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Title: Associations between brain structure and sleep patterns across adolescent development

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KEY POINTS

Question: Does age modulate associations between gray matter structure and actigraphic sleep patterns across adolescent development?

Findings: This cross-sectional study reports stable associations between regional gray matter structure and shorter duration, later timing, and poorer continuity of sleep from ages 9 to 25 years-old, as well as developmentally-specific associations that are present only from late childhood to early-to-mid adolescence.

Meaning: Stronger coupling of gray matter and sleep patterns from late childhood to early-to-mid adolescence potentially implicates this discrete developmental window as a period of vulnerability to adverse sleep-brain interactions. Sleep intervention during this developmental stage may support healthier neurodevelopmental trajectories.

74 **ABSTRACT**

75
76 **Importance:** Structural brain maturation and sleep are complex processes that exhibit
77 significant changes over adolescence and are linked to healthy physical and mental
78 development. The precise timing and magnitude of these changes influence function throughout
79 the lifespan. However, the relationships between gray matter structure and sleep patterns
80 during adolescence are not fully understood. A detailed characterization of brain-sleep
81 associations during this sensitive period is crucial for understanding factors contributing to
82 optimal neurodevelopmental trajectories in adolescence.

83 **Objective:** To investigate whether sleep-gray matter relationships are developmentally-invariant
84 (i.e., stable across age) or developmentally-specific (i.e., only present during discrete time
85 windows) from late childhood through young adulthood.

86 **Setting:** The Neuroimaging and Pediatric Sleep Databank was constructed from 8 research
87 studies conducted at the University of Pittsburgh between 2009 and 2020.

88 **Participants:** The final sample consisted of 240 participants without current psychiatric
89 diagnoses (9-25 years), and with good quality sleep tracking and structural MRI (sMRI) data.

90 **Design:** Participants completed a sMRI scan and 5-7 days of wrist actigraphy to assess
91 naturalistic sleep. We examined cross-sectional associations between sMRI measures and
92 sleep patterns, as well as the effects of age, sex, and their interaction with sMRI measures on
93 sleep.

94 **Main Outcome(s) and Measure(s):** Using Freesurfer software, we extracted cortical thickness
95 and subcortical volumes from T1-weighted MRI. Sleep patterns (duration, timing, continuity,
96 regularity) were estimated from wrist actigraphy.

Results. Shorter sleep duration, later sleep timing, and poorer sleep continuity were associated with a stable pattern of thinner cortex and altered subcortical volumes in diverse brain regions across adolescence. In a discrete subset of regions (e.g., posterior cingulate), thinner cortex was associated with these sleep patterns from late childhood through early-to-mid adolescence, but not in late adolescence and young adulthood.

Conclusions and Relevance: In childhood and adolescence, developmentally-invariant and developmentally-specific associations exist between sleep patterns and gray matter structure, in a wide array of brain regions linked to many sensory, cognitive, and emotional processes. Sleep intervention during specific developmental periods could potentially promote healthier neurodevelopmental outcomes.

INTRODUCTION

Structural brain maturation and sleep are complex processes that exhibit significant changes during adolescent development. The precise timing and amount of these changes in youths likely influences multiple adult outcomes. Optimal sleep and brain maturation are each known to influence adolescent health and functioning, including academic/vocational achievement, mental health, and/or risk behaviors^{1–10}. However, relationships between gray matter structure and sleep patterns over adolescence are not fully understood; furthermore, it is unknown whether these relationships vary as a function of age. A detailed characterization of brain-sleep relationships in adolescence is important for understanding factors contributing to optimal neurodevelopmental trajectories during this sensitive period.

Many brain regions implicated in cognitive and emotional outcomes show a protracted developmental course through adolescence^{11–15}, indicating that periods of heightened plasticity also come with greater vulnerability^{15,16}. Cortical thickness usually peaks by age 9-10 and then decreases until early adulthood, particularly in frontal, parietal, and temporal regions^{4,12,17–23}. Most subcortical regions increase in volume until ~14-15 years, with growth plateauing afterwards^{13,24,25}. Deviations from these normative trajectories may increase vulnerability to diverse negative outcomes, including poorer academic performance, mental health difficulties, and/or risky behaviors.

