AWARD NUMBER: W81XWH-16-1-0259

TITLE: When Sleep Isn’t Perfect: Risk and Resilience for Cognitive Consequences of Imperfect Sleep Duration and Suboptimal Timing of Tasks in Circadian Rhythm

PRINCIPAL INVESTIGATOR: Anne Richards, MD, MPH

RECIPIENT: Northern California Institute for Research and Education
4150 Clement St 151NC, San Francisco CA 94121-1545

REPORT DATE: APRIL 2020

TYPE OF REPORT: Final Technical Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE
APRIL 2020

2. REPORT TYPE
Final

3. DATES COVERED
1 Jul 2016 -31 Dec 2019

4. TITLE AND SUBTITLE
When Sleep Isn't Perfect: Risk and Resilience for Cognitive Consequences of Imperfect Sleep Duration and Suboptimal Timing of Tasks in Circadian Rhythm

5a. CONTRACT NUMBER
W81XWH-16-1-0259

5b. GRANT NUMBER
PR150478

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Anne Richards, MD, MPH

E-Mail: anne.richards@ucsf.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Northern California Institute for
Research and Education
4150 Clement St 151NC
San Francisco CA 94121-1545

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This DOD-funded project has produced compelling and important findings with respect to sleep and cognitive performance. We have published two peer-reviewed manuscripts and presented our findings at the World Sleep 2019 annual meeting. As per our published results, we believe our most interesting findings pertain to the effects of sleep duration, and deviation from typical sleep duration, on cognitive performance across the lifespan. Our findings demonstrate the utility of large-scale data to reveal relationships between sleep duration and cognitive performance with a resolution that laboratory samples and more typically powered epidemiological studies cannot provide. We did not observe the hypothesized effects of chronotype, or chronotype synchrony, with cognitive performance. We did however observe interesting findings with respect to time of day, showing that task complexity may also impact the effects of time of day on task performance. Contrary to expectations, our initial analyses did not show marked effects of sleep duration on *learning* (or change in performance over time). We are not sufficiently confident in these negative results to disseminate these at this juncture. We continue to collaborate with our industry partner Lumos labs, with whom we are working to implement a revised chronotype measure, and to pursue research opportunities to build on positive findings and to better understand negative findings.

15. SUBJECT TERMS Sleep Duration, Chronotype, Cognitive Performance, Learning

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	20	**19b. TELEPHONE NUMBER** ***(include area code)***

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

1. INTRODUCTION:

Our DoD Discovery Award study has utilized large-scale internet-based cognitive performance data of adult men and women to examine how sleep and chronotype affect cognitive performance, and to uncover non-sleep factors contributing to cognitive risk and resilience in the setting of deviations from habitual sleep duration as well as misalignment of task timing with participants' endogenous circadian rhythmicity. The primary aims of this proposal are to examine the relationship of habitual sleep duration (HSD), deviations from habitual sleep duration, self-reported chronotype, and the degree to which task performance is aligned with chronotype (task-timing alignment to chronotype, (TTAC), also known as a chronotype "synchrony effect") with cognitive performance and improvement in performance (i.e.: learning) of cognitive tasks in adult male and female users of an internet-based cognitive training program. The design involves both cross-sectional and longitudinal assessment of cognitive performance on internet cognitive training tasks in adult men and women to examine the contributions of sleep, chronotype, demographic, lifestyle, and mood variables to cognitive performance and improvement in cognitive performance (i.e. learning) in adult male and female users of an internet cognitive training program

2. KEYWORDS:

Sleep Duration
Chronotype
Cognitive Performance
Learning

3. ACCOMPLISHMENTS:

Major Goals of Project: The primary scientific aims of our study are as follows:

