TITLE PAGE

Title:

A multidimensional investigation of sleep and biopsychosocial profiles with associated neural signatures

Authors:

Aurore A. Perrault[1,2,3Δ*], Valeria Kebets[4,5,6,7,8Δ*], Nicole M. Y. Kuek[4,5,6], Nathan E. Cross[1,2,9], Rackeb Tesfaye[8], Florence B. Pomares[1,2], Jingwei Li[4,5,6,10,11], Michael W.L. Chee[5], Thien Thanh Dang-Vu[1,2], B.T. Thomas Yeo[4,5,6,12,13]

Affiliations:

1. Sleep, Cognition and Neuroimaging Lab, Department of Health, Kinesiology and Applied Physiology & Center for Studies in Behavioral Neurobiology, Concordia University, Montreal, QC, Canada
2. Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, CIUSSS Centre-Sud-de-l'Ile-de-Montréal, QC, Canada
3. Sleep & Circadian Research Group, Woolcock Institute of Medical Research, Sydney, NSW, Australia
4. Department of Electrical and Computer Engineering, National University of Singapore, Singapore
5. Centre for Sleep & Cognition & Centre for Translational Magnetic Resonance Research, Yong Loo Lin School of Medicine, Singapore
6. N.1 Institute for Health & Institute for Digital Medicine, National University of Singapore, Singapore
7. McConnell Brain Imaging Centre (BIC), Montreal Neurological Institute (MNI), McGill University, Montreal, QC, Canada
8. McGill University, Montreal, QC, Canada
9. School of Psychology, University of Sydney, NSW, Australia
10. Institute of Neuroscience and Medicine (INM-7: Brain and Behavior), Research Center Jülich, Germany
11. Institute of Systems Neuroscience, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Germany
12. Integrative Sciences and Engineering Programme (ISEP), National University of Singapore, Singapore
13. Athinoula A. Martinos Center for Biomedical Imaging, Massachussetts General Hospital, Charlestown, MA, USA

Δ Authors contributed equally.

*Corresponding authors:
Aurore A. Perrault, Valeria Kebets
aurore.perrault@gmail.com ; valkebets@gmail.com

ABSTRACT

Sleep is essential for optimal functioning and health. Interconnected to multiple biological, psychological and socio-environmental factors (i.e., biopsychosocial factors), the multidimensional nature of sleep is rarely capitalized on in research. Here, we deployed a data-driven approach to identify sleep-biopsychosocial profiles that linked self-reported sleep patterns to inter-individual variability in health, cognition, and lifestyle factors in 770 healthy young adults. We uncovered five profiles, including two profiles reflecting general psychopathology associated with either reports of general poor sleep or an absence of sleep complaints (i.e., sleep resilience) respectively. The three other profiles were driven by sedative-hypnotics-use and social satisfaction, sleep duration and cognitive performance, and sleep disturbance linked to cognition and mental health. Furthermore, identified sleep-biopsychosocial profiles displayed unique patterns of brain network organization. In particular, somatomotor network connectivity alterations were involved in the relationships between sleep and biopsychosocial factors. These profiles can potentially untangle the interplay between individuals' variability in sleep, health, cognition and lifestyle — equipping research and clinical settings to better support individual's well-being.

Keywords: sleep, biopsychosocial outcomes, multivariate, profile, psychopathology, cognition

INTRODUCTION

While the effects of sleep are intimately recognized by all, decades of research have established that sleep is interconnected to multiple biological, psychological and socio-environmental factors[1,2] (i.e., biopsychosocial factors)[3,4]. Importantly, sleep difficulties are among the most common comorbidities of mental and physical disorders[5–8], highlighting the central role of sleep in health. Despite the recognition that sleep is a unique marker for optimal health[9,10] and a potential transdiagnostic therapeutic target, its multidimensional and transdisciplinary nature is rarely capitalized on in research. Traditionally, single association studies have been used to investigate the relationship between a single measure of sleep (e.g., duration, quality, onset latency) and a single biopsychosocial outcome of interest. Such studies have demonstrated links between insufficient or poor sleep with a multitude of negative outcomes, including cognitive difficulties (e.g., reaction time, performance accuracy)[11,12], decreased physical health (e.g., body mass index, diabetes mellitus)[7,13], mental health and well-being (e.g., self-reported clinical symptoms)[8,14], as well as increased risks for cardiovascular disease[7,15,16], neurodegenerative disease[17,18] and psychiatric disorders[8,19]. However, given these uni-dimensional approaches and the varying effect sizes reported, it is unclear which biopsychosocial factors are most robustly associated with sleep traits and if they underlie similar mechanisms.

Adding to the complexity of these relationships is how sleep and good sleep health are defined. Defining sleep is a challenging task, firstly because of the different ways it can be measured (i.e., objective recordings, subjective reports), but also due to its multidimensional nature[20]. Sleep can be characterized by quantity (i.e., sleep duration) and quality (i.e., satisfaction, efficiency), as well as in terms of regularity, timing, and alertness. These dimensions are deemed particularly relevant when defining sleep health[9], as they each have been related to biopsychosocial outcomes. Different sleep dimensions can also be described as either "good" or "bad" sleep, without necessarily affecting one another (e.g., short sleep duration is not systematically associated with poor sleep quality). Another important aspect of sleep is how it is subjectively characterized. For instance, our perception of sleep can influence daytime functioning[21] and can be ascribed to certain behaviors that differ from objective reports[22,23].

Reconciling the multiple components of sleep and the complex connections to a myriad of biopsychosocial factors will require adopting frameworks grounded in a multidimensional approach. The biopsychosocial model has long been used to assert that biological (e.g., genetics and intermediate brain phenotypes), psychological (e.g., mood and behaviors), and social factors (e.g., social relationships, economic status), are all significant contributors to health and disease[3,4]. Indeed, the biopsychosocial model has been used to establish current diagnostic and clinical guidelines, such as the World Health Organization's International Classification of Functioning, Disability and Health, and is considered central to person-centered care[24]. Hence, statistical methods that enable us to interrogate the complex interconnected relationships within and between sleep and biopsychosocial factors can advance our understanding of optimal health and functioning across the lifespan. Multivariate data-driven techniques can help disentangle these complex interrelations, by deriving latent components that optimally relate multidimensional data sets in a single integrated analysis. In recent years, a few studies have used such techniques to account for the multidimensional components of sleep and biopsychosocial factors separately[25–30] suggesting that such profiling approaches may lead to better-tailored interventions. However, no current study has yet integrated both multidimensional components of sleep and biopsychosocial factors to derive profiles that can account for the dynamic interplay among biopsychosocial factors and thus provide more clinical utility.

Deploying multivariate data-driven techniques requires a large sample size to identify latent components that can generalize well[31–33]. However, few existing large-scale datasets compile sufficient measures of sleep alongside an extensive battery of biopsychosocial measures, although this is slowly changing (e.g., Adolescent Brain Cognitive Development data repository, UK Biobank). One such optimal

dataset is the Human Connectome Project dataset (HCP)[34] as it comprises a wide range of self-reported questionnaires about lifestyle, mental and physical health, personality and affect, as well as objective measures of physical health and cognition from over a thousand healthy young adults. Moreover, the HCP dataset stands out as one of the rare large-scale datasets that implemented a detailed assessment of sleep health, i.e., the Pittsburg Sleep Quality Index (PSQI)[35]. This standardized sleep questionnaire, used both by clinicians and researchers, assesses different dimensions of sleep health in 19 individual items, creating 7 sub-components, including sleep duration, satisfaction, and disturbances. Beyond sleep-biopsychosocial profiling, the HCP dataset also provides the opportunity to explore the neural signatures of these sleep-biopsychosocial profiles using in vivo imaging. Magnetic resonance imaging (MRI) is widely used to probe brain network organization at the structural and functional level. Moreover, multiple studies have shown that brain structure (e.g., white matter connectivity, cortical thickness), as well as signal fluctuation patterns during task or rest (i.e., resting-state functional connectivity; RSFC) are sensitive to sleep[29,36,37], but also predictive of psychopathology[38,39] and cognitive performance[36,37]. By investigating patterns of brain network organization associated with the different sleep-biopsychosocial profiles, we have a chance to untangle the interplay between individuals' variability in sleep, psychopathology, cognition, and brain connectivity. Such holistic biopsychosocial approaches are not only in line with established diagnostic frameworks, but also with initiatives such as the NIMH's Research Domain Criteria (RDoC) that encourage investigating mental disorders as continuous dimensions rather than distinct categories by integrating data from genomics, neural circuitry and behavior[40–42].

Identifying vulnerability markers constitutes a first step towards forecasting disease trajectories and designing multimodal multidimensional targeted therapies. Given the increasing recognition that sleep has a central role in health and well-being, we believe that sleep profiles should be included as a core aspect of these markers. Hence, in this study, we sought to take a multidimensional data-driven approach to identify sleep-biopsychosocial profiles that simultaneously relate self-reported sleep patterns to biopsychosocial factors of health, cognition, and lifestyle in a large cohort of healthy young adults. We further explored patterns of brain network organization associated with each profile and hypothesized that whole-brain RSFC will be differently associated with distinct sleep-biopsychosocial profiles.

RESULTS

We applied canonical correlation analysis (CCA) to derive latent components (LCs) linking the 7 sub-components of the PSQI to 118 biopsychosocial measures (spanning cognitive performance, physical and mental health, personality traits, affects, substance use, and demographics; **Table S1**) in 770 healthy adults from the HCP N1200 dataset[34] (**Figure 1A**). Participants were young adults between 22 and 36 years old (mean 28.86 ± 3.61 years old, 53.76% female), were generally employed full time (70.7%) and mostly white (78%; see **Table 1** for Demographics).

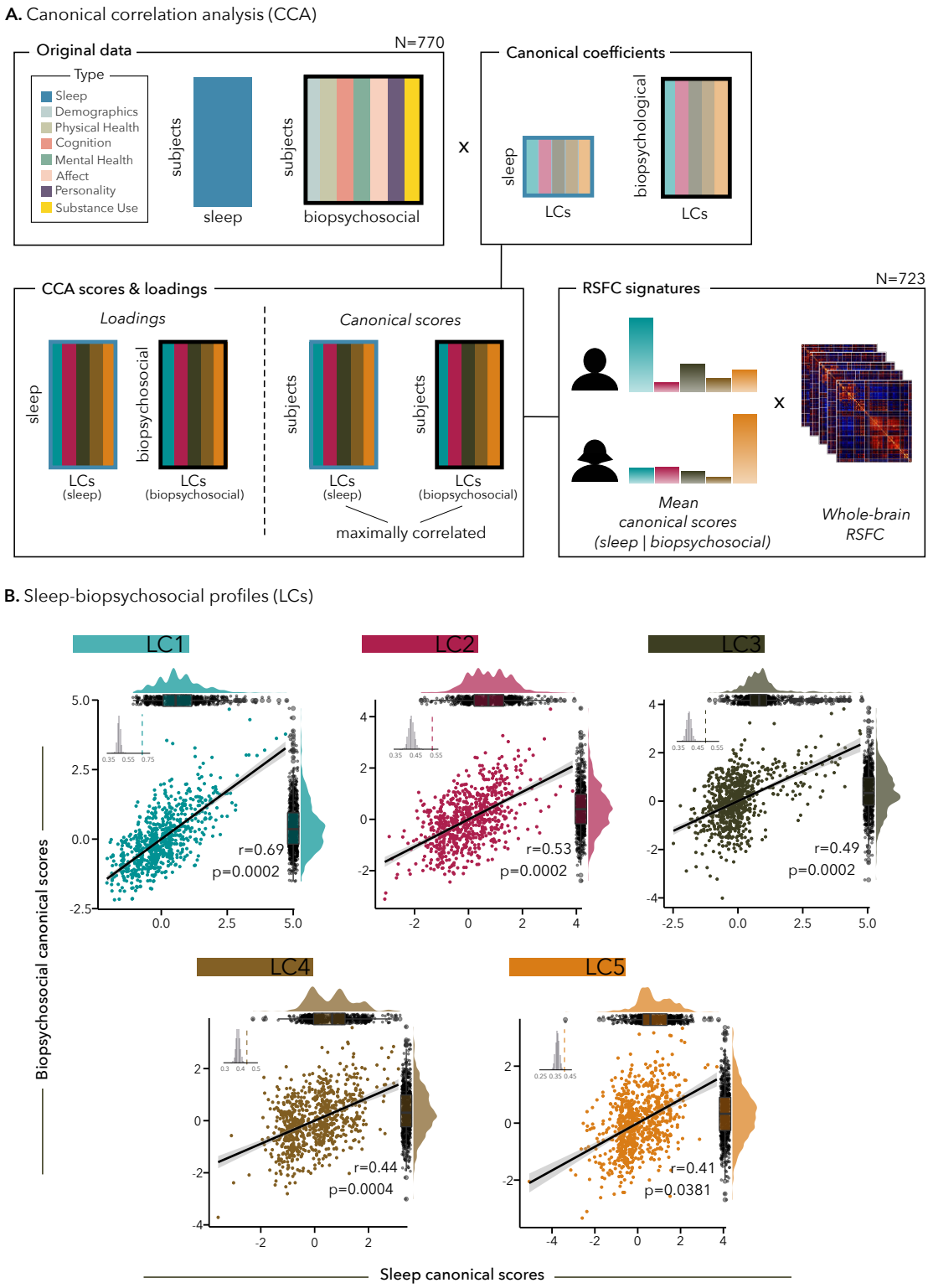


Figure 1 - Canonical correlation analysis reveals five sleep-biopsychosocial profiles (LCs).
(A) Canonical correlation analysis (CCA) flowchart and RSFC signatures; (B) Scatter plots showing correlations between biopsychosocial and sleep canonical scores. Each dot represents a different participant. Inset shows the null distribution of canonical correlations obtained by permutation testing; note that the null distribution is not centered at zero. The dashed line indicates the actual canonical correlation computed for each LC. The distribution of sleep (top) and biopsychosocial (right) canonical scores is shown on rain cloud plots.

Five latent components (LCs) linking sleep and biopsychosocial factors.

Out of the seven significant LCs that were derived, 5 were interpretable LCs delineating multivariate relationships between sleep and biopsychosocial factors (**Figure 1B**). While LC1 and LC2 were defined by general patterns of sleep (either general poor sleep or sleep resilience), LCs 3-5 reflected more specific sub-components of the PSQI, all associated with specific patterns of biopsychosocial factors. The 5 LCs respectively explained 88%, 4%, 3%, 2%, 1% of covariance between the sleep and biopsychosocial data.