During adolescence, brain structural maturation is accompanied by multiple cognitive, behavioral, and emotional changes, including changes in sleep. Adolescence is characterized by a circadian phase delay and reduced homeostatic sleep drive, contributing to later sleep timing^{26,27}. These biological shifts converge with psychosocial and behavioral factors (e.g., school start times, peer socializing) to result in insufficient sleep and, at times, poorer sleep regularity or continuity^{26,27}. Disruptions to the timing, duration, continuity, and regularity of sleep predict and track with the severity of adverse cognitive and emotional outcomes (e.g., poor school performance, depression, substance use)^{28–32}.

Developmental shifts in sleep characteristics may possess reciprocal relationships with brain structural maturation^{33–36}, ultimately influencing diverse outcomes. While sleep serves multiple purposes, one such function is to support synaptic plasticity and reorganization of brain circuitry²⁴. Sleep disruption was originally considered a *consequence* of brain structural abnormalities; however, recent animal data indicate that sleep disruption during periods of heightened developmental plasticity also *cause* deviations in brain maturation^{37–39}. These translational studies imply stronger brain-sleep relationships in certain developmental windows^{37,40}. Yet, in humans it is unknown whether brain-sleep relationships are stable across adolescent development (i.e., developmentally-invariant relationships) or only occur during a discrete window of development (i.e., developmentally-specific relationships). Developmentally-specific brain-sleep relationships could inform the optimal timing of brain and/or sleep-based interventions that promote healthier neurodevelopmental outcomes. Several initial reports have identified ties between diverse gray matter structures and sleep in pediatric populations^{41–48}. However, developmentally-specific relationships have not been examined and these studies have been restricted to retrospective self-report or lab-based sleep measures that do not reflect usual sleep. An important next step is to evaluate how brain structure relates to objective, ecologically-valid sleep patterns (as captured by wrist actigraphy) through a developmental lens.

To address these open questions, we created the Neuroimaging and Pediatric Sleep (NAPS) Databank, a large, harmonized cross-sectional databank comprised of healthy children, adolescents, and young adults (ages 9-25yr). We estimated sleep from wrist actigraphy and sMRI measures from T1-weighted MRI. Given that a wide array of sMRI measures have been associated with sleep, we conducted data-driven regularized regression analyses, to test many potential predictors while minimizing the issues of predictor inter-correlation and multiple comparisons. We explored developmentally-invariant and developmentally-specific associations between sMRI measures (subcortical volume, cortical thickness) and core sleep dimensions (sleep duration, timing, continuity, regularity). Because there are important sex differences in

sleep and brain development^{17,49–54}, we also explored the interaction between self-reported sex and neuroimaging measures on sleep outcomes.

METHODS

Participants

The initial NAPS databank includes a total of 307 participants drawn from eight University of Pittsburgh studies conducted between the years of 2009 to 2020. Studies were considered for inclusion in NAPS if they included: a) actigraphic sleep monitoring; b) a sMRI scan; c) a baseline assessment reflecting naturalistic sleep; and d) participants aged 8-30 years-old (inclusive). Participant-level inclusion criteria were: a) 8-25 years-old; b) absence of current psychiatric diagnosis based on clinical interview (i.e., KSADS, SCID); c) no current psychotropic or hypnotic medication use; d) ≥5 days of good quality actigraphic sleep monitoring composed of both weekday and weekend days; e) good quality MRI scan. Demographics of the final analytic sample of N=240 are described in **Table 1**. Demographics by protocol are reported in **eTable 1** and reasons for participant exclusion are documented in the **eMethods**.