Primary Aim 1: To assess the effects of habitual sleep duration (HSD), as defined by average sleep duration over a period of 4 months, and naturalistic deviation from habitual sleep duration, as determined by sleep duration immediately prior to task performance, on performance score and/or improvement in performance (i.e. learning) in tasks of working memory, task-shifting, response inhibition and verbal memory in adult male and female users of an internet cognitive training program.
Primary Aim 2: To assess the effects of chronotype, based on self-reported evening and morning preference, as well as degree of task-timing alignment to chronotype (TTAC score), as determined by chronotype and time-of-day of task performance, on performance score and/or improvement in performance (i.e. learning) in tasks of working memory, task shifting, response inhibition and verbal memory in adult male and female users of an internet cognitive training program.
Primary Aim 3: To assess the interaction of habitual sleep duration and degree of task-timing alignment to chronotype (TTAC score) on performance in tasks of working memory, task shifting, response inhibition and verbal memory in adult male and female users of an internet cognitive training program.
Primary Aim 4: To determine whether age moderates the effects of habitual sleep duration (HSD), deviations from habitual sleep duration, and degree of task-timing alignment with chronotype (TTAC score) on task performance and improvement in task performance (i.e. learning).

We described our major tasks and target dates of achievement of these tasks as follows:
Major Task 1 (Months 1-3): Study Start-Up and Approvals: Completed
We obtained required approvals for the study and established a strong working relationship with collaborators at Lumos Labs, who are committed to continue working with us in future projects.
Major Task 2 (Months 1-6): Obtain Data and Prepare Data for Analysis: Completed
We have successfully obtained data for analysis. We worked with our industry colleagues to identify the most suitable cognitive tasks for use in our analyses. Due to insufficient sample size available for some cognitive tasks

("brain games"), we focused our repeated-measures analyses on a cognitive task of executive function and response inhibition. We did not obtain an adequate sample size of quality data to perform rigorous analyses on a task of verbal memory or to rigorously analyze the contributions of mood and lifestyle variables such as exercise and caffeine use to the outcomes of interest.

Major Task 3: Data Analysis (Months 7-13): Completed

We successfully accomplished the major objectives of our study, and determined that some findings were consistent with our hypotheses while others were not (See details below, under "What was accomplished under these goals?").

Major Task 4 (Months 14-18): Dissemination of Findings and Preparation of Follow-Up Grants: In Progress

We have already published findings from this project in 2 high-profile peer-reviewed sleep journals. These results are compelling and success in publication demonstrates that findings are of relevance and interest to the sleep and broader scientific research community. We have submitted two LOI's to follow up on these findings and will continue to pursue opportunities to leverage this academic-industry partnership to advance understanding of sleep and circadian effects on cognitive performance.

We are currently working with our industry partner to 1. Revise their chronotype measure to provide a more evidence-based measure of subjective chronotype. Our *negative* findings with respect to chronotype, and task-timing alignment with chronotype (the "synchrony effect") *may* be due to a suboptimal measure of chronotype. 2. Incorporate health and mental health variables in our analyses, to understand how health variables contribute to the relationships of interest. We are particularly interested in the effects of posttraumatic stress and other conditions of high prevalence amongst DoD beneficiaries on sleep-cognition relationships. 3. As our industry partner continues to collect more data, lifestyle variables may become more adequate for large-scale analyses.

What was accomplished under these goals?

1) Major Activities: Obtained all approvals for performance of research; data analysis for Primary Aims 1-4 (cognitive performance and learning); publication of results using cross-sectionally and prospectively collected data for cognitive performance data.
2) Specific Objectives: Our specific objectives were consistent with our major activities. Our industry partner's data science team has been highly collaborative with respect to this project. The team has provided data to the investigators free of charge and without any expectations or pressures with respect to interpretation of data or authorship rights. Staffing changes, both for our industry partner and the investigator's team at various time points during the funding period contributed to some delays in study progress. Additionally, our industry partner has not designed their braingame platform specifically for the purposes of research and therefore data quantity and/or quality varied across cognitive domains and predictor variables. For example, large-scale data included scores for games performed on both desktop computers and mobile apps. Because data-collection hardware could affect scores, steps had to be taken to ensure consistency in data collection methods. These factors did not impact the team's ability to carry out the project's main objectives. Data were closely scrutinized to ensure satisfaction of data quality inclusion criteria and only the highest quality data were utilized for analysis. For example, to address the above-described device issue, we only included participants whose initial 20 game plays were performed on desktop computers.
3) Significant results/Key outcomes: Both published and preliminary analyses yielded compelling simple and/or interaction effects for predictors of interest. Primary Aims 1,2 and 4 describe objectives with respect to cognitive performance as well as aims with respect to change in cognitive performance over time (i.e. learning). We did not observe the expected effects on learning. We start by describing our most compelling findings, pertaining to cognitive performance.