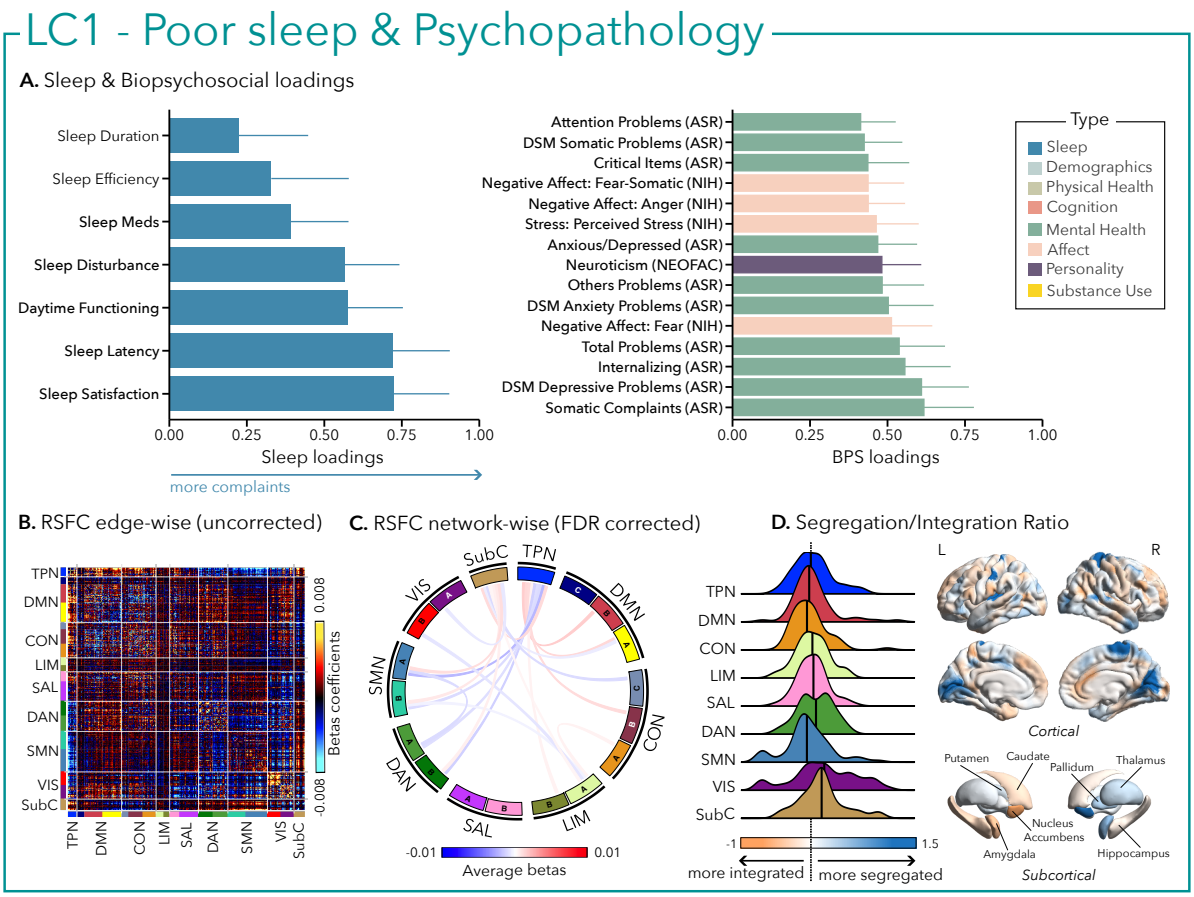


Figure 2 – First latent component (LC1) reflects poor sleep and psychopathology.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC1. Greater loadings on LC1 were associated with higher measures of poor sleep and psychopathology. Higher values on sleep (blue) and biopsychosocial (green, purple, pink) loadings indicate worse outcomes. Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance (after FDR correction q<0.05); (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC1 (left). The dashed line indicates the median of all parcels, and

the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

LC1 was characterized by a general pattern of poor sleep, including decreased sleep satisfaction, longer time to fall asleep, greater complaints of sleep disturbances and daytime impairment, as well as greater (i.e., worse) psychopathology (e.g., depression, anxiety, somatic complaints, internalizing behavior) and negative affect (e.g., fear, anger, stress – **Figure 2A**).
Similarly, LC2 was also driven by greater psychopathology, especially attentional problems (e.g., inattention, ADHD), low conscientiousness, and negative affect (**Figure 3A**). In terms of sleep however and in contrast to the first LC, greater psychopathology was only related to higher complaints in daytime impairment without sleep difficulties, suggesting sleep resilience.

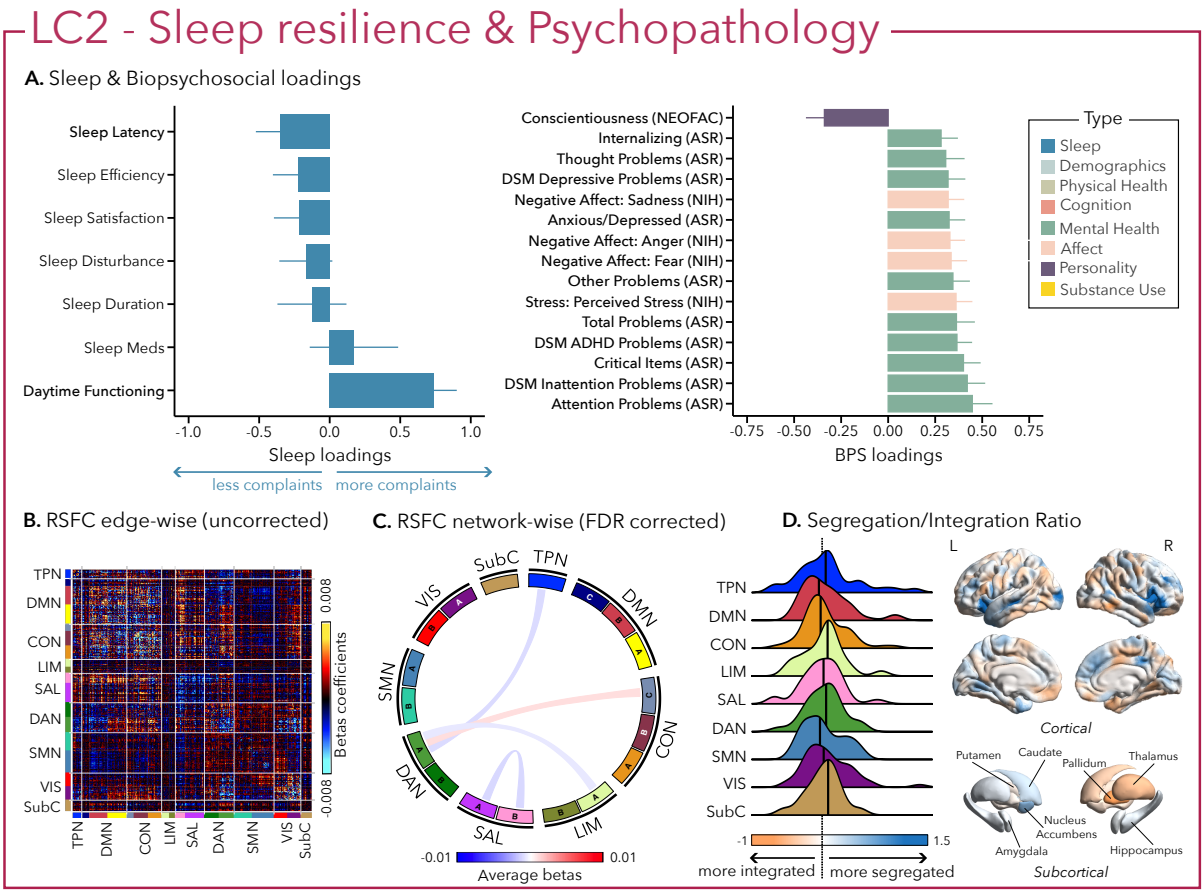


Figure 3 – Second latent component (LC2) reflects sleep resilience and psychopathology.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC2. Greater loadings on LC2 were associated with higher measures of complaints of daytime dysfunction and psychopathology. Positive values on sleep (blue) loadings indicate worse outcomes while positive values on biopsychosocial (green, purple, pink) loadings reflect higher magnitude on these measures. Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC2 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

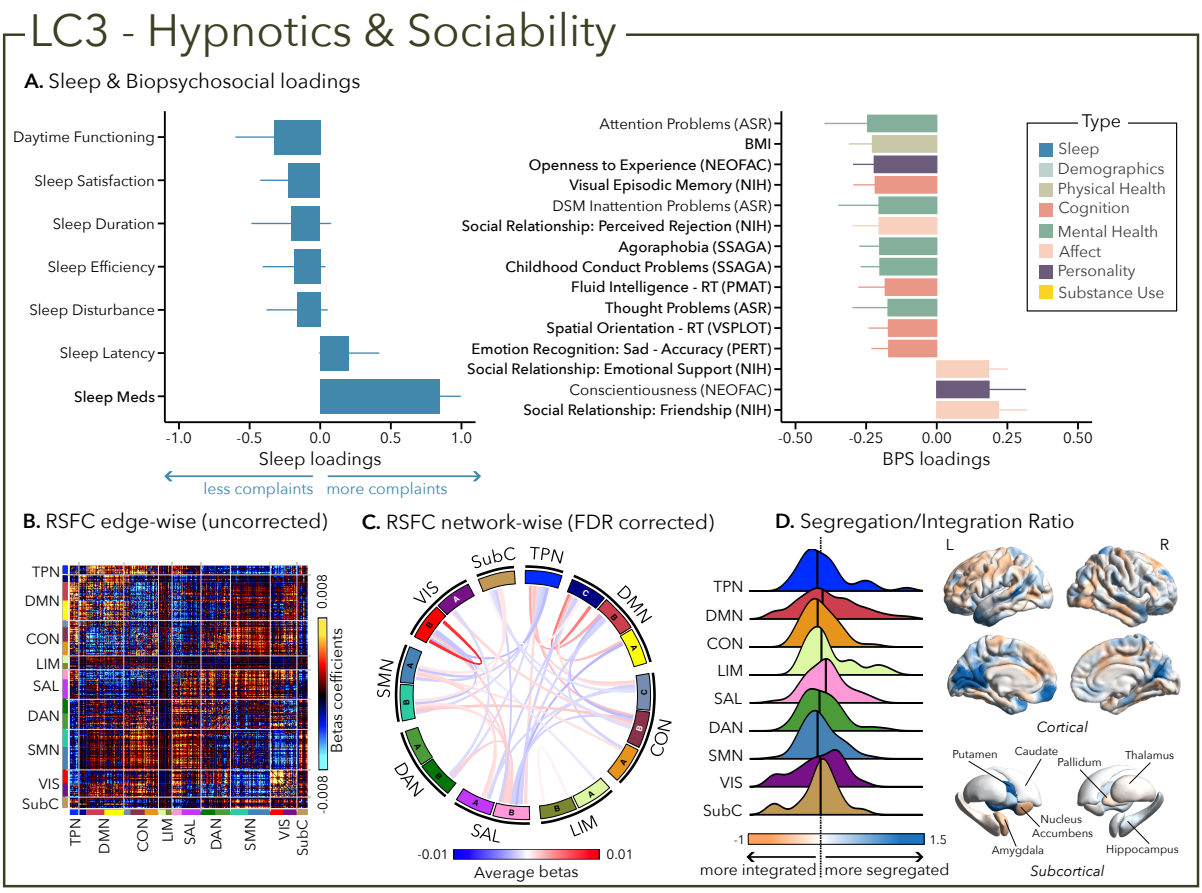


Figure 4 – Third latent component (LC3) reflects hypnotics and sociability.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC3. Greater loadings on LC3 were associated with the use of sedative-hypnotics and measures of positive social relationships, lower body mass index (BMI) and poor visual episodic memory performance. Positive values on sleep (blue) loadings indicate worse outcomes while positive values on the mental health (green), affect (pink) and personality (purple) categories of biopsychosocial loadings reflect higher magnitude on these measures. Positive value in the physical health (olive) category represents higher value and positive values in the cognition (orange) category indicate either higher accuracies or slower reaction times (RT). Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC3 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

LC3 was mostly characterized by hypnotic-sedative drugs intake (i.e., sleep meds PSQI sub-component) and to a lesser extent a lack of daytime functioning complaint. Surprisingly, LC3 was not driven by any attentional problem but was related to worse performance in visual episodic memory and emotional recognition. Moreover, hypnotics intake was mainly related to satisfaction in social relationships (**Figure 4A**).

While LC4 was solely driven by sleep duration (i.e., not sleeping enough - reporting <6-7h per night), LC5 was mostly characterized by the presence of sleep disturbances that can encompass multiple awakenings, nocturia and breathing issues as well as pain or temperature imbalance. In LC4, short sleep duration was associated with worse accuracy and longer reaction time at multiple cognitive tasks tapping into emotional processing, delayed reward discounting, language, fluid intelligence, and social

cognition. LC4 was also characterized by higher aggressive behavior and lower agreeableness (**Figure 5A**).

Interestingly, sleep disturbances in LC5 were also associated with aggressive behavior and worse cognitive performance (e.g., in language processing and working memory), but was mostly characterized by critical items on mental health assessments (i.e., anxiety, thought problems, internalization) and substance abuse (i.e., alcohol and cigarette use – **Figure 6A**).

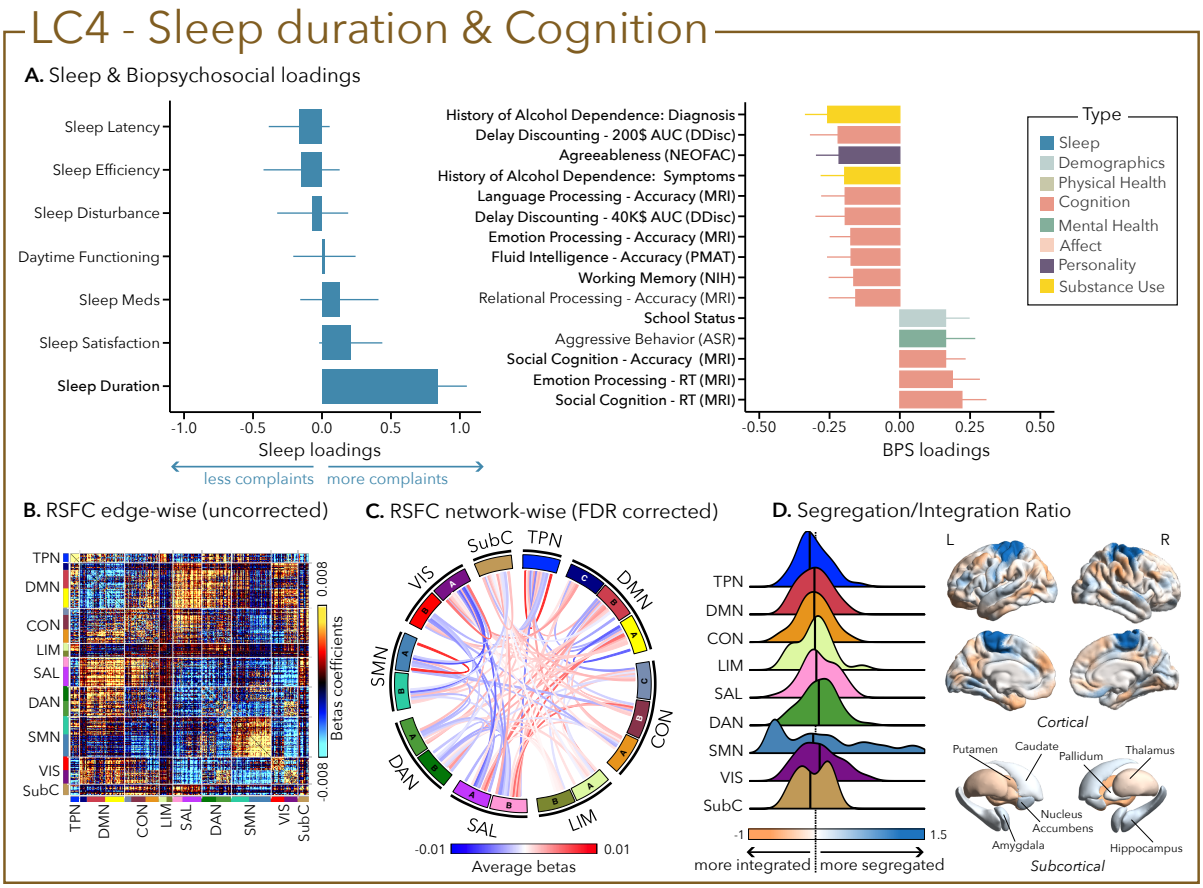


Figure 5 – Fourth latent component (LC4) reflects sleep duration and cognition.