Neuroimaging Methods and Outcomes

Please see **eTable 2** for sMRI protocol parameters. We used the FreeSurfer analysis software^{55–58} (v6.0) to extract measures of cortical thickness (Desikan-Killiany atlas⁵⁹, n=34 measures) and subcortical volume (aseg.mgz atlas, n=8 measures) averaged across two hemispheres. We implemented a quality assessment pipeline developed by and used for the Enhancing Neuroimaging Genetics through Meta-Analysis consortium^{60–70}. An automated MRIQC T1w-classifier determined individual scan quality based on a reference template⁷¹. We adjusted neuroimaging data for scanner protocol effects with ComBat^{72,73}.

Wrist Actigraphy

Actigraphy is a well-validated and widely-used tool for objectively assessing naturalistic sleep in children, adolescents, and adults^{74–76}. Participants continuously wore wrist actigraphs

on their non-dominant wrist during a monitoring period of 5 or more consecutive days⁷⁷. **eTable 1** describes the number of participants who wore watches from Philips Respironics (PR; Actiwatch-64, Actiwatch2, Spectrum series) or Ambulatory Monitoring, Inc. (AMI; Basic Octagonal Motionlogger). Wrist activity was sampled in 1-minute intervals (epochs). Participants were asked to indicate via button press the start and end of each sleep interval.

We estimated sleep from wrist actigraphy using a combination of validated brand-specific sleep algorithms (PR Medium Threshold; AMI Sadeh) and standardized visual editing procedures^{78–80}. Trained scorers blinded to neuroimaging data manually identified rest intervals based on a combination of event markers indicated by participants and clear changes in activity and (if available) environmental light level recorded by the device. Brand-specific sleep scoring algorithms estimated sleep within each rest interval^{74,75,79,81–83}. We implemented additional semi-automated quality assurance procedures using in-house R scripts, including identification of the main rest interval (defined as the longest rest interval each day), removal of invalid sleep intervals containing ≥ 1 hour of off-wrist time or recording errors^{79,84}, time adjustment for daylight savings time, and final visual inspection of sleep intervals on raster plots.

Sleep Outcomes

Primary actigraphy sleep outcomes were based on the main rest interval. We selected four sleep outcomes corresponding to key dimensions of sleep health⁸⁵: sleep duration (total sleep time in minutes), timing (midpoint between sleep onset and offset in minutes from midnight), continuity (minutes awake after sleep onset; WASO), and regularity (intra-individual standard deviation of midpoint in minutes). The first three outcomes were averaged over the 5-7 tracking days most proximal to their MRI scan; regularity was calculated from the available days of recording. Sleep variables were natural log transformed to normalize distributions.

Statistical Analyses

We first conducted general additive models to confirm that the four sleep outcomes showed age-associated patterns consistent with prior research (**eFigure 1**). We observed the

characteristic decline in sleep duration, delay in sleep timing, and increased sleep variability over adolescent development. Sleep continuity did not vary with age.

We were interested in developmentally-invariant effects (i.e., main effects) of neuroimaging measures on the four sleep outcomes, as well as developmentally-specific effects (i.e., interactions between age and neuroimaging measures). Due to the large number of and multicollinearity amongst neuroimaging measures, we used regularized regression⁸⁶ to identify non-zero predictors associated with sleep outcomes. We used the R package, Group-Lasso-INTERaction-NET (glinternet^{87,88}) to examine main effects of structural neuroimaging measures, as well as their interaction with age and sex, for each sleep variable. Only potential interactions between non-zero main effects are considered. We included multiple actigraphy covariates (i.e., tracking days, season, ratio of weekday to weekend days, actigraph model) as potential predictors in the models. **eTable 3** contains the full list of 48 predictors. We repeated 10-fold cross validation 100 times, using the penalty parameter (λ) one standard deviation away from the minimal cross-validation error. The final model was the model was selected most often during this procedure. Regularized regression selects variables based on minimizing error in the model as opposed to statistical significance as in standard regression. Thus, p-values are not reported for non-zero coefficients.