For **Primary Aim 1**: Our proposed aim sought to examine the effects of sleep duration on cognitive performance. Our initial cross-sectional analyses based on each participant's first attempt at a game showed significant effects of sleep duration on cognitive performance and an age-by-sleep-duration interaction effects on cognitive performance across multiple tasks. These initial cross-sectional analyses predicted single-play cognitive performance from self-reported “typical” sleep duration. The most compelling findings from these analyses included: 1) the inverted u-shaped relationship between sleep and cognitive performance, 2) the peak in performance at 7-hours typical sleep duration, 8) evidence of a *steeper deterioration* in performance with longer sleep durations, in younger participants relative the older participants, with longer sleep durations. The latter finding runs counter to the expectation that young people need more sleep. (See **Figure 1**, modified from *Richards et al., 2017, Figure 1).*

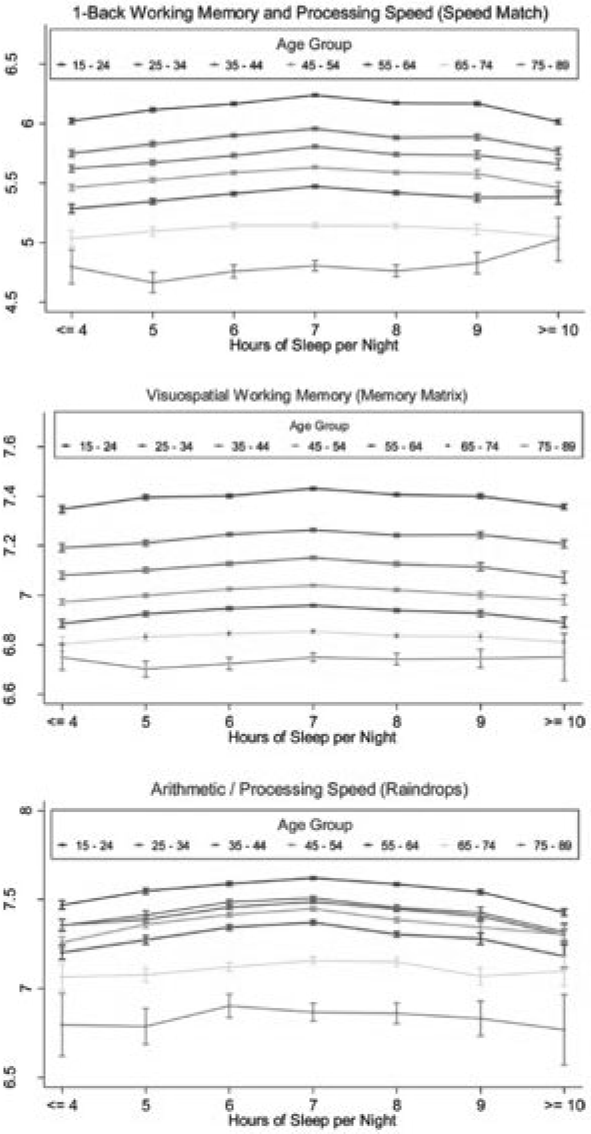

Figure 1. Effect of sleep duration on performance. We found an overall effect of age on performance, and that 7 hours average sleepers showed the best performance per age group. This pattern was consistent across three task domains of working memory and processing speed. *Modified from Richards et al., 2017).*

