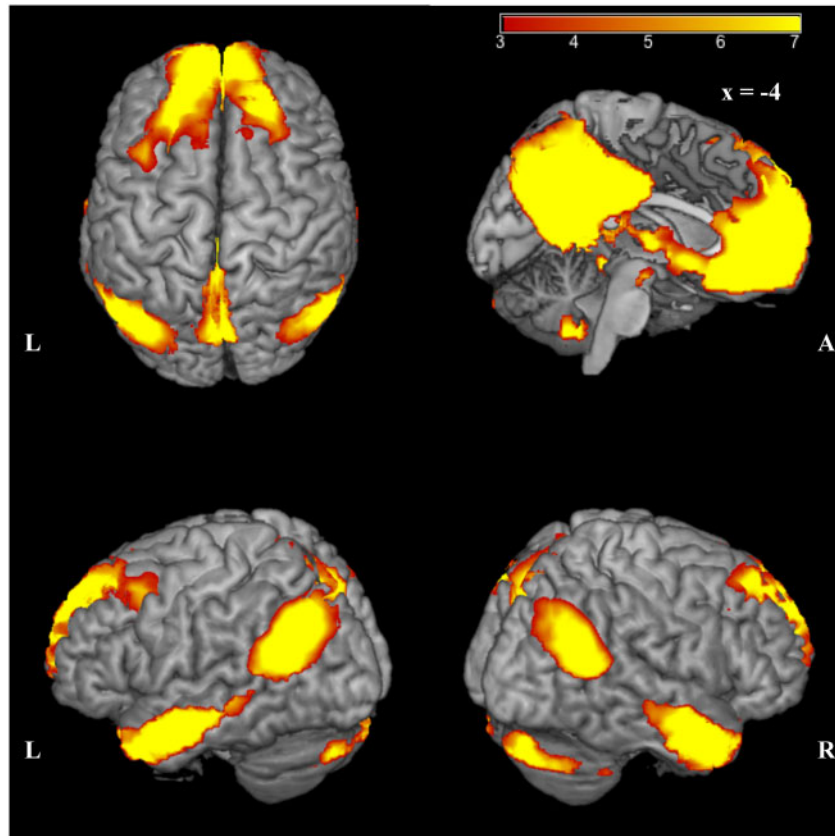[a]Variability scores calculated as intra-individual standard deviations across the study.

Fig. 2. Regions of the DMN that demonstrate positive connectivity with the PCC/precuneus seed. Results were masked with the adolescent specific DMN mask from Sherman et al. (2014). *P < .05, corrected. Color bar indicates *t* intensity values. L, R = left and right hemispheres, A = anterior.

Table 3. Regions of the DMN that have weaker connectivity with the PCC/precuneus seed as a function of poor sleep quality (PCA sleep component)

Region label	R/L	Peak MNI coordinates			Voxel	Cluster	Voxels
		x	*y*	*z*	*t*-value		(mm³)
Cingulate gyrus, anterior division	L	−10	32	4	6.00	1	1225
Cingulate gyrus, anterior division	L	−8	26	10	5.07	1	
Frontal pole	L	−24	54	−2	4.75	1	
Frontal pole	L	−24	48	0	4.21	1	
Caudate	L	−14	16	−4	3.96	2	27
Caudate	L	−10	12	−4	3.62	2	
Paracingulate gyrus	L	−2	48	10	4.20	3	13

Note: x, y and *z* refer to MNI coordinates; top four local maxima regions are listed in order of highest to lowest *t*-value; Voxels refer to each significant cluster; L, R = left and right hemispheres. All regions are significant at *P* < .05, corrected. N = 55.

understanding (Killgore *et al.*, 2007, 2008; Talbot *et al.*, 2010; van der Helm *et al.*, 2010; Beebe, 2011; Baum *et al.*, 2014). Our prior work indicates the way sleep relates to the interaction between the DMN and other brain regions is important for buffering against impulsivity in adolescents (Tashjian *et al.*, 2017). Together with the current study, we demonstrate the important link between DMN functioning and poor sleep quality during a transitional period of development. Our data call for future work on the interplay between sleep-related differences in DMN connectivity and commonly reported characteristics of deficient sleep like difficulty sustaining attention, mood variability and memory deficits.