(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC4. Greater loadings on LC4 were associated with shorter sleep duration and measures of poor cognitive performance. Positive values on sleep loadings indicate worse outcomes while positive values on the mental health (green), substance use (yellow), demographics (light blue) and personality (purple) categories of biopsychosocial loadings reflect higher magnitude on the measures. Positive values in the cognition (orange) category indicate either higher accuracies or slower reaction times (RT). Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC4 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

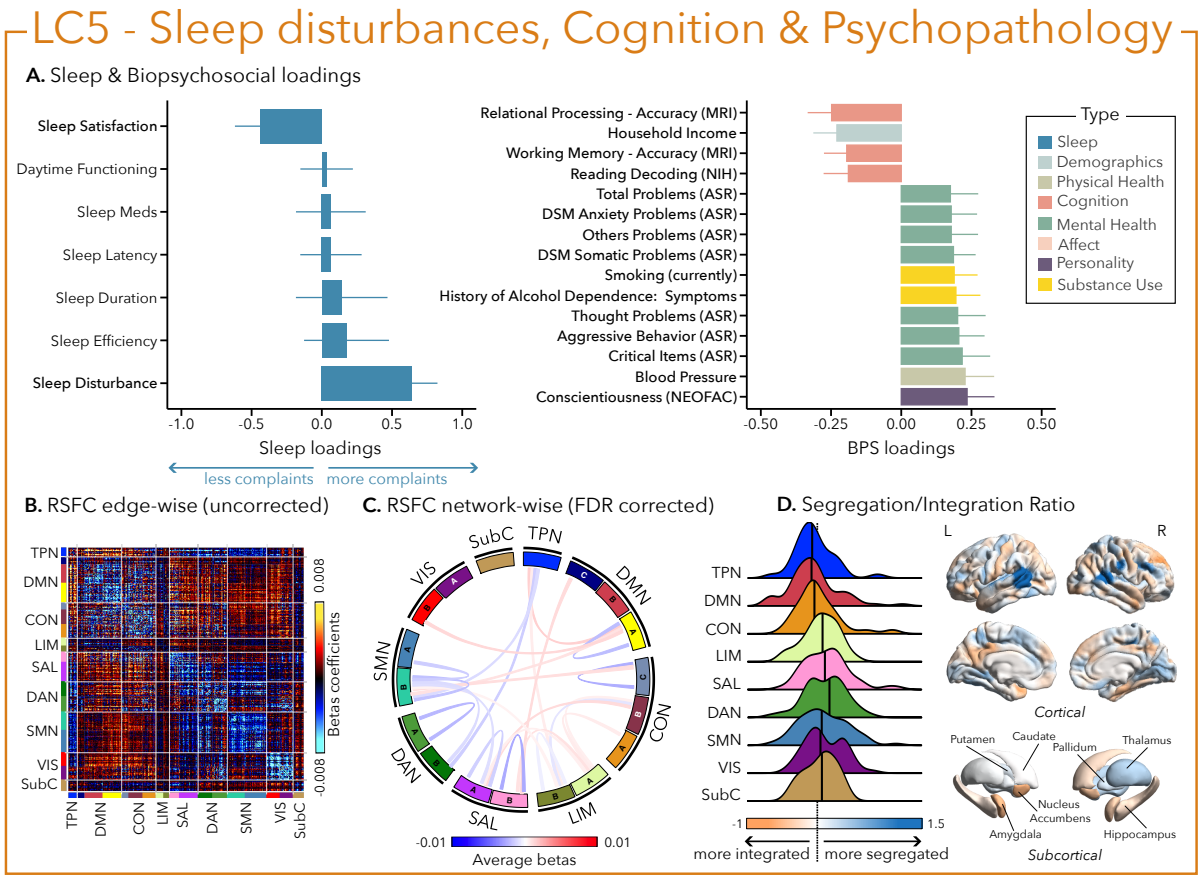


Figure 6 – Fifth latent component (LC5) reflects sleep disturbance, cognition and psychopathology.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC5. Greater loadings on LC5 were associated with the presence of sleep disturbances, higher measures of psychopathology and lower cognitive performance. Positive values on sleep loadings indicate worse outcomes while positive values on the mental health (green), substance use (yellow) and personality (purple) categories of biopsychosocial loadings reflect higher magnitude on these measures. Positive values in the cognition (orange) category indicate either higher accuracies or slower reaction times (RT), while positive values in the demographics (light blue) and physical health (olive) categories represent higher values. Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC5 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

Sleep and biopsychosocial profiles exhibit signatures of resting state brain connectivity.

In terms of brain organization, the 5 LCs revealed distinct patterns of network connectivity. Specifically, we examined patterns of both within-network and between-network connectivity (see **Figure S1** for subcortical-cortical patterns).

Greater (averaged) biopsychosocial and sleep composite scores on LC1 were associated with increased RSFC between subcortical areas and the somatomotor and dorsal attention networks (**Figures 2B** and **2C**), and a decreased RSFC between the temporoparietal network and these two networks. The visual network showed a flattened distribution of segregation/integration ratio (i.e., more variability in segregation and integration among the parcels of the network). The amygdala and nucleus accumbens exhibited asymmetrical patterns in the segregation/integration ratio with the left side being more segregated (**Figure 2D**). Meanwhile, LC2 was associated with increased RSFC between the dorsal

attention and control network but decreased RSFC between dorsal attention and the temporoparietal and limbic networks (**Figures 3B** and **3C**), a higher segregation of nodes within the tempoparietal network and increased integration within the right thalamus (**Figure 3D**). Higher composite scores in LC3 were associated with increased RSFC within the visual and default mode networks (**Figures 4B** and **4C**). The segregation/integration ratio within the default mode exhibited a flattened distribution (i.e., high variability in segregation and integration among parcels) but there was an increased segregation in the limbic and visual networks (**Figure 4D**). While greater composite scores in LC4 were associated with widespread patterns of hypo- or hyper-connectivity within and between every network the somatomotor network specifically exhibited an altered pattern of segregation and integration (**Figures 5B** to **5D**). Finally, we found that greater averaged composite scores in LC5 were mainly associated with reduced within-network connectivity in the somatomotor, dorsal and ventral attention networks (**Figures 6B and 6C**) but no strong pattern of segregation/integration ratio change (**Figure 6D**).

Post-hoc associations with socio-demographics, health, and family history of mental health

We found a number of significant associations between LC composite scores and socio-economic (e.g., education level, household income) and socio-demographic factors (e.g., race, ethnicity; see **Table S4** and **Supplemental Results**). In brief, most profiles (LCs 1,4,5) showed significant associations between sleep-biopsychosocial composite scores and education level, where lower education level was associated with a higher composite score in LCs 1,4,5 (all $q<0.05$). Similarly, lower household income correlated with a higher composite score in LCs 1-2 (all $q<0.05$). Race and ethnicity groups revealed differences in composite sleep and biopsychosocial scores for LCs 1,3-5 (all $q<0.05$). Finally, while the presence of a family history of psychopathology was associated with higher biopsychosocial scores in LCs 1-2, we only found biological sex differences in LC5, with higher sleep and biopsychosocial composite scores in female participants ($q<0.05$).

Control analyses

We summarize several analyses that demonstrate the robustness of our findings. First, LC1 and LC2 successfully generalized in our cross-correlation scheme (mean across 5 folds: $r=0.49$, $p=0.001$; $r=0.19$, $p=0.039$ respectively), but not LCs 3-5 (see **Table S3**), suggesting that LCs 3-5 might not be as robust and generalizable, possibly due to these LCs being driven by a single sleep dimension. Second, we re-computed the CCA analysis after (i) applying quantile normalization on sleep and behavior measures; (ii) excluding participants that had tested positive for any substance on the day of the MRI; (iii) excluding physical health measures (i.e., body mass index, hematocrit, blood pressure) or (iv) sociodemographic variables (i.e., employment status, household income, school status, relationship status) from the behavior matrix. The CCA loadings remained mostly unchanged (**Table S5**). We also assessed the robustness of our imaging results in several ways. First, we re-computed the GLM analysis using RSFC data that underwent CompCor[43] instead of GSR. The RSFC patterns were not much altered, as shown by generally high correlations with the main analysis ($r=0.75$, $r=0.76$, $r=0.78$, $r=0.51$, $r=0.77$ for LCs 1-5 respectively; **Figure S2**). Next, excluding subjects that likely fell asleep in the scanner did not impact our findings ($r=0.90$, $r=0.87$, $r=0.95$, $r=0.95$, $r=0.95$ for LCs 1-5 respectively; **Figure S2**); however, we found that these participants had higher sleep and biopsychosocial composite scores on LC4 compared to participants that likely stayed awake during the scan (**Figure S3**). Finally, we re-computed the GLM analyses by using sleep and behavior canonical scores instead of averaged scores. We found moderate to high correlations with the main GLM analysis ($r=0.69$, $r=0.62$, $r=0.63$, $r=0.46$, $r=0.67$ for LCs 1-5 respectively; **Figure S2**).

DISCUSSION

Leveraging a multidimensional data-driven approach in a large cohort of healthy young adults, we uncovered five distinct sleep profiles linked to biopsychosocial factors encompassing health, cognition, and lifestyle. We found that the first two profiles reflected general psychopathology (or *p factor*) associated with either reports of general poor sleep (LC1) or an absence of sleep complaints, which we defined as sleep resilience (LC2). Meanwhile, the three other profiles were driven by a specific dimension of sleep such as sedative-hypnotics-use (LC3), sleep duration (LC4), or sleep disturbances (LC5), which were associated with distinct patterns of health, cognition, and lifestyle factors. Furthermore, identified sleep-biopsychosocial profiles displayed unique patterns of brain network organization. Our findings emphasize the crucial interplay between biopsychosocial outcomes and sleep, and the necessity to integrate sleep history to contextualize research findings and to inform clinical intake assessments along with subsequent intervention approaches[44].

The dominance of psychopathology markers in most of the profiles is not surprising as the RDoC framework proposed arousal and regulatory systems (i.e., circadian rhythms and sleep/wakefulness) as one of the five key domains of human functioning likely to affect mental health[45], which is consistent with a large literature reporting significant disruption of sleep across multiple psychiatric disorders[8,46]. Although individuals with a neuropsychiatric diagnosis (e.g., schizophrenia or major depression disorder) were not included in the HCP dataset[34], the presence of the *p* factor, defined as an individual's susceptibility to develop any common form of psychopathology, exists on a continuum of severity and chronicity within the general population[47]. Symptoms of psychopathology mirrored each other across LC1 and LC2 but the paradoxical contrast in sleep loadings suggests that some individuals might have more resilient sleep (LC2), whereby they might be able to maintain healthy sleep patterns in the face of psychopathology. However, the cause of such resilience is unclear. Up to 80% of individuals experiencing an acute phase of mental disorder (e.g., depressive and/or anxiety episode) report sleep issues[8,48,49], leaving a minority of individuals that do not report abnormal sleep during such episodes. The identification of LC2 supports this and suggests there might be biological or environmental protective factors in some individuals who would otherwise be considered at risk for sleep issues. However, our understanding of such protective factors is limited[50–52]. These findings also highlight the need to appreciate the complexity of psychopathology, in line with the current view that psychiatric disorders are typically comorbid and heterogeneously expressed. Nonetheless, whether this profile of sleep resilience is a stable latent component or a cross-sectional observation of fluctuating symptoms that may develop into psychopathology-related sleep complaints, needs to be further tested.

Within the profiles driven by a specific sleep sub-component, LC5 also reflected some dimensions of psychopathology (i.e., anxiety, critical items and thought problems) that were only associated with the presence of global sleep disturbances. The sleep disturbance sub-component of the PSQI is broad and encompasses complaints of sleep-related breathing problems as well as multiple awakenings that could be due to nycturia, pain, nightmares, or difficulties maintaining optimal body temperature[35]. Altogether, the sleep disturbances dimension is thought to represent sleep fragmentation[53], and thus, sleep quality. This is in line with a recent study in a large community-based cohort (i.e., UK Biobank) that found that lifetime diagnoses of psychopathology and psychiatric polygenic risk scores were more strongly associated with accelerometer-derived measures of sleep quality (i.e., fragmentation) than with sleep duration per se[54]. In a similar manner, we found that sleep duration (driving LC4) was not associated with measures of psychopathology but rather with cognitive performance. Whether studied in the form of acute sleep deprivation or chronic sleep restriction, the consequences of lack of sleep on daytime functioning and health are well-known and substantial[11–13,55,56]. Sleep duration affects, in varying effect sizes, both accuracy and reaction time in most cognitive tasks[11,12,56]. In our study, reports of regular short sleep duration, defined as <6-7h of total sleep time, was associated with reduced accuracy in working memory, emotional processing, language processing, delay discounting, fluid intelligence as

well as longer reaction times during social cognition and emotional processing, mimicking results found in the sleep deprivation and sleep restriction literature[11,12,37,56–61].

Finally, beyond sleep measures and sleep-related daytime functioning, the PSQI also evaluates the use of medication to help sleeping[35], whether prescribed or over the counter (e.g., gamma-aminobutyric acid $GABA_A$ receptor modulators, selective melatonin receptor agonists, selective histamine receptor antagonists, cannabinoid products)[62]. We found that LC3 was driven by the use of sedative-hypnotics to aid sleep and was mostly associated with reports of satisfaction in social relationships. Interestingly, while we would have expected more links between the use of sedative-hypnotics and cognitive impairment, especially in older adults[63,64], we only found an association with visual working memory deficits but not with attentional problems. This profile specifically highlights a sub-group of young adults (22-36 years old) who experience sleep complaints and seek pharmacological solutions to manage them. As such, the associated biopsychosocial factors, in particular high sociability, could result from the effect of the drug itself on social behavior and positive mood (e.g., via potentiation of GABA transmission)[65,66] or as a consequence of the drugs on sleep complaints[67], which may support better emotional regulation and well-being, and consequently translate to greater satisfaction in social relationships and support systems[67,68]. We did not have information on the type nor duration of drug usage as the PSQI only assesses sleep habits in the past month, which may not be a substantial period of time to observe robust changes in cognitive functioning as previously documented[64,69].

Such distinctions between profiles were also present in the neural signatures of RSFC, which may assist in the neurobiological interpretation of the profiles. Directly comparing LC1 and LC2 suggested an underlying increase in subcortical-cortical connectivity when sleep disturbances are associated with psychopathology. This is in alignment with the known neurophysiology of the ascending arousal system, and possibly implies the existence of some level of hyperarousal in these pathways that may contribute to disturbances in sleep. However, this speculation requires further targeted research to be confirmed. The profile with the strongest RSFC loadings was LC4, driven by sleep duration and cognition. Interestingly, this RSFC pattern consisting of a global increase in connectivity, with localized segregation of part of the somatomotor network, has been previously reported in neuroimaging studies of acute total sleep deprivation[59,70]. Hence, this suggests that LC4 may be exposing an underlying level of sleep deprivation in the general population. Finally, alteration to the segregation/integration ratio of the somatomotor and visual cortex was common in most profiles. Highly interconnected to the whole brain, the somatomotor network is crucial for processing external stimuli and producing motor responses but is also functionally involved in bodily self-consciousness and interoception. Altered dysconnectivity patterns of the somatomotor network have been linked to variation in several domains, including general psychopathology[71,72], cognitive dysfunction related to sleep deprivation[59], as well as the total PSQI score[73,74]. Overall, these findings suggest that alterations to RSFC in the somatomotor network are also involved in the relationships between sleep and biopsychosocial factors and highlight the importance of understanding the role of this brain network in overall mental health.