The above analyses were performed in a cross-sectional sample of hundreds of thousands of participants using only 1 (each participant’s first) gameplay. For our subsequent analyses, based on a thorough assessment of available data, we selected data from a flanker-style task. We determined that most tasks test a variety of cognitive domains, and therefore isolating specific cognitive functions would be difficult. Our review of the literature indicates that probing a single cognitive domain in isolation is difficult, since cognitive functions, especially higher cognitive functions such as executive function, rely on multiple other functions (such as attention and working memory) to be carried out. Based on the availability of a large sample of quality data with repeated measures of sleep duration and cognitive performance, we focused on the flanker-style task to address our questions. The flanker task is a well-documented measure of executive function which tests task-switching and response inhibition. In particular, some of our analyses showed differences in task performance for trials that required more, as opposed to less, response inhibition.

Our subsequent published analyses are based on a sample of over 48,000 participants with approximately 1 million repeated measures of sleep duration and cognitive performance. Using this sample, we first examined the relationship between average sleep duration and performance using multiple repeated measures of *prior-night sleep duration* and next-day cognitive performance (**Figure 2)**. These findings strengthened our confidence in initial findings, bolstering our conclusion that 1) there is an inverted u-shaped relationship between sleep duration and cognitive performance, 2) the peak in performance occurs at 7 hours average sleep in the sample as a whole, and 3) this effect is *more* rather than less pronounced in younger people, relative to older people, as the decrements in performance with longer sleep durations are more pronounced in younger age groups as compared to older age groups**)**.

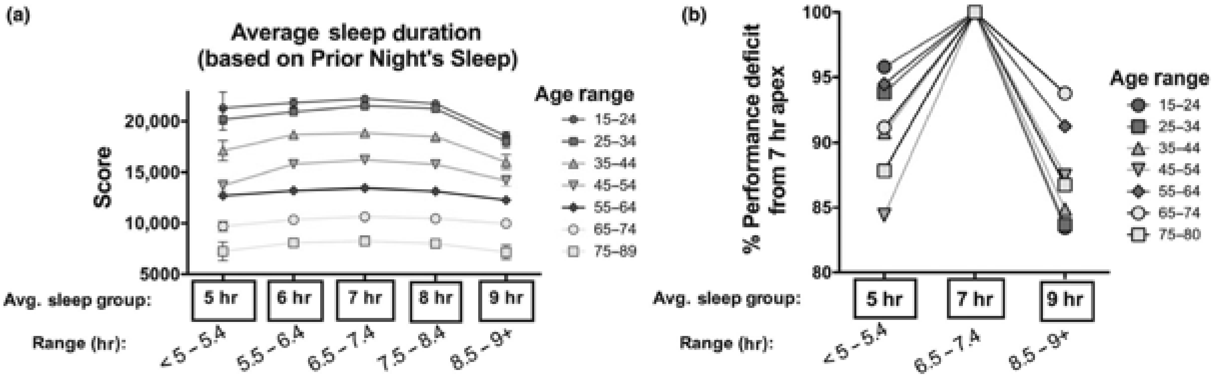

Figure 2. Effect of habitual sleep duration on performance. As in prior published study, we revealed a significant effect of age on performance. We also found that younger players had a greater deficit in performance at higher average sleep durations (relative to 7-hour sleep duration within their age category). *Modified from Richards et al., 2019).*

Aim 1 objectives also included the examination of *deviations* from typical sleep duration and their impact on cognitive performance. These analyses also yielded compelling results. They indicate that the effects of deviations from average sleep depend on one's average sleep duration. While 7-hour-average sleepers show deteriorations in performance when their prior night of sleep deviates upwards or downwards from their average, 6-hour-average sleepers show an improvement with 7 hours of prior night's sleep, and deteriorations at other sleep durations. In contrast, 8-hour average sleepers demonstrated a deterioration in performance (on average), when their prior-night sleep was 7 hours. Despite this, the peak performance for 8-hour sleepers was lower than it was for 7-hour-average sleepers even when controlling for demographic factors of gender, age and education (**Figure 3)**.