Non-zero predictors selected by group-lasso models were entered into linear regression models, as in prior reports^{89,90}. R-squared was computed to estimate variance explained by the full model as well as groups of predictors (i.e., demographics, neuroimaging measures, actigraphy covariates). We assessed non-zero interactions between age and neuroimaging predictors with the Johnson-Neyman technique, which obtains parameter estimates and points of significance from the interaction between two continuous variables⁹¹⁻⁹³. Non-zero interactions between sex and neuroimaging predictors were probed by comparing estimated marginal means⁹⁴.

RESULTS

All neuroimaging measures, and their interactions with age and sex, selected as non-zero predictors of sleep outcomes are reported in **Table 2**. Non-zero actigraphy covariates (e.g., season, actigraph type) are reported in **eTable 4**.

Sleep Duration (Total Sleep Time)

The main effects of neuroimaging measures, age, sex, and their respective interactions accounted for 25% of the total variance in sleep duration (**Table 2A**). Shorter sleep duration was associated with older age and males had shorter sleep duration in comparison to females.

We observed several developmentally-invariant relationships between brain structure and sleep duration. From 9-25 years old, greater volume in the pallidum, hippocampus, and amygdala was associated with shorter sleep duration. Additionally, thinner medial orbitofrontal and isthmus (posterior) cingulate cortices were associated shorter sleep duration. Thinner cortex in the posterior cingulate was associated with shorter sleep duration in both sexes, but there was a stronger relationship in males. Conversely, thinner parahippocampal cortex and shorter sleep duration were associated in females, but not males.

We also found developmentally-specific relationships between gray matter structure and sleep duration (**Figure 2A**). In late childhood through middle adolescence, thinner cortex in the cuneus (9-17.3 years) and superior parietal regions (9-16.0 years) was associated with shorter sleep duration; however, this relationship was not observed at older ages. From 21.9-25.9 years old, greater lateral ventricle volume was associated with longer sleep duration.

Sleep Timing (Midsleep)

The main effects of neuroimaging measures, age, and their interactions accounted for 20% of the variance in midsleep (**Table 2B**). Midsleep was later in males and among older participants.

Developmentally-invariant relationships were identified for several brain regions. Specifically, lower thalamus volume was associated with later midsleep; this was relationship driven by males. In females only, greater lateral ventricle volume was associated with later midsleep. Thinner superior parietal and lateral occipital cortices were associated with later sleep timing.

Developmentally-specific relationships were also observed between neuroimaging measures and sleep timing (**Figure 2B**). From late childhood through middle adolescence, thinner cortex in the pars orbitalis (9-15.2 years), rostral middle frontal (9-14.1 years), and posterior cingulate regions (9-14.5 years) was associated with later midsleep. Thinner medial orbitofrontal cortex in late childhood (9-10 years) was also associated with later midsleep. Greater pallidum volume was associated with later midsleep only from ages 9 to 16.8 years.

Sleep Continuity (WASO)

The combined effects of neuroimaging measures, age, sex, and their interactions accounted for 16% of the variance in sleep continuity (**Table 2C**). WASO was longer among older participants and in females.

With regard to developmentally-invariant relationships, greater palladium and thalamus volume was associated with greater WASO. Thinner cortex in middle temporal, precentral, and lateral occipital regions was associated with greater WASO. Greater precentral and entorhinal cortical thickness was associated with greater WASO in females.

Thinner parahippocampal (9-14.6 years) and superior parietal cortices (9-16.0 years) were associated with greater WASO from late childhood to mid-adolescence, but not in older adolescents and young adults (**Figure 2C**).

Sleep Regularity (Midsleep Variability)

Regularized regression did not identify any nonzero predictors of midsleep regularity.

DISCUSSION

Using a large sample of typical adolescent development (9.0-25.9 years), we identified developmentally-invariant and developmentally-specific relationships between gray matter structure and naturalistic sleep patterns. Shorter sleep duration, later sleep timing, and poorer sleep continuity — all of which are associated with adverse health outcomes — were associated with a stable pattern of thinner cortex and altered subcortical volumes in diverse brain regions over adolescent development. In discrete regions, developmentally-specific relationships were also observed. In these regions, thinner cortex from late childhood through early-to-mid adolescence — a pattern associated with accelerated maturation — was associated with less optimal sleep, but these relationships were not detected in late adolescence and young adulthood. Our results provide a novel view of brain-sleep structure relationships within brain structures implicated in a wide array of cognitive, emotional, and psychological processes over adolescent development^{2,95–100}.