These profiles contribute to a deeper understanding of the current debate that oppose sleep quality and sleep duration[7,75]. In line with previous studies[11,12,76], we found that cognitive functioning was more related to sleep duration than subjective sleep quality; in addition, we found that sleep disturbances, alone (LC5) or in combination with other sleep dimensions (LC1), can be associated with the presence of psychopathology. Moreover, it is also important to note that complaints of poor sleep quality and/or short sleep duration have been both associated with increased risks of physical health outcomes and all-cause mortality[6,7]. While LC1 and LC2 presented sleep dimensions as being inextricably linked, LC3, LC4 and LC5 respectively revealed distinct facets of sleep, suggesting that while sleep dimensions are related, they can also be separable domains with specific connections to biopsychosocial factors. This is likely reflected in the finding that only LC1 and LC2 were replicable in cross-validation analyses, which may be due to LC3, LC4 and LC5 being driven by a single sleep dimension and thus, contributing only marginally to the variance. While unidimensional association studies have been informative, these

findings reinforce the notion that sleep health is multidimensional and distinct measures of sleep quantity or quality should be considered together when investigating their influence on biopsychosocial aspects of health, cognition, and lifestyle. Future work should extend these findings and further explore the multidimensional nature of sleep health, for instance, taking into consideration the U-shaped relationship of sleep duration with biopsychosocial measures. Given the design of the PSQI, only short sleep duration (<5-6h) was considered as a sleep difficulty, neglecting the potential consequences of long sleep duration (>9h). Long sleep duration is commonly observed in hypersomnia disorders and psychopathology (e.g., schizophrenia, depression)[6,77], as well as being associated with increased risk of cardiovascular heart disease and mortality[7,78,79] and cognitive decline[6,17]. This U-shape observation, whereby both short and long sleep durations are associated with negative health and cognitive consequences as well as increasing markers of cerebrovascular burden (e.g., white matter hyper-intensities)[51], may provide a window to identify mechanisms that underlie the interplay between sleep and biopsychosocial factors.

Other considerations moving forward include sleep regularity and sleep timing, which are not part of the computation of the sub-components of PSQI[35], hence their association with biopsychosocial outcomes were not investigated in this study. A final important distinction to be addressed is that sleep and biopsychosocial outcomes were mostly self-reported through questionnaires. Both objectively recorded and subjectively perceived estimations provide different yet meaningful information that tend to positively correlate[80]. However, it has been shown that when compared to objective estimates (i.e., polysomnography and/or actigraphy recordings), individuals with sleep complaints (i.e., chronic insomnia, obstructive sleep apnea) tend to subjectively misperceive their sleep (i.e., duration, sleep latency)[22,23,81,82]. The degree of discrepancy between objective and subjective measures (i.e., sleep state misperception) has been correlated with worse sleep quality[83,84] as well as compromised reports of daytime functioning[21]. While objective measurements might have exposed divergent associations between sleep and biopsychosocial factors, the profiles reported here arguably support greater clinical validity, where the subjective complaints are often what drives an individual to seek out healthcare. Our study emphasizes that considering individuals' sleep experience can support clinicians to make more accurate initial assessments and navigate the course of treatment and interventions.

The awareness and interest surrounding sleep as a crucial pillar of health is growing rapidly[85]. However, the role of sleep in general health is complex and multifaceted, and largely unknown. The multidimensional approach applied in this large sample of healthy young adults is a first step that we argue should be implemented in future research incorporating sleep. We highlight the observation of five distinct sleep patterns associated with specific combinations of biological, psychological and socio-environmental factors. These findings support that sleep is emerging as a distinguishable factor that can assist in disentangling the complex heterogeneity of human health. As the capacity for large-scale human research continues to grow, integrating sleep dimensions at such a scale is not only feasible in terms of evaluation, but presents a unique opportunity for translational application. Sleep is a modifiable lifestyle factor and can be investigated in model organisms as well as in humans, and as such is well positioned to identify potential converging mechanisms and intervention pathways or tools. The current study emphasizes that by using a multidimensional approach to identify distinct sleep-biopsychosocial profiles we can begin to untangle the interplay between individuals' variability in sleep, health, cognition, lifestyle, and behaviour—equipping research and clinical settings to better support individuals' well-being.

METHODS

Participants

Data for this study were obtained from the publicly available Human Connectome Project (HCP) S1200 release[34]. The HCP dataset comprises multimodal MRI data, including structural MRI, diffusion MRI, resting-state and task fMRI data, as well as a broad range of behavioral measures collected in young healthy subjects (aged 22-36). Details about imaging acquisition parameters and data collection[34] as well as the list of available behavioral and demographics measures (HCP S1200 Data Dictionary)[86] can be found elsewhere. Of note, the HCP dataset comprises a large number of related individuals (i.e., siblings and twins). Of the 1,206 total subjects available from the HCP S1200 release, we excluded 403 participants with missing/incomplete data, and 33 participants with visual impairment that might have impacted their task performance in the scanner. Our final sample comprised 770 participants (53.76% female, 28.86 ± 3.61 years old). We decided to keep participants (N=94) that tested positive for any substance (including alcohol, marijuana, and other drugs) on the day of the MRI, as substance use has intricate links to sleep, and we did not want to exclude the possibility of finding potential substance use-related sleep profiles. However, we also re-computed our analyses after excluding these individuals (N=676) and found very similar results (see **Table S5**). Out of these 770 participants, 723 passed MRI quality control and were included in the *posthoc* RSFC analyses.

Sleep assessment

Participants were administered the Pittsburgh Sleep Quality Index[35] (PSQI) to assess different aspects of their sleep over the past month. Total PSQI score ranges from 0 to 21 (with higher scores indicating worse sleep quality). We used the 7 sub-components of the PSQI, namely (i) sleep satisfaction, (ii) sleep latency, (iii) sleep duration, (iv) sleep efficiency, (v) sleep disturbance, (vi) sleep medication, and (vii) daytime functioning. Sub-components are calculated through 4 questions on the timing of sleep habits and 6 Likert-scale questions from 0 to 3, 0 being best and 3 being worst. The mean PSQI total score in our sample was 5.14 ± 2.17 with 287 participants (37.2%) above the clinical cut-off (>5). We did not find any effect of age (rho=0.02, p=0.55) or sex (w=70208, p=0.25) on the PSQI score.

Behavioral assessment

118 behavioral measures were selected from the HCP dataset (see complete list in **Table S1**). These behavioral measures included self-reported assessments of current and past mental health and substance use, questionnaires on personality, affect, lifestyle and demographics, cognitive tasks tapping on different processes such as working memory or social cognition performed either inside or outside the MRI, and physical assessments (e.g., blood pressure). Behavioral measures with large amounts of missing data were excluded, as well as similar measures that were likely to be redundant.

Canonical correlation analysis

Canonical Correlation Analysis (CCA)[87,88], a multivariate data-driven approach, was applied to the sleep and behavioral measures. CCA derives latent components (LCs, i.e., canonical variates), which are optimal linear combinations of the original data, by maximizing *correlation* between two data matrices (i.e., sleep and behavioral measures). Each sleep-behavior LC is characterized by a pattern of sleep weights and a corresponding pattern of behavioral weights (i.e., canonical coefficients). Linear projection of sleep (or behavioral) data onto sleep (or behavioral) weights yielded participant-specific composite scores for sleep (or behavioral) measures (i.e., canonical scores). The contribution of original sleep and behavioral loadings to each LC was determined by computing Pearson's correlations between sleep (or behavioral) data and participant-specific scores for sleep (or behavior) to obtain sleep and behavioral *loadings* (i.e., canonical structure coefficients)[89,90]. Canonical structure coefficients reflect the direct contribution of a predictor (e.g., one sleep dimension) to the predictor criterion (e.g., LC1) independently of other predictors (e.g., the other sleep dimensions, which can be critical when

predictors are highly correlated between each other (i.e., in presence of multicollinearity)[91]. Statistical significance of each of the 7 LCs was determined by permutation testing (10,000 permutations) followed by FDR correction. Given the high prevalence of related participants in the HCP dataset, family structure was maintained during permutations (using the PALM package[92,93]), whereby monozygotic twins, dizygotic twins, and non-twin siblings were only permuted within their respective groups. Finally, the loadings' stability was determined using bootstrap resampling to estimate confidence intervals for the loadings, by deriving 1,000 samples with replacement from participants' sleep and behavioral data.

MRI acquisition and processing

All imaging data were acquired on a customized Siemens 3T Skyra scanner at Washington University (St Louis, MI). Four runs of rs-fMRI were collected over two sessions across two separate days. Each run included 1,200 frames using a multi-band sequence at 2-mm isotropic spatial resolution with a TR of 0.72 s for 14.4 minutes. The structural images were acquired at 0.7-mm isotropic resolution. Further details of the data collection and HCP preprocessing are available elsewhere[34,94,95]. Notably, cortical and subcortical data underwent ICA-FIX[96,97] and were saved in the CIFTI grayordinate format. The surface (fs_LR) data were aligned with MSM-All[98]. As ICA-FIX does not fully eliminate global motion-related and respiratory-related artifacts[99,100], additional censoring and nuisance regression were performed[101,102]. In particular, volumes with framewise displacement (FD) > 0.2mm, and root-mean-square of voxel-wise differentiated signal (DVARS) > 75 were marked as outliers and censored, along with one frame before and two frames after the outlier volume[103,104]. Any uncensored segment of data that lasted fewer than five contiguous volumes were also excluded from analysis, as well as runs with >50% censored frames. Additionally, global signal obtained by averaging signal across all cortical vertices and its temporal derivatives (ignoring censored frames) were also regressed out from the data because previous studies have suggested that global signal regression strengthens association between RSFC and behavioral traits[101]. As there is ongoing debate on the use of global signal regression (GSR) as a means of fMRI preprocessing[101,105–107], additional reliability analysis was performed on data preprocessed using a component-based noise correction method (CompCor)[43] instead of GSR.

RSFC was computed among 400 cortical parcels[108] and 19 subcortical regions[109] using Pearson's correlation (excluding the censored volumes). The subcortical regions were in subject-specific volumetric space as defined by FreeSurfer[109], and comprised the left and right cerebellum, thalamus, caudate, putamen, pallidum, hippocampus, accumbens, amygdala, ventral diencephalon, and brainstem. For each participant, RSFC was computed for each run, Fisher z-transformed, and then averaged across runs and sessions, yielding a final 419 x 419 RSFC matrix for each participant.

RSFC analyses

To investigate whether the sleep-behavioral profiles were associated with distinct RSFC signatures, we computed generalized linear models (GLM) between participant's canonical scores (i.e., averaged sleep and behavior scores) and their RSFC data. Age, sex, and level of education were first regressed out from the RSFC data.

To obtain an analysis at the large-scale network level and limit the number of multiple comparisons, we computed a network-wise GLM, whereby the whole-brain RSFC data was averaged within and between the 17 Yeo networks[108] and subcortical regions[109], resulting in 18 x 18 RSFC matrices. Next, we applied a GLM for each network edge (i.e., average connectivity between two brain networks), with participants' component-specific canonical scores as the predictor and RSFC edge as the response. Each GLM yielded a beta coefficient and associated T statistic, as well as an F statistic and associated p value obtained from a hypothesis test that all coefficient estimates were equal to zero. Statistical significance for each RSFC network edge was determined by applying FDR correction ($q < 0.05$) on all p values (along with other posthoc analyses). For a more granular view, we also computed a GLM for each RSFC edge (i.e., connectivity between two brain regions) using whole-brain RSFC between all 419 brain regions. For a

complete view of the component-specific RSFC signatures, we plotted both the uncorrected region-wise GLM beta coefficients (e.g., **Figure 2C**) and FDR-corrected network-wise GLM beta coefficients (e.g., **Figure 2D**).

Measures of integration and segregation were computed on the GLM beta coefficient connectivity matrix associated with each LC using functions from the Brain Connectivity Toolbox[110]. Firstly, the input weighted connection matrix was normalized. Next, each 419 cortical parcel was assigned to one of the 7 Yeo functional networks and subcortical regions [111]. Within-network connectivity was estimated by calculating the module-degree Z score (within-module strength) for each region. The extent to which a parcel connects across all networks was quantified using the participation coefficient, (between-module strength). For each cortical parcel, the ratio of normalized within:between module strength values was calculated and interpreted as a measure for the balance of integration and segregation of functional brain connectivity[112]. Nodes with high within- but low between-module strength are likely to facilitate network segregation, while nodes with higher between-module strength (i.e., connector hubs) are likely to facilitate global integration[110].

Control analyses

We ran several control analyses to evaluate the robustness of our findings. First, we applied 5-fold cross-validation (accounting for family structure) to assess the generalizability of our sleep-behavior profiles by training a CCA model on 80% of the data and testing it on the remaining 20% of the data. For each fold, we projected the sleep and behavior canonical coefficients of the training data on the sleep and behavior data of the test data, to obtain sleep and behavior scores, and computed Pearson's correlations between these scores. Second, we evaluated the impact of the covariates on our profiles as well as the impact of other potential confounds, including race, ethnicity, and familial psychiatric history. Third, we re-computed the CCA analysis after excluding participants that had tested positive for any substance use on the day of the MRI. Fourth, we re-computed the CCA analysis after excluding physical health (i.e., body mass index, hematocrit, blood pressure) and sociodemographic (i.e., employment status, household income, in school, relationship status) variables from the behavior matrix. Fifth, we re-computed the CCA analysis after applying quantile normalization on sleep and behavior measures. We also assessed the robustness of our imaging results in several ways. As GSR is a controversial preprocessing step[101,106,107], we re-computed the GLM analysis using RSFC data that underwent CompCor[43] instead of GSR. Some subjects were noticed to have likely fallen asleep during scanning (list not publicly available[113]). As a first step, we re-computed the GLM after excluding these subjects (N=100); next, we sought to determine whether these participants scored high on any of the profiles, by comparing their sleep/behavior composite scores with awake participants using t-tests. We re-computed the GLM analyses by using sleep and behavior canonical scores instead of averaged scores. Finally, integration and segregation measures were also computed on the average RSFC matrix of the whole sample. FDR correction ($q < 0.05$) was applied to all posthoc tests.