We discuss the strengths and value of these findings in our published work. Smaller scale studies do not have the statistical power to examine the subtle effects of differences in average sleep duration on cognitive performance, nor the effects of deviations from typical sleep duration on cognitive performance. Our data are consistent with the expert recommendations that individuals should obtain at least 7 hours' sleep duration, however they also clearly indicate that 7-hour-average sleepers may have an edge over individuals with different sleep durations, and that there may be a cost to more sleep. At the same time, 8-hour-average sleepers may also experience detrimental effects if they sleep less than their average.

We recognize that these initial analyses should be interpreted with some caution, given that the data were not collected initially for purposes of research. Reliance on self-report and uncertainty about whether sleep on reporting days reflects typical sleep remain. Lacking from these analyses are health variables that may contribute to sleep-duration-cognitive-performance dynamics. We intend to examine these in future analyses in the context of our ongoing partnership with Lumos Labs.

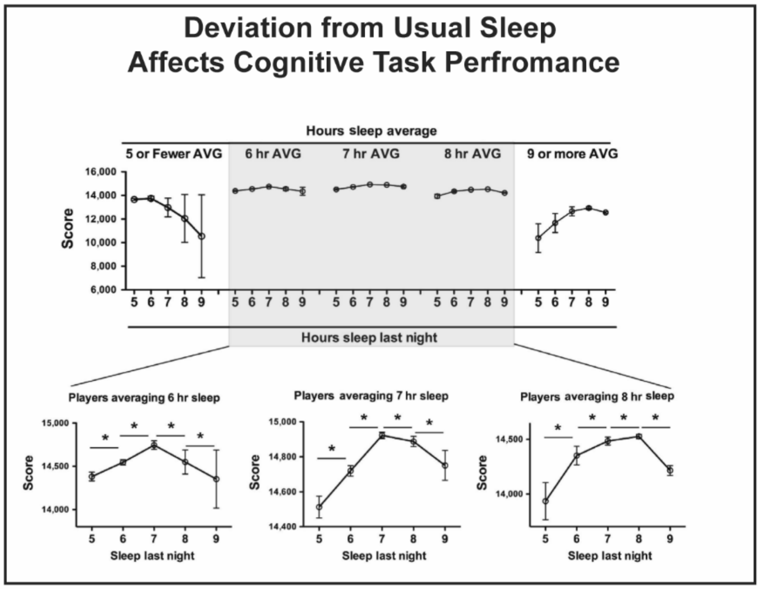

Figure 3. Assessment of performance when deviating from one's average sleep. Findings show effects of deviations vary by average sleep duration (linear mixed model, covariate adjusted for age, education and age by education, * p < 0.05). *Modified from Richards et al., 2019).*

For **Primary Aim 2**: Our proposed Aim was to examine the role of chronotype, assessed subjectively based on a self-report item, on cognitive performance and learning. We did *not* find evidence for our hypotheses regarding an overall chronotype effect on cognitive performance in two different tasks (**Figure 4**), nor did we find a "synchrony effect": alignment of task timing to chronotype did not improve performance. While this effect could be considered present for the morning chronotypes, this was not true for the evening chronotypes. This essentially revealed that, for the group as a whole, participants performed better in the morning than in the evening. We also assessed whether the effect of habitual sleep duration on performance was different for synchronous and asynchronous task alignment, and found no significant interaction effect (**Figure 5).**

.