Few adolescents in this study averaged the 8+ hours of sleep recommended by the National Sleep Foundation, consistent with a wealth of evidence that adolescents chronically experience insufficient sleep. Our results extend these findings with data on nighttime awakenings. Although the average number of awakenings in our study was 5, the range was up to 22 awakenings per night. The average number of minutes awake during these awakening was 21 min but some reports were as high as an hour and a half. Because we collected sleep data over 2 weeks, we can be reassured that these data are not anomalies. The use of actigraphy allowed assessment of metrics of sleep quality, specifically micro-awakenings, of which the participant
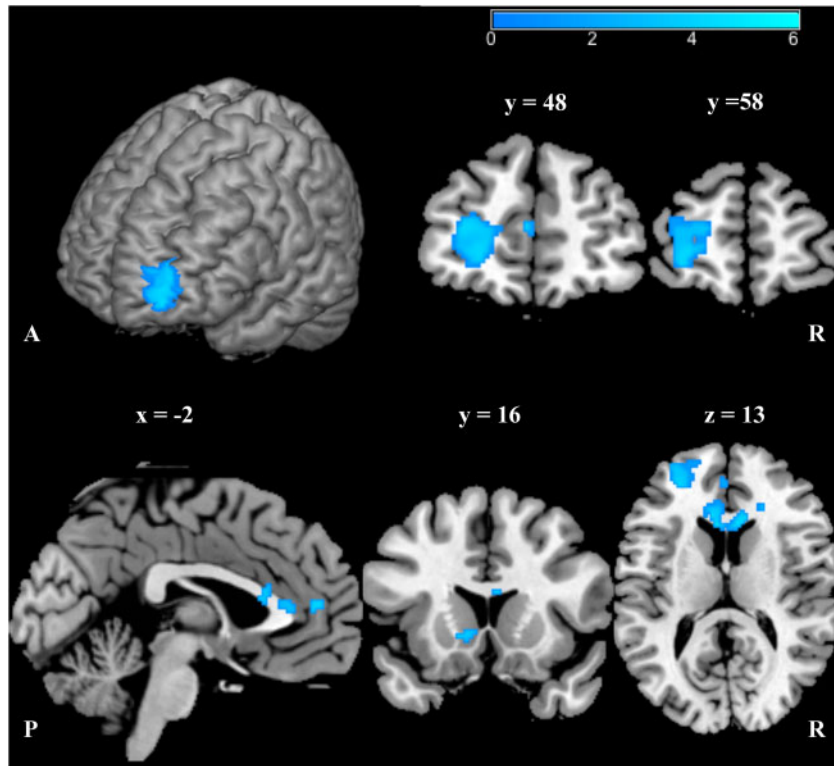
Fig. 3. Regions of the DMN that demonstrate weaker connectivity with the PCC/precuneus seed as a function of poor sleep quality (PCA sleep component). *$P < .05$, corrected. Color bar indicates t intensity values. R = right hemisphere, A = anterior, P = posterior.
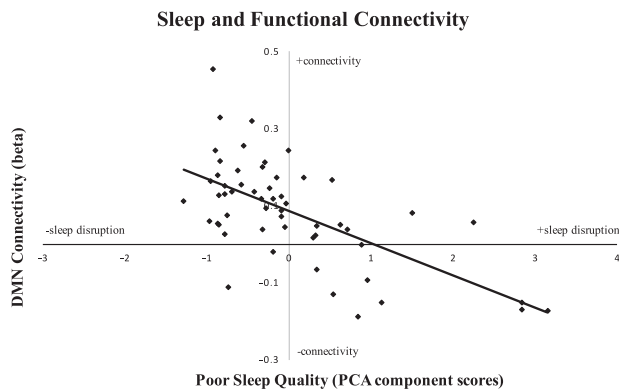

Fig. 4. Visual depiction of the relation between PCA sleep component scores (poor sleep quality) and regions of the DMN that demonstrate weaker connectivity with the PCC/precuneus seed as a function of poor sleep quality (betas extracted using a binarized mask of significant voxels from the analysis including sleep quality component scores). N = 55.

might not have been aware. Consistent with biological changes in sleep patterns occurring after puberty, our sample had a greater percentage of poor sleepers than comparable research in younger children (Sadeh *et al.*, 2000). These data signal a problem with adolescent sleep that goes beyond shorter sleep duration and highlight the importance of understanding factors contributing to poor sleep quality in adolescence.

We found no relation between sleep duration and DMN connectivity. This was surprising given prior research and may be due to relatively less variability in sleep duration among our participants than in previous studies. Our assessment of sleep

duration represented naturalistic differences rather than extreme and artificial sleep restriction reported in previous studies, making it possible that everyday differences in duration are not disruptive enough to replicate the weaker DMN connectivity in adult sleep-restriction studies. Additionally, our aim was to assess normative sleep patterns over a 2-week period rather than sleep immediately prior to the MRI scan. It is possible that sleep duration is more closely linked to next-day neural connectivity rather than the later assessment employed in this study. Nonetheless, our findings suggest research assessing sleep duration alone may be missing a key component of sleep, namely sleep quality.