Data and code availability

Data from the HCP dataset is publicly available (https://www.humanconnectome.org/). The brain parcellation can be obtained here (https://github.com/ThomasYeoLab/CBIG/tree/master/stable_projects/brain_parcellation/Schaefer2018_LocalGlobal), while the code for the CCA analysis and figures can be found here (https://github.com/valkebets/sleep_biopsychosocial_profiles). Chord diagrams were generated using previously published code: https://github.com/ThomasYeoLab/CBIG/tree/master/stable_projects/predict_phenotypes/ChenTam2022_TRBPC/figure_utilities/chord

AUTHOR CONTRIBUTION STATEMENT

Conceptualization: NMYK, BTTY, VK, AAP; Data curation: VK, NMYK, JL, AAP; Formal analysis: VK, NMYK, NEC, AAP; Methodology: VK, NMYK, NEC; Visualization: AAP, VK, NEC; Interpretation: AAP, VK, NEC, RT; Writing original draft: AAP, VK – editing and reviewing: AAP, VK, RT, NEC, BTTY, FBP, TTDV, JL, MWLC, NMYC

ACKNOWLEDGEMENT

Any opinions, findings and conclusions or recommendations expressed in this material are those of the authors and do not reflect the views of the Singapore NRF, Singapore NMRC, MOH or Temasek Foundation. Our research also utilized resources provided by the Center for Functional Neuroimaging Technologies, P41EB015896 and instruments supported by 1S10RR023401, 1S10RR019307, and 1S10RR023043 from the Athinoula A. Martinos Center for Biomedical Imaging at the Massachusetts General Hospital. The computational work was partially performed using resources of the National Supercomputing Centre, Singapore (www.nscc.sg). Data were provided by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University. AAP has been supported by the American Academy of Sleep Medicine (AASM), Fondation Lemaire and fellowships from Concordia University, Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal (CRIUGM) and PERFORM Center. VK has been supported by the Transforming Autism Care Consortium and the Montreal Neurological Institute. NC has been supported by the Fonds de Recherche du Québec – Santé and fellowship from the CRIUGM. TDV is currently supported by CIHR grants, the Natural Sciences and Engineering Research Council of Canada, the Canada Foundation for Innovation and the Fonds de Recherche du Québec – Santé. BTTY is currently supported by the NUS Yong Loo Lin School of Medicine (NUHSRO/2020/124/TMR/LOA), the Singapore National Medical Research Council (NMRC) LCG (OFLCG19May-0035), NMRC CTG-IIT (CTGIIT23jan-0001), NMRC STaR (STaR20nov-0003), Singapore Ministry of Health (MOH) Centre Grant (CG21APR1009), the Temasek Foundation (TF2223-IMH-01), and the United States National Institutes of Health (R01MH120080 & R01MH133334). Finally, we thank Dr. Joshua Gooley for his helpful comments in the previous versions of the work.

LEGENDS: FIGURES & TABLES

Table 1 - Demographics

Figure 1 - Canonical correlation analysis reveals five sleep-biopsychosocial profiles (LCs).

(A) Canonical correlation analysis (CCA) flowchart and RSFC signatures; (B) Scatter plots showing correlations between biopsychosocial and sleep canonical scores. Each dot represents a different participant. Inset shows the null distribution of canonical correlations obtained by permutation testing; note that the null distribution is not centered at zero. The dashed line indicates the actual canonical correlation computed for each LC. The distribution of sleep (top) and biopsychosocial (right) canonical scores is shown on rain cloud plots.

Figure 2 – First latent component (LC1) reflects poor sleep and psychopathology.

(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC1. Greater loadings on LC1 were associated with higher measures of poor sleep and psychopathology. Higher values on sleep (blue) and biopsychosocial (green, purple, pink) loadings indicate worse outcomes. Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance (after FDR correction $q<0.05$); (B) Unthresholded edge-wise beta

coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC1 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

Figure 3 – Second latent component (LC2) reflects sleep resilience and psychopathology.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC2. Greater loadings on LC2 were associated with higher measures of complaints of daytime dysfunction and psychopathology. Positive values on sleep (blue) loadings indicate worse outcomes while positive values on biopsychosocial (green, purple, pink) loadings reflect higher magnitude on these measures. Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC2 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

Figure 4 – Third latent component (LC3) reflects hypnotics and sociability.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC3. Greater loadings on LC3 were associated with the use of sedative-hypnotics and measures of positive social relationships, lower body mass index (BMI) and poor visual episodic memory performance. Positive values on sleep (blue) loadings indicate worse outcomes while positive values on the mental health (green), affect (pink) and personality (purple) categories of biopsychosocial loadings reflect higher magnitude on these measures. Positive value in the physical health (olive) category represents higher value and positive values in the cognition (orange) category indicate either higher accuracies or slower reaction times (RT). Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC3 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

Figure 5 – Fourth latent component (LC4) reflects sleep duration and cognition.
(A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC4. Greater loadings on LC4 were associated with shorter sleep duration and measures of poor cognitive performance. Positive values on sleep loadings indicate worse outcomes while positive values on the mental health (green), substance use (yellow), demographics (light blue) and personality (purple) categories of biopsychosocial loadings reflect higher magnitude on the measures. Positive values in the cognition (orange) category indicate either higher accuracies or slower reaction times (RT). Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from

generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC4 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

Figure 6 – Fifth latent component (LC5) reflects sleep disturbance, cognition and psychopathology. (A) Sleep loadings (left) and top 15 strongest biopsychosocial (BPS) loadings (right) for LC5. Greater loadings on LC5 were associated with the presence of sleep disturbances, higher measures of psychopathology and lower cognitive performance. Positive values on sleep loadings indicate worse outcomes while positive values on the mental health (green), substance use (yellow) and personality (purple) categories of biopsychosocial loadings reflect higher magnitude on these measures. Positive values in the cognition (orange) category indicate either higher accuracies or slower reaction times (RT), while positive values in the demographics (light blue) and physical health (olive) categories represent higher values. Error bars indicate bootstrapped-estimated confidence intervals (i.e., standard deviation) and measures in bold indicate statistical significance. (B) Unthresholded edge-wise beta coefficients obtained from generalized linear models (GLM) between participants' LC1 canonical scores (i.e., averaged sleep and behavior canonical scores) and their RSFC data; (C) FDR-corrected network-wise beta coefficients computed with GLMs within and between 17 Yeo networks[111] and subcortical regions[109]. (D) Distribution of the integration/segregation ratio in each of the 7 Yeo networks and subcortical regions associated with LC5 (left). The dashed line indicates the median of all parcels, and the bold black lines represent the median for each network. The integration/segregation ratio values for the 400 Schaeffer parcellation[108] and 7 subcortical regions are projected on cortical and subcortical surfaces (right).

REFERENCES

1. Becker, S. P., Langberg, J. M. & Byars, K. C. Advancing a Biopsychosocial and Contextual Model of Sleep in Adolescence: A Review and Introduction to the Special Issue. *J. Youth Adolesc.* **44**, 239–270 (2015).
2. Verma, K., Singh, D. & Srivastava, A. Sleep disorders and its consequences on biopsychosocial health: A narrative review. *Yoga Mimamsa* **54**, 101 (2022).
3. Havelka, M., Luanin, J. D. & Luanin, D. Biopsychosocial Model – The Integrated Approach to Health and Disease. *Coll Antropol* (2009).
4. Bolton, D. & Gillett, G. *The Biopsychosocial Model of Health and Disease: New Philosophical and Scientific Developments*. (Springer International Publishing, Cham, 2019). doi:10.1007/978-3-030-11899-0.

5. Roth, T. *et al.* Sleep Problems, Comorbid Mental Disorders, and Role Functioning in the National Comorbidity Survey Replication (NCS-R). *Biol. Psychiatry* **60**, 1364–1371 (2006).
6. Chaput, J.-P. *et al.* Sleep duration and health in adults: an overview of systematic reviews. *Appl. Physiol. Nutr. Metab.* **45**, S218–S231 (2020).
7. Gao, C. *et al.* Sleep Duration/Quality With Health Outcomes: An Umbrella Review of Meta-Analyses of Prospective Studies. *Front. Med.* **8**, (2022).
8. Freeman, D., Sheaves, B., Waite, F., Harvey, A. G. & Harrison, P. J. Sleep disturbance and psychiatric disorders. *Lancet Psychiatry* **7**, 628–637 (2020).
9. Buysse, D. J. Sleep Health: Can We Define It? Does It Matter? *Sleep* **37**, 9–17 (2014).
10. Papadopoulos, D., Sosso, F. E., Khoury, T. & Surani, S. R. Sleep Disturbances Are Mediators Between Socioeconomic Status and Health: a Scoping Review. *Int. J. Ment. Health Addict.* **20**, 480–504 (2022).
11. Hudson, A. N., Van Dongen, H. P. A. & Honn, K. A. Sleep deprivation, vigilant attention, and brain function: a review. *Neuropsychopharmacology* **45**, 21–30 (2020).
12. Killgore, W. D. S. Effects of sleep deprivation on cognition. in *Progress in Brain Research* (eds. Kerkhof, G. A. & Dongen, H. P. A. van) vol. 185 105–129 (Elsevier, 2010).
13. Liew, S. C. & Aung, T. Sleep deprivation and its association with diseases- a review. *Sleep Med.* **77**, 192–204 (2021).
14. Ong, A. D., Kim, S., Young, S. & Steptoe, A. Positive affect and sleep: A systematic review. *Sleep Med. Rev.* **35**, 21–32 (2017).
15. Song, Q. *et al.* The Lifestyle-Related Cardiovascular Risk Is Modified by Sleep Patterns. *Mayo Clin. Proc.* **97**, 519–530 (2022).
16. Fan, M. *et al.* Sleep patterns, genetic susceptibility, and incident cardiovascular disease: a prospective study of 385 292 UK biobank participants. *Eur. Heart J.* **41**, 1182–1189 (2020).
17. Shi, L. *et al.* Sleep disturbances increase the risk of dementia: A systematic review and meta-analysis. *Sleep Med. Rev.* **40**, 4–16 (2018).

18. Wang, C. & Holtzman, D. M. Bidirectional relationship between sleep and Alzheimer's disease: role of amyloid, tau, and other factors. *Neuropsychopharmacology* (2019) doi:10.1038/s41386-019-0478-5.

19. Gregory, A. M. *et al.* Associations between sleep quality and anxiety and depression symptoms in a sample of young adult twins and siblings. *J. Psychosom. Res.* **71**, 250–255 (2011).

20. van de Langenberg, S. C. N., Kocevska, D. & Luik, A. I. The multidimensionality of sleep in population-based samples: a narrative review. *J. Sleep Res.* **31**, e13608 (2022).

21. Semler, C. N. & Harvey, A. G. Misperception of sleep can adversely affect daytime functioning in insomnia. *Behav. Res. Ther.* **43**, 843–856 (2005).

22. Castelnovo, A. *et al.* The paradox of paradoxical insomnia: A theoretical review towards a unifying evidence-based definition. *Sleep Med. Rev.* **44**, 70–82 (2019).

23. Perrault, A. A. *et al.* Effects of cognitive behavioral therapy for insomnia on subjective and objective measures of sleep and cognition. *Sleep Med.* **97**, 13–26 (2022).

24. Wade, D. T. & Halligan, P. W. The biopsychosocial model of illness: a model whose time has come. (2017).

25. Smith, C. E. & Lee, S. Identifying diverse forms of (un)healthy sleep: Sleep profiles differentiate adults' psychological and physical well-being. *Soc. Sci. Med.* **292**, 114603 (2022).

26. Blanken, T. F. *et al.* Insomnia disorder subtypes derived from life history and traits of affect and personality. *Lancet Psychiatry* **6**, 151–163 (2019).

27. Appleton, S. L. *et al.* Multidimensional sleep health is associated with mental well-being in Australian adults. *J. Sleep Res.* **31**, e13477 (2022).

28. Katori, M., Shi, S., Ode, K. L., Tomita, Y. & Ueda, H. R. The 103,200-arm acceleration dataset in the UK Biobank revealed a landscape of human sleep phenotypes. *Proc. Natl. Acad. Sci.* **119**, e2116729119 (2022).

29. Tahmasian, M. *et al.* The interrelation of sleep and mental and physical health is anchored in grey-matter neuroanatomy and under genetic control. *Commun. Biol.* **3**, 1–13 (2020).

30. Wang, Y. *et al.* Covariance patterns between sleep health domains and distributed intrinsic functional connectivity. *Nat. Commun.* **14**, 7133 (2023).
31. McIntosh, A. R. Comparison of Canonical Correlation and Partial Least Squares analyses of simulated and empirical data. *aRXiv* **3**, 58–66 (2019).
32. Marek, S. *et al.* Reproducible brain-wide association studies require thousands of individuals. *Nature* **603**, 654–660 (2022).
33. Helmer, M. *et al.* On stability of Canonical Correlation Analysis and Partial Least Squares with application to brain-behavior associations. 2020.08.25.265546 Preprint at https://doi.org/10.1101/2020.08.25.265546 (2023).
34. Van Essen, D. C. *et al.* The WU-Minn Human Connectome Project: An overview. *NeuroImage* **80**, 62–79 (2013).
35. Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R. & Kupfer, D. J. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* **28**, 193–213 (1989).
36. Grumbach, P. *et al.* Sleep duration is associated with white matter microstructure and cognitive performance in healthy adults. *Hum. Brain Mapp.* **41**, 4397–4405 (2020).
37. Curtis, B. J., Williams, P. G., Jones, C. R. & Anderson, J. S. Sleep duration and resting fMRI functional connectivity: examination of short sleepers with and without perceived daytime dysfunction. *Brain Behav.* **6**, e00576 (2016).
38. Deco, G. & Kringelbach, M. L. Great Expectations: Using Whole-Brain Computational Connectomics for Understanding Neuropsychiatric Disorders. *Neuron* **84**, 892–905 (2014).
39. Cheng, C. P. W. *et al.* Relationship between cortical thickness and neuropsychological performance in normal older adults and those with mild cognitive impairment. *Aging Dis.* **9**, 1020–1030 (2018).
40. Cuthbert, B. N. The RDoC framework: Facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. *Ann. Med. Psychol. (Paris)* **179**, 75–85 (2021).

41. Insel, T. *et al.* Research Domain Criteria (RDoC): Toward a New Classifi ation Framework for Research on Mental Disorders. *Am. J. Psychiatry Online* 748–751 (2010).

42. Plomin, R., Haworth, C. M. A. & Davis, O. S. P. Common disorders are quantitative traits. *Nat. Rev. Genet.* **10**, 872–878 (2009).

43. Behzadi, Y., Restom, K., Liau, J. & Liu, T. T. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage* **37**, 90–101 (2007).

44. Garg, H. Sleep History Taking and Examination. *Int. J. Head Neck Surg.* **10**, 9–17 (2019).

45. Kozak, M. J. & Cuthbert, B. N. The NIMH Research Domain Criteria Initiative: Background, Issues, and Pragmatics: NIMH Research Domain Criteria initiative. *Psychophysiology* **53**, 286–297 (2016).

46. Baglioni, C. *et al.* Sleep and mental disorders: a meta-analysis of polysomnographic research. *Psychol. Bull.* **142**, 969–990 (2016).

47. Caspi, A. *et al.* The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders? *Clin. Psychol. Sci.* **2**, 119–137 (2014).

48. Del Rio João, K. A., Jesus, S. N. de, Carmo, C. & Pinto, P. The impact of sleep quality on the mental health of a non-clinical population. *Sleep Med.* **46**, 69–73 (2018).

49. Palagini, L., Hertenstein, E., Riemann, D. & Nissen, C. Sleep, insomnia and mental health. *J. Sleep Res.* **31**, e13628 (2022).

50. He, Y. *et al.* The Transcriptional Repressor DEC2 Regulates Sleep Length in Mammals. *Science* **325**, 866–870 (2009).

51. Li, Y. *et al.* The brain structure and genetic mechanisms underlying the nonlinear association between sleep duration, cognition and mental health. *Nat. Aging* **2**, 425–437 (2022).

52. Lunansky, G. *et al.* The Mental Health Ecosystem: Extending Symptom Networks With Risk and Protective Factors. *Front. Psychiatry* **12**, (2021).

53. Ting, L. & Malhotra, A. Disorders of Sleep: An Overview. *Prim. Care* **32**, 305–v (2005).

54. Wainberg, M. *et al.* Association of accelerometer-derived sleep measures with lifetime psychiatric diagnoses: A cross-sectional study of 89,205 participants from the UK Biobank. *PLOS Med.* **18**, e1003782 (2021).

55. Banks, S. & Dinges, D. F. Behavioral and physiological consequences of sleep restriction. *J. Clin. Sleep Med.* **3**, 519–528 (2007).