Cortical thickness in a diverse set of brain regions show developmentally-invariant relationships with sleep

Across adolescent development, thinner cortex in frontal, temporal, parietal, and visual processing areas was associated with shorter sleep duration, later sleep timing, and longer time awake after sleep onset. These brain regions are implicated in salience detection (pars orbitalis), motor function (precentral), memory (entorhinal, middle temporal), and attention and visuospatial perception (superior parietal cortex, lateral occipital)¹⁰¹. Given that sleep is associated with diverse range of mental, cognitive and physical health outcomes in adolescence^{1–10}, it is reasonable that naturalistic sleep is related to brain structure in regions that support multiple functions. Some of these relationships were modulated by self-reported sex, consistent with reported sex differences in sleep patterns and brain development^{17,49–54}. Future studies should also examine the extent to sex effects may be better explained by pubertal maturation.

Increased cortical thickness was associated with healthier sleep patterns from late childhood to middle adolescence

This is the first study, to our knowledge, to demonstrate that brain structure is related to individual differences in naturalistic sleep patterns at different ages, from late childhood through adulthood. Thicker cortex in multiple brain regions was associated with “healthier” sleep (as indicated by longer, more continuous, and earlier sleep) during late childhood and early adolescence. These findings, in conjunction with other work¹⁰², present the possibility that biological factors exert differential influences on behavior at distinct points in development. Accelerated cortical thinning/growth patterns in discrete brain regions could contribute to disruptions in sleep characteristics during late childhood and early adolescence, but not during other periods. Alternatively, disruptions in the typical age-related changes in sleep could lead to accelerating cortical thinning, particularly during this late childhood-early adolescence age range, but not during others. Multiple neurobiological mechanisms likely underlie individual differences in cortical thickness. Cortical thinning is traditionally believed to be caused by synaptic pruning, a re-wiring of synapses^{103,104}. Translational models find that, in mice, synaptic pruning is *higher* during sleep than wakefulness in adolescents, but not adults¹⁰⁵. More recent data suggest that age-associated changes in cortical thickness may also be driven by white matter maturational processes, i.e. myelination¹⁰⁶. Sleep disruption is detrimental to the formation and maintenance of myelin in murine models^{107,108}. Future longitudinal within-person investigations, particularly during late childhood and early adolescence, will be necessary to disentangle the directionality and neurobiological mechanisms of relationships between sleep, cortical thickness measures, and white matter integrity.

Unexpected relationships between poorer sleep and larger subcortical volumes

Surprisingly, in many cases, we also discovered that *larger* subcortical (i.e., hippocampal, amygdala, thalamus, and caudate) volumes are associated with more disrupted sleep patterns. One possibility is that exposure to sleep disruption at certain developmental

stages may be correlated with or cause *accelerated* subcortical growth patterns, akin to the acceleration-deceleration hypothesis of chronic stress and neurodevelopment^{109–111}. Importantly, this result stands in contrast with prior research showing lower subcortical gray matter volumes in relation to poor sleep⁴⁶ and mental health conditions^{60,112,113}. Thus, replication of these findings, as well as work examining the relationship between structural brain measures and sleep, needs to be further explored in informative subgroups such as individuals with mental disorders.

We also observed subcortical volume-sleep relationships in the expected direction. In females, larger lateral ventricle volume was associated with shorter sleep duration and later midsleep. Greater ventricle size has been linked to serious mental health conditions, including schizophrenia¹¹⁴. Furthermore, study of older adults also found longitudinal reduction in sleep duration corresponded to ventricular expansion over the follow-up period¹¹⁵.