A major innovation of this study is the novel and comprehensive examination of normative sleep as it relates to intrinsic connectivity in the adolescent DMN. By collecting daily sleep metrics via actigraphy, this study deviates from studies that focused on one snapshot (e.g. questionnaire) to assess adolescent sleep (e.g. Telzer *et al.*, 2013) or that used artificial sleep restriction approaches (e.g. Beebe *et al.*, 2009). Self-reported sleep quality can be a poor indicator of objective sleep patterns (Short *et al.*, 2013), and individuals may not be aware of all of the short awakenings they experience during the night, necessitating objective measures like actigraphy to provide a more precise picture of sleep quality. Functional connectivity methods provided additional insight into the relation between DMN connectivity and differences in sleep quality independent of task-induced differences.

Our findings call for future work investigating the DMN as a potential mediator of problem sleep and behavioral outcomes. Sleep deficiencies and DMN connectivity have been separately implicated in similar behavioral domains. For example, greater connectivity between the PCC and mPFC is associated with

better performance during working memory (Sambataro *et al.*, 2010) and sleep deprivation has a negative effect on working memory capacity (Banks and Dinges, 2007). Prior literature in adults demonstrating alterations in resting state functional connectivity after experimental sleep deprivation (De Havas *et al.*, 2012) suggests DMN connectivity can be altered by severe restrictions in sleep. Our findings add to this literature by demonstrating an association between intrinsic DMN connectivity and differences in normative sleep quality in a sample of healthy adolescents.

Our findings have potential implications for informing the growing discourse about how best to support sleep health in adolescence. Rates of chronic sleep deprivation in adolescents are alarmingly high (Basch *et al.*, 2014) and educators, parents and policymakers alike grapple with how to ameliorate this growing health concern. However, these efforts largely focus only on improving sleep duration (NSF, 2014), overlooking contributors to poor sleep quality in non-clinical adolescent populations. Although the effects of sleep on the developing brain may not always be acutely detectable, now is the time to underscore the importance of sleep and to further probe whether differences in DMN connectivity mediate the association between sleep and teens' health and well-being.

Interpretation of the current findings should be considered in the context of potential limitations. We did not collect data on daytime naps. Although it is unclear whether naps act as restorative sleep (Saletin *et al.*, 2017), it is possible that adolescents who nap ameliorate some of their nighttime sleep debt. Conversely, it is possible that naps exacerbate sleep problems by contributing to inconsistent sleep habits. Although prior work suggests the relation between sleep deprivation and functional connectivity is not specific to adolescents (De Havas *et al.*, 2012), that work did not assess DMN connectivity associated with naturalistic sleep patterns and this study did not include a comparison group of children or adults. Thus, we cannot determine whether the effects reported here would be more or less pronounced during different developmental periods. This study focused on late-adolescence due to evidence suggesting sleep is most altered during these ages. However, future work should determine whether this finding holds in pre- or early pubertal adolescents. This study cannot establish a causal direction for the relation between sleep and DMN connectivity, which can only be determined with experimental manipulations. Longitudinal within-subject changes in sleep and DMN connectivity during adolescence can lend insight into whether these findings are stable or whether adequate sleep could possibly reverse these effects, particularly given the plasticity of the adolescent brain (Spear, 2013). DMN intra-network and inter-network connectivity fluctuates depending on sleep stage (Haimovici *et al.*, 2017), with some studies finding participants experience transient states of wakefulness during resting state scans (Tagliazucchi and Laufs, 2014). It is possible that adolescents who experience chronic poor sleep quality have greater difficulty sustaining wakefulness during scanning and future studies should combine real-time measures of sleep to determine whether DMN connectivity differences are due to wakefulness during scanning.

In conclusion, this study provides new evidence for the association between sleep quality and adolescent neural network functioning. We used objective actigraphy and PCA to investigate multiple components of sleep in adolescence, and explored functional connectivity in the large-scale DMN rather than assessing neural functioning in discrete brain regions or during a behavioral task. The association between poor sleep and DMN connectivity are particularly important given connectivity of the DMN is critical for numerous key psychological constructs (e.g. Hampson *et al.*, 2006; Mason *et al.*, 2007; Spreng and Grady, 2010; Li *et al.*, 2014), because the DMN continues to develop throughout adolescence (Fair *et al.*, 2008, 2009; Stevens *et al.*, 2009; Sherman *et al.*, 2014), and because adolescence is a period of significant alterations in sleep patterns (Carskadon, 2011b).

Supplementary data

Supplementary data are available at *SCAN* online.

Conflict of interest. None declared.

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