56. Durmer, J. S. & Dinges, D. F. Neurocognitive Consequences of Sleep Deprivation. *Semin. Neurol.* **25**, 117–129 (2005).

57. Lim, J., Choo, W.-C. & Chee, M. W. L. Reproducibility of Changes in Behaviour and fMRI Activation Associated with Sleep Deprivation in a Working Memory Task. *Sleep* **30**, 61–70 (2007).

58. Chee, M. W. L. & Chuah, L. Y. M. Functional neuroimaging insights into how sleep and sleep deprivation affect memory and cognition. *Curr. Opin. Neurol.* **21**, 417–423 (2008).

59. Cross, N. E. *et al.* An altered balance of integrated and segregated brain activity is a marker of cognitive deficits following sleep deprivation. *PLoS Biol.* **19**, 2020.11.28.402305 (2021).

60. Dorrian, J., Centofanti, S., Smith, A. & McDermott, K. D. Chapter 4 - Self-regulation and social behavior during sleep deprivation. in *Progress in Brain Research* (eds. Van Dongen, H. P. A., Whitney, P., Hinson, J. M., Honn, K. A. & Chee, M. W. L.) vol. 246 73–110 (Elsevier, 2019).

61. Cross, N. *et al.* Cortical gradients of functional connectivity are robust to state-dependent changes following sleep deprivation. *NeuroImage* **226**, 117547 (2021).

62. Neubauer, D. N., Pandi-Perumal, S. R., Spence, D. W., Buttoo, K. & Monti, J. M. Pharmacotherapy of Insomnia. *J. Cent. Nerv. Syst. Dis.* **10**, 1179573518770672 (2018).

63. Vermeeren, A. & Coenen, A. M. L. Effects of the use of hypnotics on cognition. in *Progress in Brain Research* (eds. Van Dongen, H. P. A. & Kerkhof, G. A.) vol. 190 89–103 (Elsevier, 2011).

64. Crowe, S. F. & Stranks, E. K. The Residual Medium and Long-term Cognitive Effects of Benzodiazepine Use: An Updated Meta-analysis. *Arch. Clin. Neuropsychol.* **33**, 901–911 (2018).

65. Lee, J. S. *et al.* Is the GABA System Related to the Social Competence Improvement Effect of Aripiprazole? An 18F-Fluoroflumazenil PET Study. *Psychiatry Investig.* **10**, 75–80 (2013).

66. Mielnik, C. A., Horsfall, W. & Ramsey, A. J. Diazepam improves aspects of social behaviour and neuron activation in NMDA receptor-deficient mice. *Genes Brain Behav.* **13**, 592–602 (2014).

67. Pillai, V. *et al.* Effectiveness of Benzodiazepine Receptor Agonists in the Treatment of Insomnia: An Examination of Response and Remission Rates. *Sleep* **40**, zsw044 (2017).

68. Hajak, G. *et al.* Effects of hypnotics on sleep quality and daytime well-being. Data from a comparative multicentre study in outpatients with insomnia. *Eur. Psychiatry* **10**, 173s–179s (1995).

69. Watson, N. F. *et al.* Do Insomnia Treatments Improve Daytime Function? *J. Clin. Med.* **12**, 3089 (2023).

70. Yeo, B. T. T., Tandi, J. & Chee, M. W. L. Functional connectivity during rested wakefulness predicts vulnerability to sleep deprivation. *NeuroImage* **111**, 147–158 (2015).

71. Kebets, V. *et al.* Somatosensory-Motor Dysconnectivity Spans Multiple Transdiagnostic Dimensions of Psychopathology. *Biol. Psychiatry* **86**, 779–791 (2019).

72. Van Dam, N. T. *et al.* Data-Driven Phenotypic Categorization for Neurobiological Analyses: Beyond DSM-5 Labels. *Biol. Psychiatry* **81**, 484–494 (2017).

73. Bai, Y. *et al.* Resting-state functional connectivity of the sensory/somatomotor network associated with sleep quality: evidence from 202 young male samples. *Brain Imaging Behav.* **16**, 1832–1841 (2022).

74. Zhang, L., Li, D. & Yin, H. How is psychological stress linked to sleep quality? The mediating role of functional connectivity between the sensory/somatomotor network and the cingulo-opercular control network. *Brain Cogn.* **146**, 105641 (2020).

75. Bin, Y. S. Is Sleep Quality More Important than Sleep Duration for Public Health? *Sleep* **39**, 1629–1630 (2016).

76. Zavecz, Z., Nagy, T., Galkó, A., Nemeth, D. & Janacsek, K. The relationship between subjective sleep quality and cognitive performance in healthy young adults: Evidence from three empirical studies. *Sci. Rep.* **10**, 4855 (2020).

77. Faulkner, S. & Sidey-Gibbons, C. Use of the Pittsburgh Sleep Quality Index in People With Schizophrenia Spectrum Disorders: A Mixed Methods Study. *Front. Psychiatry* **10**, (2019).

78. Krittanawong, C. *et al.* Sleep Duration and Cardiovascular Health in a Representative Community Population (from NHANES, 2005 to 2016). *Am. J. Cardiol.* **127**, 149–155 (2020).

79. Clark, A. J. *et al.* Onset of Impaired Sleep and Cardiovascular Disease Risk Factors: A Longitudinal Study. *Sleep* **39**, 1709–1718 (2016).

80. Baker, M., Stabile, M. & Deri, C. What Do Self-Reported, Objective, Measures of Health Measure? *J. Hum. Resour.* **39**, 1067–1093 (2004).

81. Trimmel, K. *et al.* The (mis)perception of sleep: factors influencing the discrepancy between self-reported and objective sleep parameters. *J. Clin. Sleep Med.* **17**, 917–924 (2021).

82. Lee, S.-A., Im, K. & Yang, H. Factors associated with sleep state misperception in patients with obstructive sleep apnea. *Sleep Breath.* **26**, 1921–1930 (2022).

83. Lecci, S. *et al.* Electroencephalographic changes associated with subjective under- and overestimation of sleep duration. *SLEEP* **43**, zsaa094 (2020).

84. Andrillon, T. *et al.* Revisiting the value of polysomnographic data in insomnia: more than meets the eye. *Sleep Med.* **66**, 184–200 (2020).

85. Lim, D. C. *et al.* The need to promote sleep health in public health agendas across the globe. *Lancet Public Health* **8**, e820–e826 (2023).

86. Barch, D. M. *et al.* Function in the human connectome: Task-fMRI and individual differences in behavior. *NeuroImage* **80**, 169–189 (2013).

87. Kettenring, J. R. Canonical analysis of several sets of variables. *Biometrika* **58**, 433–451 (1971).

88. Hotelling, H. Relations Between Two Sets of Variates. in *Breakthroughs in Statistics: Methodology and Distribution* (eds. Kotz, S. & Johnson, N. L.) 162–190 (Springer, New York, NY, 1992). doi:10.1007/978-1-4612-4380-9_14.

89. Courville, T. & Thompson, B. Use of Structure Coefficients in Published Multiple Regression Articles: β is not Enough. (2001).

90. Henson, R. K. The logic and interpretation of structure coefficients in multivariate general linear model analyses. in (New Orleans, 2002).

91. Sherry, A. & Henson, R. K. Conducting and Interpreting Canonical Correlation Analysis in Personality Research: A User-Friendly Primer. *J. Pers. Assess.* **84**, 37–48 (2005).

92. Winkler, A. M. *et al.* Non-parametric combination and related permutation tests for neuroimaging. *Hum. Brain Mapp.* **37**, 1486–1511 (2016).

93. Winkler, A. M., Ridgway, G. R., Webster, M. A., Smith, S. M. & Nichols, T. E. Permutation inference for the general linear model. *NeuroImage* **92**, 381–397 (2014).

94. Glasser, M. F. *et al.* The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage* **80**, 105–124 (2013).

95. Smith, S. M. *et al.* Resting-state fMRI in the Human Connectome Project. *NeuroImage* **80**, 144–168 (2013).

96. Griffanti, L. *et al.* ICA-based artefact removal and accelerated fMRI acquisition for improved resting state network imaging. *NeuroImage* **95**, 232–247 (2014).

97. Salimi-Khorshidi, G. *et al.* Automatic denoising of functional MRI data: combining independent component analysis and hierarchical fusion of classifiers. *NeuroImage* **90**, 449–468 (2014).

98. Robinson, E. C. *et al.* MSM: A new flexible framework for Multimodal Surface Matching. *NeuroImage* **100**, 414–426 (2014).

99. Burgess, G. C. *et al.* Evaluation of Denoising Strategies to Address Motion-Correlated Artifacts in Resting-State Functional Magnetic Resonance Imaging Data from the Human Connectome Project. *Brain Connect.* **6**, 669–680 (2016).

100. Siegel, J. S. *et al.* Data Quality Influences Observed Links Between Functional Connectivity and Behavior. *Cereb. Cortex* **27**, 4492–4502 (2017).

101. Li, J. *et al.* Global signal regression strengthens association between resting-state functional connectivity and behavior. *NeuroImage* **196**, 126–141 (2019).

102. Kong, R. *et al.* Spatial Topography of Individual-Specific Cortical Networks Predicts Human Cognition, Personality, and Emotion. *Cereb. Cortex N. Y. NY* **29**, 2533–2551 (2019).

103. Jenkinson, M., Bannister, P., Brady, M. & Smith, S. Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. *NeuroImage* **17**, 825–841 (2002).

104. Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L. & Petersen, S. E. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage* **59**, 2142–2154 (2012).

105. Li, X. & Huang, X. Linear mode regression with covariate measurement error. *Can. J. Stat.* **47**, 262–280 (2019).

106. Liu, T. T., Nalci, A. & Falahpour, M. The global signal in fMRI: Nuisance or Information? *NeuroImage* **150**, 213–229 (2017).

107. Murphy, K. & Fox, M. D. Towards a consensus regarding global signal regression for resting state functional connectivity MRI. *NeuroImage* **154**, 169–173 (2017).

108. Schaefer, A. *et al.* Local-Global Parcellation of the Human Cerebral Cortex from Intrinsic Functional Connectivity MRI. *Cereb. Cortex* **28**, 3095–3114 (2018).

109. Fischl, B. FreeSurfer. *NeuroImage* **62**, 774–781 (2012).

110. Rubinov, M. & Sporns, O. Complex network measures of brain connectivity: Uses and interpretations. *NeuroImage* **52**, 1059–1069 (2010).

111. Yeo, B. T. *et al.* The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J. Neurophysiol.* **106**, 1125–1165 (2011).

112. Shine, J. M. *et al.* The Dynamics of Functional Brain Networks: Integrated Network States during Cognitive Task Performance. *Neuron* **92**, 544–554 (2016).

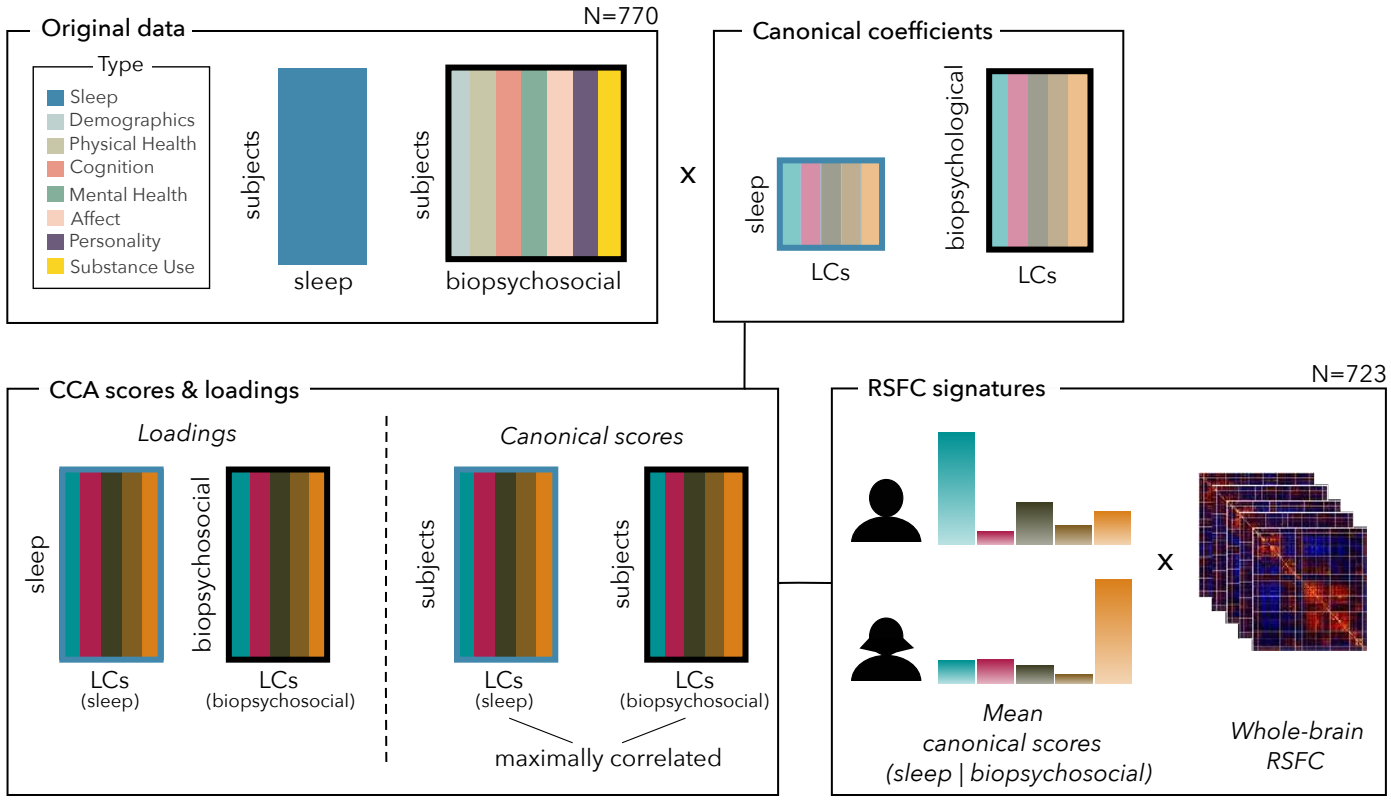
113. Glasser, M. F. *et al.* Using temporal ICA to selectively remove global noise while preserving global signal in functional MRI data. *NeuroImage* **181**, 692–717 (2018).