Implications for optimal timing and targets for sleep intervention

If sleep patterns prove to be a causal contributor to individual differences in sMRI measures, our findings have the potential to inform developmentally-sensitive optimization of evidence-based behavioral sleep interventions¹¹⁶. As an example, both shorter sleep duration and later sleep timing were associated with thinner cortex in default mode network (DMN) regions (medial orbitofrontal and posterior cingulate cortices), a neural signature tied to outcomes such as depression, insomnia, and poor cognitive function^{98,117}. DMN cortical thickness and sleep duration relationships were developmentally-invariant. However, DMN cortical thickness-sleep timing association were only present in late childhood/mid-adolescence. Thus, a sleep treatment geared toward promoting healthy DMN-relevant outcomes should include sleep extension regardless of age but also advance sleep timing in late childhood and early/mid adolescence. Taken as a whole, our findings suggest that sleep interventions, particularly in late childhood through mid-adolescence, may be advantageous for neurodevelopment and thus downstream effects on psychological well-being.

Limitations

Our sample, while representative of the Pittsburgh Metropolitan area, was limited in its racial and ethnic diversity, factors which contribute to individual differences in brain structure and sleep^{28,118}. Although we adjusted for salient actigraphy covariates, actigraphy brand differences may have contributed noise in our data that was not captured by covarying for watch type in our models. Because our analyses were cross-sectional across a range of ages, rather than longitudinal within participants, it is unclear whether sleep patterns are a cause, correlate, or consequence of gray matter structure. Future, prospective longitudinal studies are necessary to disambiguate causal relationships between sleep and sMRI measures, and assess relationships between within-subject trajectories of sleep and brain development.

Conclusions & Future Directions

We found compelling and novel evidence for developmentally-invariant and developmentally-specific associations between sMRI measures and sleep across adolescent development. We plan to build on these findings and examine how individual differences in neuroimaging and sleep measures may identify youth at high-risk for developing adverse cognitive, mental, and physical outcomes.

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Concept and design of NAPS databank: Jalbrzikowski, Soehner

Concept, design, and funding for original research studies: Franzen, Hasler, Siegle, Buysse, Dahl, Forbes, Ladouceur, McMakin, Ryan, Silk, Goldstein, Soehner

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FIGURE CAPTIONS

Figure 1. Relationships between sleep and gray matter (cortical thickness, subcortical volume) that are developmentally-invariant (i.e., stable across age) or developmentally-specific (i.e., only present during discrete time windows) from late childhood through young adulthood.

Figure 2. Johnsyon-Neyman plots of age by neuroimaging measure interactions on sleep dimensions (A. duration, B. timing, and C. continuity). A statistically significant relationship between age and the neuroimaging measures ($p < .05$) is represented by the red color. Non-significant relationships are represented by the gray color. To aid in the interpretation of the plots, we provide one example of the age by cuneus cortical thickness interaction on sleep duration. a. From 9-17.3 years old, thicker cuneus cortex is associated with longer sleep duration ($r = 0.33$, $p = 1.0 \times 10^{-4}$). b. From 17.4-25.9 years old, this relationship is not present ($r = -0.003$, $p = 0.97$).

Table 1: NAPS sample characteristics

Variable	Mean or n (sd or %)
Sample N	240
Age (Years)	18.13 (5.26)
Self-reported Sex	
Female	133 (55%)
Male	107 (45%)
Ethnicity	
Non-Hispanic	223 (93%)
Hispanic	15 (6%)
Missing	2 (1%)
Race	
White	170 (71%)
Black	40 (17%)
Asian	11 (5%)
Multiple	16 (7%)
Unknown/Missing	3 (1%)
Wrist Actigraph Type	
AMI Octagonal MotionLogger	36 (15%)
PR/MiniMitter Actiwatch64	25 (10%)
PR Actiwatch2	113 (47%)
PR Spectrum Series	66 (28%)
Tracking Days	6.59 (0.84)
Weekdays	4.51 (0.92)
Weekend Days	2.08 (0.52)
Season	
Spring	43 (18%)
Summer	100 (42%)
Fall	52 (22%)
Winter	45 (19%)
Sleep Duration (min)	417.96 (63.52)
Wake After Sleep Onset (minutes)	56.19 (26.83)
Midsleep (minutes from midnight)	289.99 (76.59)
Midsleep Variability (minutes)	63.66 (44.06)

819 **Table 2.** Main effects and interactions between age, sex, and neuroimaging measures on
820 actigraphic sleep dimensions. Model weights are reported as standardized regression
821 coefficients.