Characteristics	N = 770
Biological sex (n | %)	
Female	414 | 53.76%
Male	356 | 46.23%
Age (years)	
mean ± SD	28.86 ± 3.61
range	[22 - 36]
Education (years)	
mean ± SD	15.02 ± 1.73
range	[11 - 17]
Race (n | %)	
Am. Indian/Alaskan Nat.	2 | 0.25%
Asian/Nat. Hawaiian/Other Pacific Is.	42 | 5.45%
Black or African Am.	90 | 11.68%
More than one	19 | 2.46%
Unknown or Not Reported	16 | 2.07%
White	601 | 78.05%
Ethnicity (n | %)	
Hispanic/Latino	78 | 10.12%
Not Hispanic/Latino	684 | 88.83%
Unknown or Not Reported	8 | 1.03%
Employment status (n | %)	
Full-time	545 | 70.77%
Part-time	132 | 17.14%
Not working	93 | 12.07%
School status (n | %)	
In school	158 | 20.51%
Not in school	612 | 79.48%
Yearly income (n | %)	
<10'000 US$	50 | 6.49%
10'000 - 20'000 US$	50 | 6.49%
20'000 - 30'000 US$	94 | 12.20%
30'000 - 40'000 US$	101 | 13.11%
40'000 - 50'000 US$	76 | 9.87%
50'000 - 75'000 US$	165 | 21.42%
75'000 - 100'000 US$	112 | 14.54%
> 100'00 US$	122 | 15.84%
Relationship status (n | %)	
In a relationship	363 | 47.14%
Not in a relationship	407 | 52.85%
PSQI total score	
mean ± SD	5.14 ± 2.17
range	[0 - 19]

PSQI, Pittsburgh sleep quality index

Table 1

A. Canonical correlation analysis (CCA)



B. Sleep-biopsychosocial profiles (LCs)

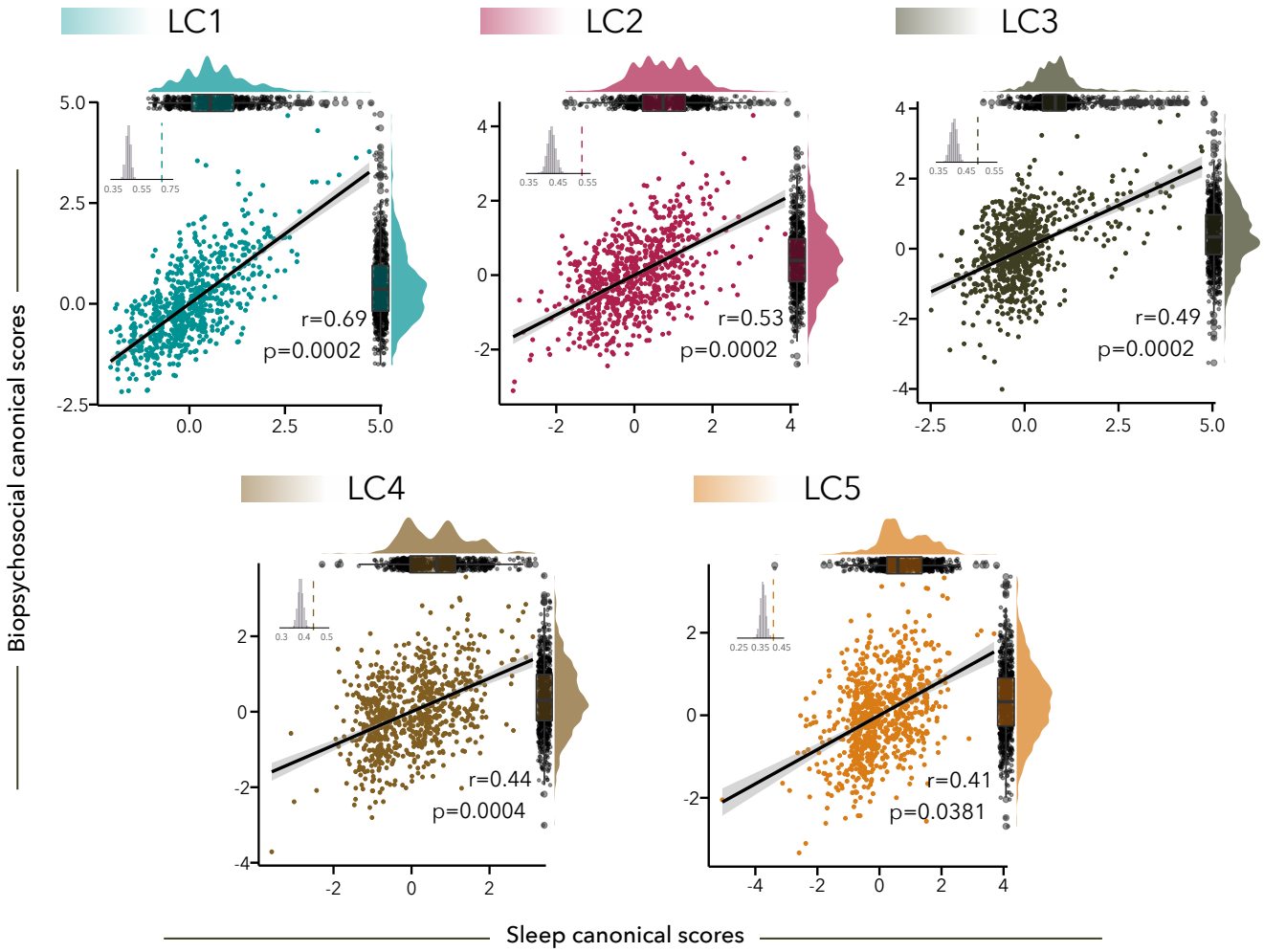


Figure 1

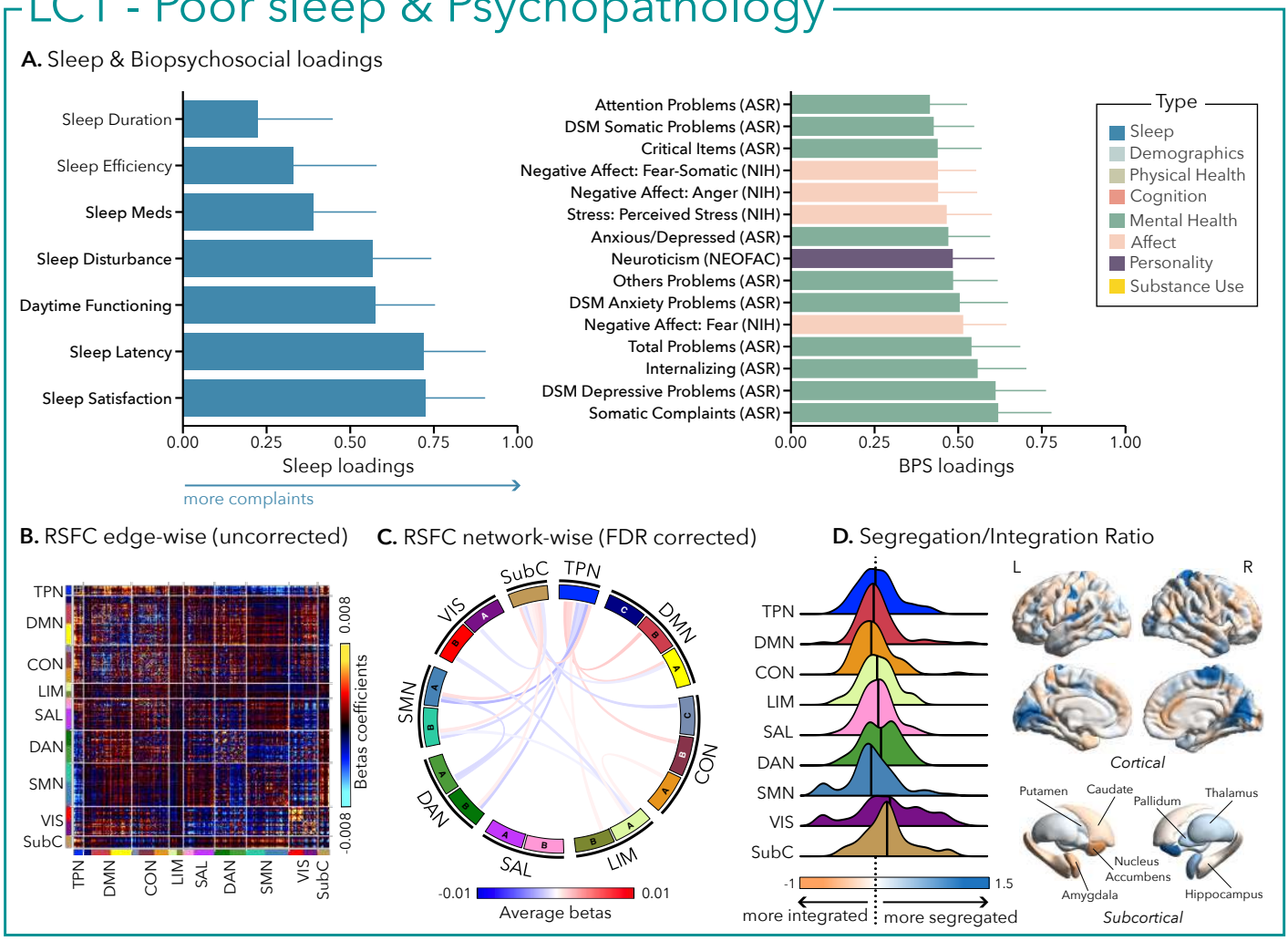

LC1 - Poor sleep & Psychopathology
A. Sleep & Biopsychosocial loadings
Sleep Duration
Sleep Efficiency
Sleep Meds
Sleep Disturbance
Daytime Functioning
Sleep Latency
Sleep Satisfaction
0.00
0.25
0.50
0.75
1.00
Sleep loadings
more complaints
Attention Problems (ASR)
DSM Somatic Problems (ASR)
Critical Items (ASR)
Negative Affect: Fear-Somatic (NIH)
Negative Affect: Anger (NIH)
Stress: Perceived Stress (NIH)
Anxious/Depressed (ASR)
Neuroticism (NEOFAC)
Others Problems (ASR)
DSM Anxiety Problems (ASR)
Negative Affect: Fear (NIH)
Total Problems (ASR)
Internalizing (ASR)
DSM Depressive Problems (ASR)
Somatic Complaints (ASR)
BPS loadings
Type
Sleep
Demographics
Physical Health
Cognition
Mental Health
Affect
Personality
Substance Use
B. RSFC edge-wise (uncorrected)
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
0.008
-0.008
Betas coefficients
C. RSFC network-wise (FDR corrected)
-0.01
0.01
Average betas
D. Segregation/Integration Ratio
-1
1.5
more integrated
more segregated
L
R
Cortical
Putamen
Caudate
Pallidum
Thalamus
Nucleus Accumbens
Amygdala
Hippocampus
Subcortical

Figure 2

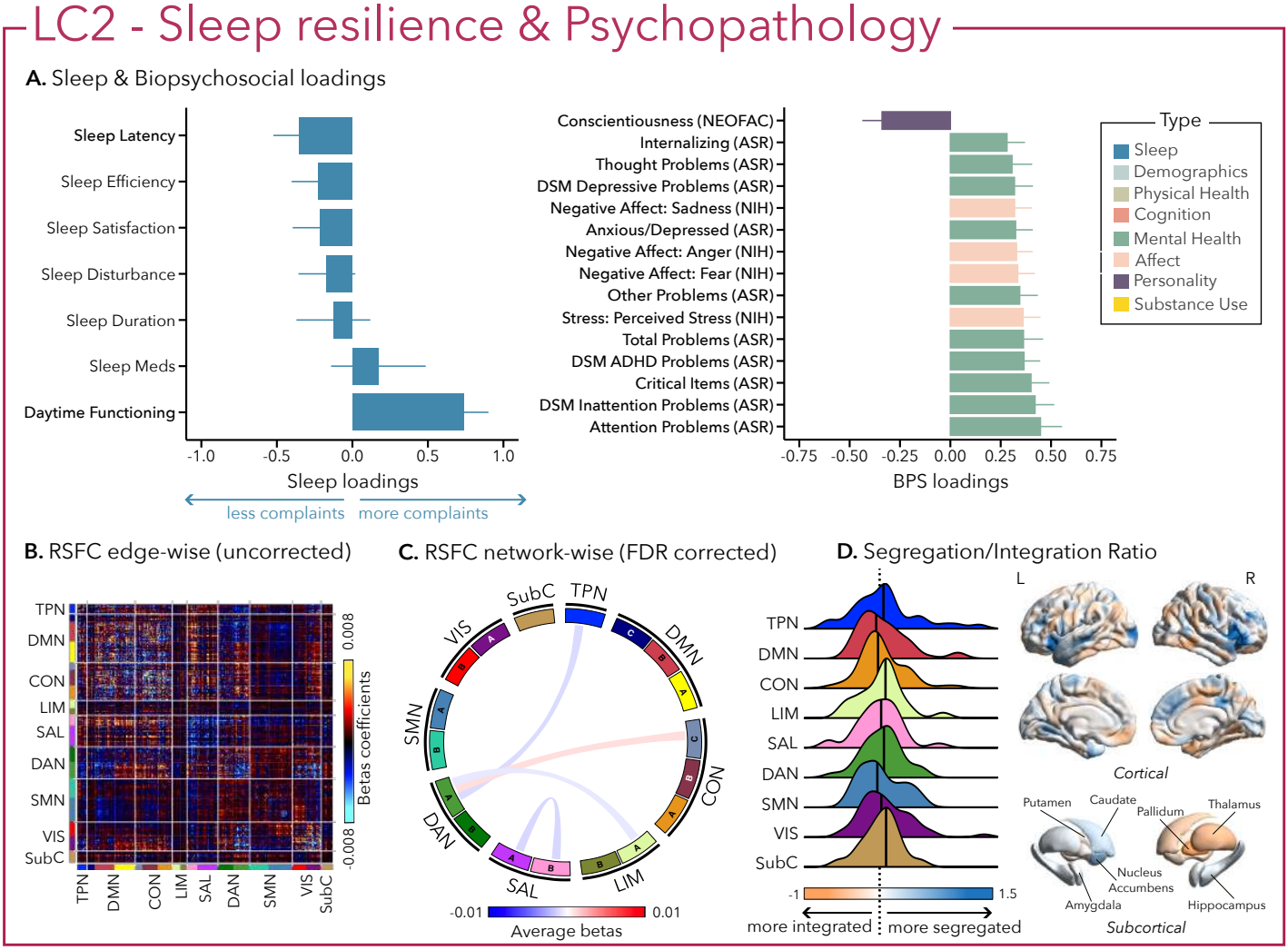

LC2 - Sleep resilience & Psychopathology
A. Sleep & Biopsychosocial loadings
Sleep Latency
Sleep Efficiency
Sleep Satisfaction
Sleep Disturbance
Sleep Duration
Sleep Meds
Daytime Functioning
-1.0
-0.5
0.0
0.5
1.0
Sleep loadings
less complaints
more complaints
Conscientiousness (NEOFAC)
Internalizing (ASR)
Thought Problems (ASR)
DSM Depressive Problems (ASR)
Negative Affect: Sadness (NIH)
Anxious/Depressed (ASR)
Negative Affect: Anger (NIH)
Negative Affect: Fear (NIH)
Other Problems (ASR)
Stress: Perceived Stress (NIH)
Total Problems (ASR)
DSM ADHD Problems (ASR)
Critical Items (ASR)
DSM Inattention Problems (ASR)
Attention Problems (ASR)
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
BPS loadings
Type
Sleep
Demographics
Physical Health
Cognition
Mental Health
Affect
Personality
Substance Use
B. RSFC edge-wise (uncorrected)
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
0.008
-0.008
Betas coefficients
C. RSFC network-wise (FDR corrected)
SubC
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
-0.01
0.01
Average betas
D. Segregation/Integration Ratio
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
-1
1.5
more integrated
more segregated
L
R
Cortical
Putamen
Caudate
Pallidum
Thalamus
Nucleus Accumbens
Amygdala
Hippocampus
Subcortical