A. Sleep Duration (Total Sleep Time)		
<i>Type of Effect</i>	<i>Variable</i>	<i>Model Weight</i>
Demographic Variable Main Effects	Sex	0.0403
	Age	-0.0732
Subcortical Volume Main Effects	Pallidum	-0.0122
	Hippocampus	-0.0529
	Amygdala	-0.0032
	Lateral Ventricles	0.0221
Cortical Thickness Main Effects	Medial Orbitofrontal Cortex	0.1090
	Parahippocampal Cortex	0.0022
	Posterior Cingulate	0.0576
	Isthmus Cingulate	0.0196
	Superior Parietal Cortex	0.0067
	Cuneus	0.0277
Sex Interactions	Sex x Parahippocampal Cortex	0.0054
	Sex by Posterior Cingulate Cortex	-0.0219
Age Interactions	Age x Lateral Ventricles	0.0234
	Age x Cuneus	-0.0332
	Age x Superior Parietal Cortex	-0.0072
Variance Accounted for by demographic measures only: $R^2=0.22$		
Variance Accounted for by neuroimaging and demographic measures, and their interactions: $R^2=0.25$		
B. Sleep Timing (Midsleep)		
<i>Type of Effect</i>	<i>Variable</i>	<i>Model Weight</i>
Demographic Variable Main Effects	Sex	-0.0601
	Age	0.1315
Subcortical Volume Main Effects	Thalamus	-0.0009
	Pallidum	0.0120
	Lateral Ventricles	0.0057
Cortical Thickness Main Effects	Medial Orbitofrontal Cortex	-0.0002
	Pars Orbitalis	-0.0136
	Rostral Middle Frontal Cortex	-0.0200
	Posterior Cingulate Cortex	-0.0089
	Superior Parietal Cortex	-0.0051
	Lateral Occipital Cortex	-0.1115
Sex Interactions	Sex x Lateral Ventricles	0.0342
	Sex x Thalamus	0.0010
Age Interactions	Age x Pallidum	-0.0431
	Age x Medial Orbitofrontal Cortex	0.0002
	Age x Pars Orbitalis	0.0187
	Age x Rostral Middle Frontal Cortex	0.0267
	Age x Posterior Cingulate Cortex	0.0189
Variance Accounted for by demographic measures only: $R^2=0.10$		
Variance Account for by neuroimaging and demographic measures, and their interactions: $R^2=0.20$		

C. Sleep Continuity (WASO)		
<i>Type of Effect</i>	<i>Variable</i>	<i>Model Weight</i>
Demographic Variable Main Effects	Sex	-0.0444
	Age	0.0244
Subcortical Volume Main Effects	Thalamus	0.0065
	Pallidum	0.0260
	Caudate	0.0083
Cortical Thickness Main Effects	Entorhinal Cortex	0.0009
	Parahippocampal Cortex	-0.0192
	Middle Temporal Cortex	-0.0086
	Precentral Cortex	-0.0283
	Superior Parietal Cortex	-0.0243
	Lateral Occipital Cortex	-0.0149
Sex Interactions	Sex x Caudate	-0.0117
	Sex x Entorhinal Cortex	-0.0021
	Sex x Precentral Cortex	-0.0151
Age Interactions	Age x Parahippocampal Cortex	0.0533
	Age x Superior Parietal Cortex	0.0622
Variance Accounted for by demographic measures only: $R^2=0.05$		
Variance Account for by neuroimaging and demographic measures, and their interactions: $R^2=0.16$		

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A. Sleep Duration (Total Sleep Time)

B. Sleep Timing (Midsleep)

C. Sleep Continuity (WASO)