Figure 3

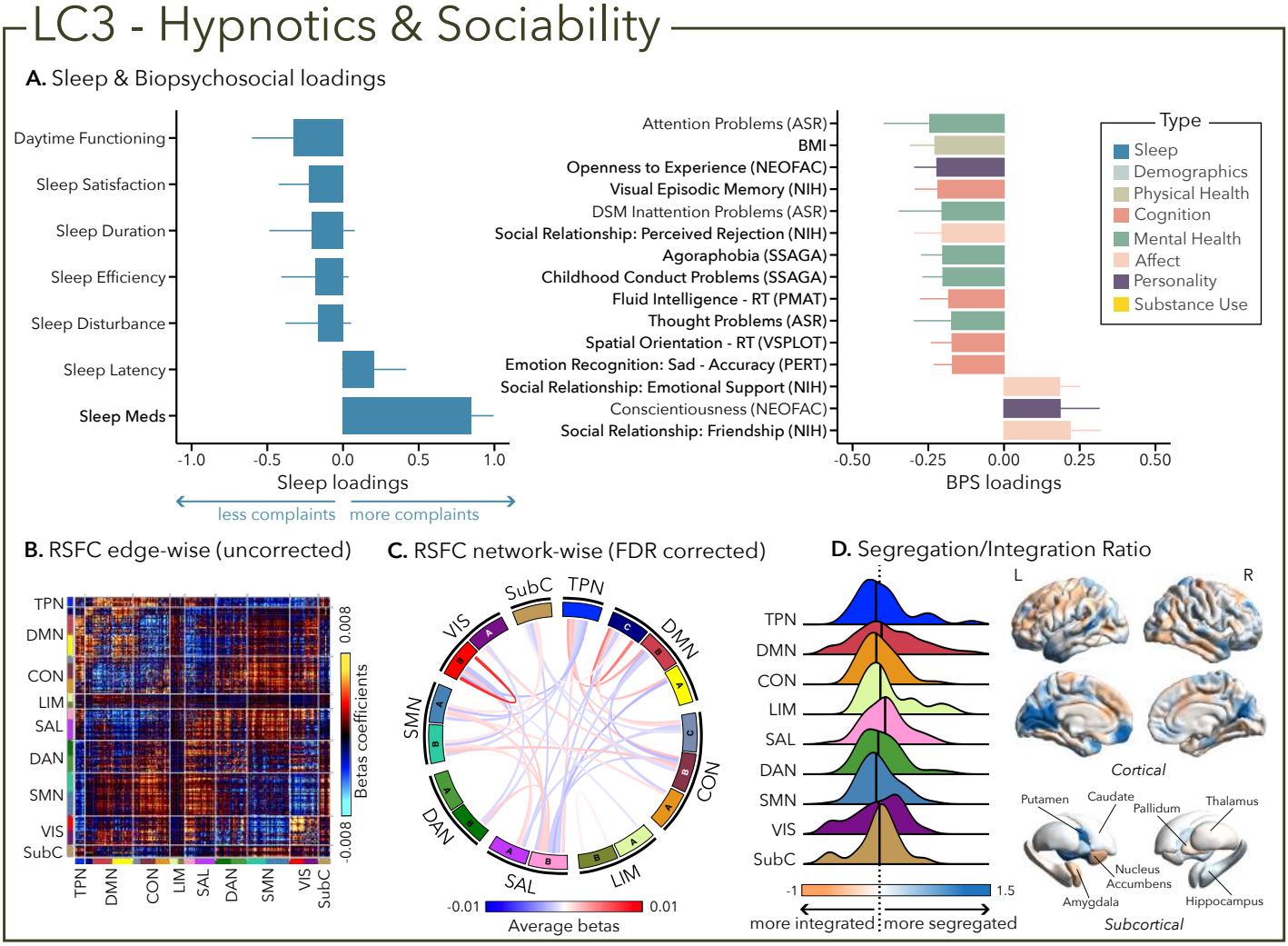

LC3 - Hypnotics & Sociability
A. Sleep & Biopsychosocial loadings
Daytime Functioning
Sleep Satisfaction
Sleep Duration
Sleep Efficiency
Sleep Disturbance
Sleep Latency
Sleep Meds
-1.0
-0.5
0.0
0.5
1.0
Sleep loadings
less complaints
more complaints
Attention Problems (ASR)
BMI
Openness to Experience (NEOFAC)
Visual Episodic Memory (NIH)
DSM Inattention Problems (ASR)
Social Relationship: Perceived Rejection (NIH)
Agoraphobia (SSAGA)
Childhood Conduct Problems (SSAGA)
Fluid Intelligence - RT (PMAT)
Thought Problems (ASR)
Spatial Orientation - RT (VSPLOT)
Emotion Recognition: Sad - Accuracy (PERT)
Social Relationship: Emotional Support (NIH)
Conscientiousness (NEOFAC)
Social Relationship: Friendship (NIH)
-0.50
-0.25
0.00
0.25
0.50
BPS loadings
Type
Sleep
Demographics
Physical Health
Cognition
Mental Health
Affect
Personality
Substance Use
B. RSFC edge-wise (uncorrected)
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
0.008
-0.008
Betas coefficients
C. RSFC network-wise (FDR corrected)
SubC
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
-0.01
0.01
Average betas
D. Segregation/Integration Ratio
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
-1
1.5
more integrated
more segregated
L
R
Cortical
Putamen
Caudate
Pallidum
Thalamus
Nucleus Accumbens
Amygdala
Hippocampus
Subcortical

Figure 4

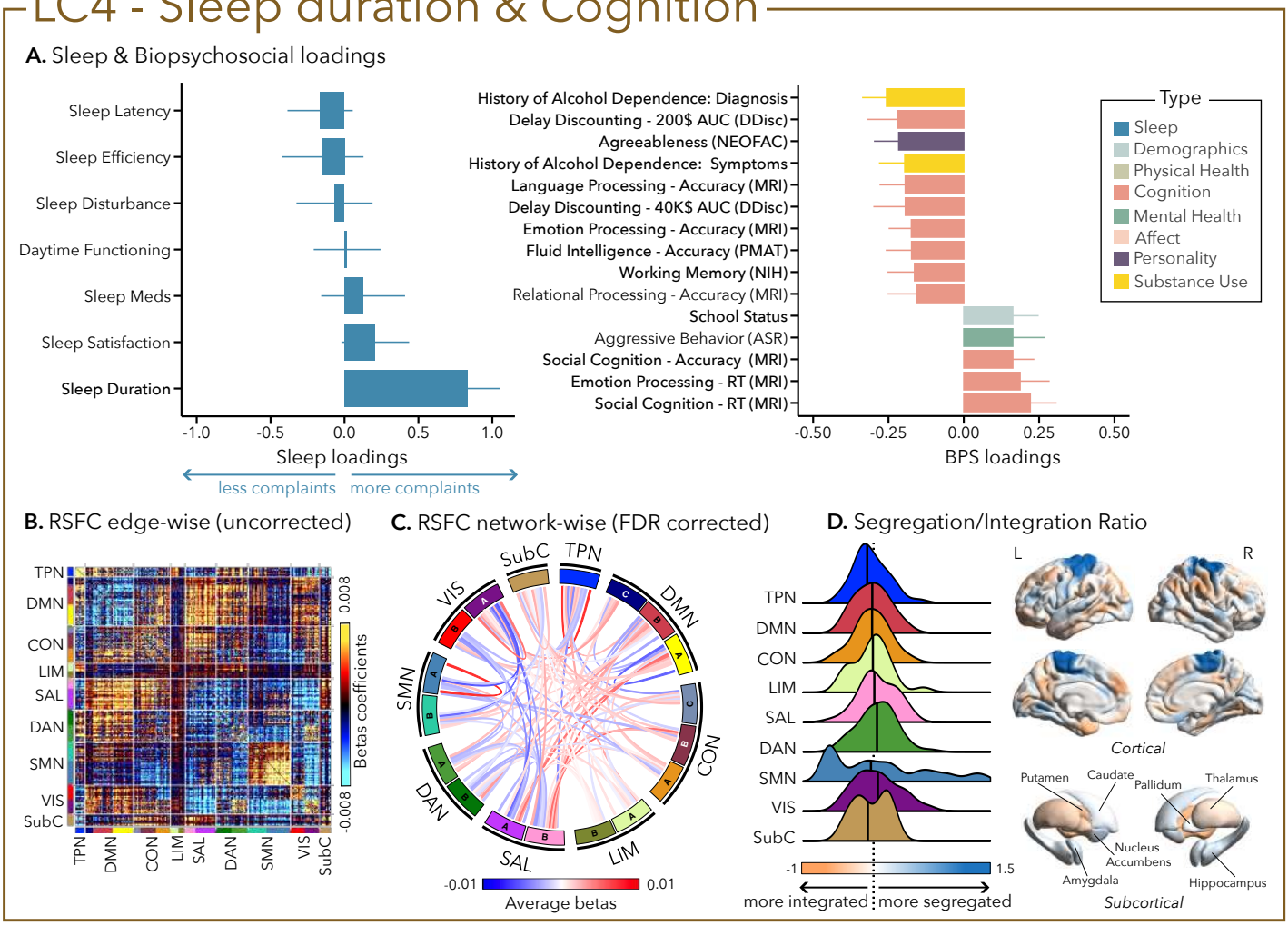

LC4 - Sleep duration & Cognition
A. Sleep & Biopsychosocial loadings
Sleep Latency
Sleep Efficiency
Sleep Disturbance
Daytime Functioning
Sleep Meds
Sleep Satisfaction
Sleep Duration
-1.0
-0.5
0.0
0.5
1.0
Sleep loadings
less complaints
more complaints
History of Alcohol Dependence: Diagnosis
Delay Discounting - 200$ AUC (DDisc)
Agreeableness (NEOFAC)
History of Alcohol Dependence: Symptoms
Language Processing - Accuracy (MRI)
Delay Discounting - 40K$ AUC (DDisc)
Emotion Processing - Accuracy (MRI)
Fluid Intelligence - Accuracy (PMAT)
Working Memory (NIH)
Relational Processing - Accuracy (MRI)
School Status
Aggressive Behavior (ASR)
Social Cognition - Accuracy (MRI)
Emotion Processing - RT (MRI)
Social Cognition - RT (MRI)
-0.50
-0.25
0.00
0.25
0.50
BPS loadings
Type
Sleep
Demographics
Physical Health
Cognition
Mental Health
Affect
Personality
Substance Use
B. RSFC edge-wise (uncorrected)
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
0.008
-0.008
Betas coefficients
C. RSFC network-wise (FDR corrected)
SubC
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
-0.01
0.01
Average betas
D. Segregation/Integration Ratio
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
-1
1.5
more integrated
more segregated
L
R
Cortical
Putamen
Caudate
Pallidum
Thalamus
Nucleus Accumbens
Amygdala
Hippocampus
Subcortical

Figure 5

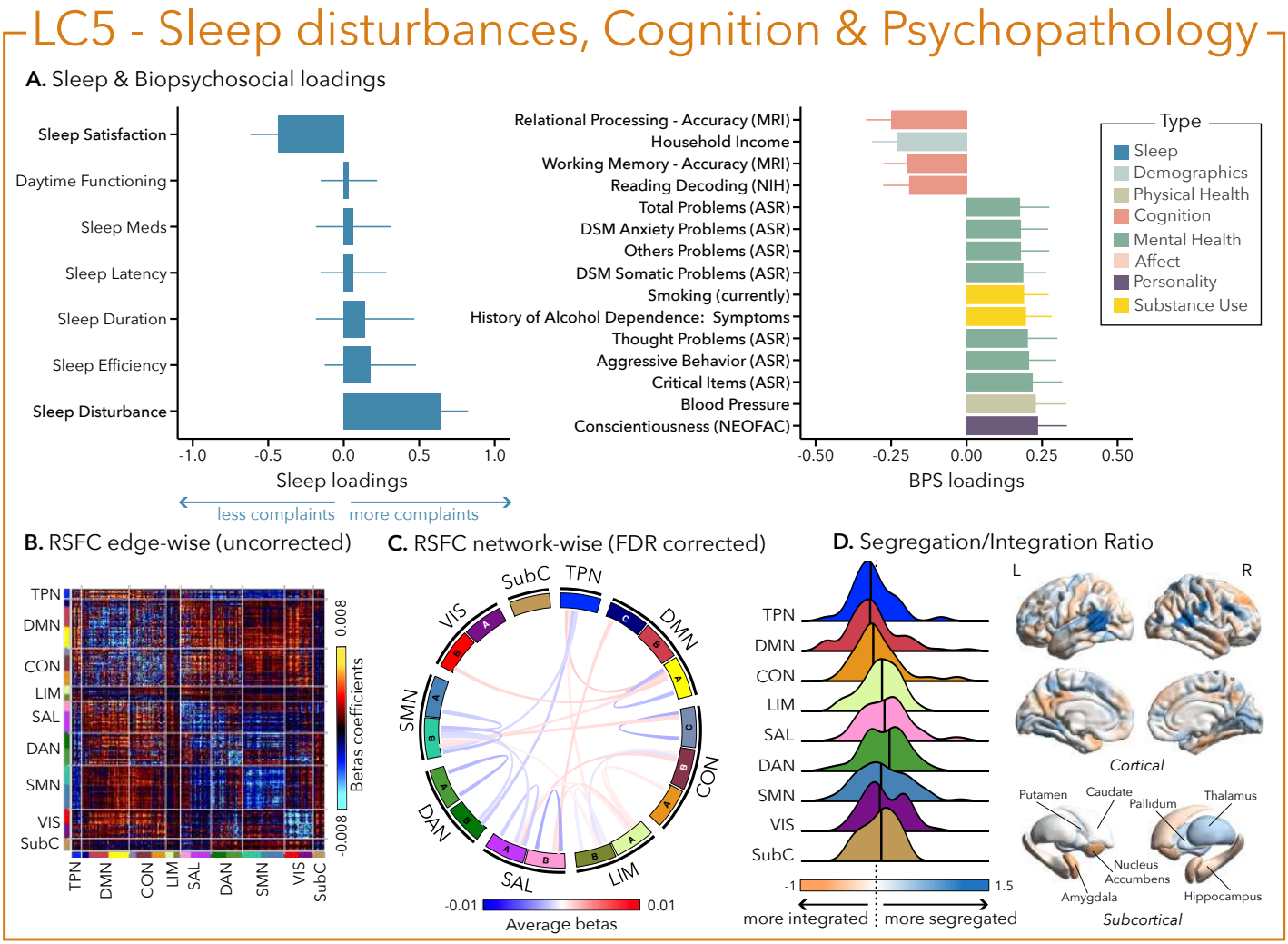

LC5 - Sleep disturbances, Cognition & Psychopathology
A. Sleep & Biopsychosocial loadings
Sleep Satisfaction
Daytime Functioning
Sleep Meds
Sleep Latency
Sleep Duration
Sleep Efficiency
Sleep Disturbance
-1.0
-0.5
0.0
0.5
1.0
Sleep loadings
less complaints
more complaints
Relational Processing - Accuracy (MRI)
Household Income
Working Memory - Accuracy (MRI)
Reading Decoding (NIH)
Total Problems (ASR)
DSM Anxiety Problems (ASR)
Others Problems (ASR)
DSM Somatic Problems (ASR)
Smoking (currently)
History of Alcohol Dependence: Symptoms
Thought Problems (ASR)
Aggressive Behavior (ASR)
Critical Items (ASR)
Blood Pressure
Conscientiousness (NEOFAC)
-0.50
-0.25
0.00
0.25
0.50
BPS loadings
Type
Sleep
Demographics
Physical Health
Cognition
Mental Health
Affect
Personality
Substance Use
B. RSFC edge-wise (uncorrected)
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
0.008
-0.008
Betas coefficients
C. RSFC network-wise (FDR corrected)
SubC
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
-0.01
0.01
Average betas
D. Segregation/Integration Ratio
TPN
DMN
CON
LIM
SAL
DAN
SMN
VIS
SubC
-1
1.5
more integrated
more segregated
L
R
Cortical
Putamen
Caudate
Pallidum
Thalamus
Nucleus Accumbens
Amygdala
Hippocampus
Subcortical

Figure 6