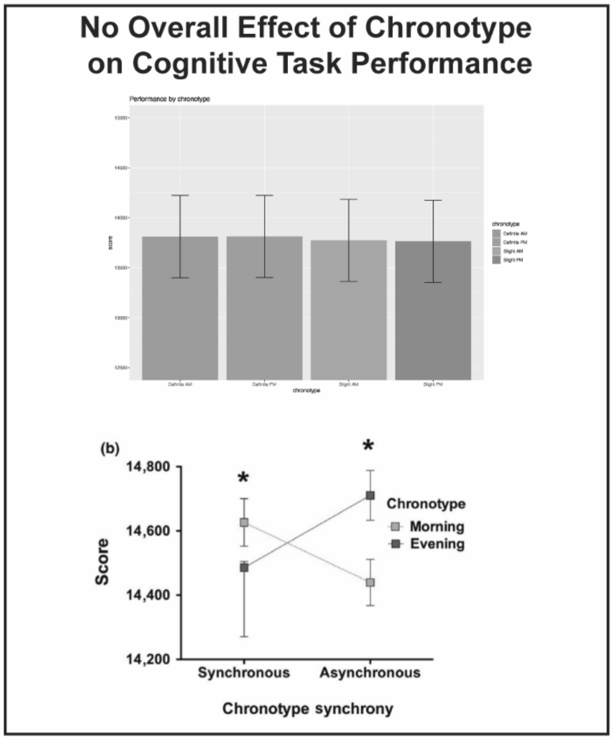

Figure 4. Assessment of chronotype on performance revealed that all chronotypes performed similarly, with no overall effect of chronotype (linear mixed model, p > 0.05). Additionally, assessment of alignment of task performance to chronotype (synchronous vs asynchronous) revealed that evening chronotypes did not perform as well as morning chronotypes when time of play aligned with chronotype (synchronous) * p < 0.05). *Modified from Richards et al., 2019.*

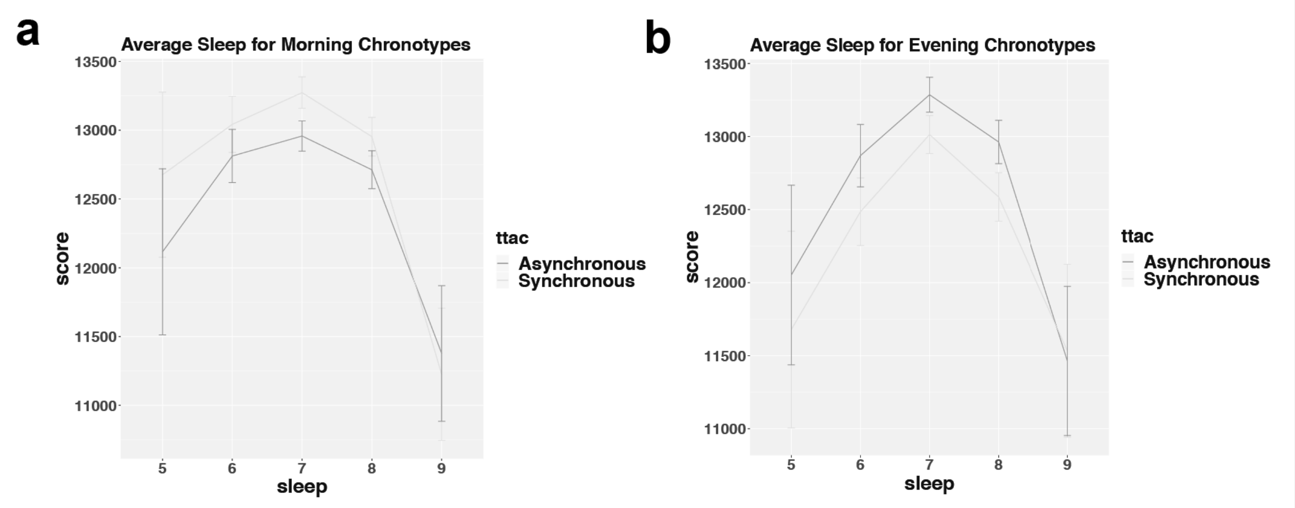

Figure 5. Effect of sleep duration on performance by task-alignment for morning and evening chronotypes. We assessed whether habitual sleep duration affects performance differently depending on whether task was performed aligned to participants' chronotype (synchronous vs. asynchronous). We found no significant interaction between sleep duration and task alignment for either morning (a) and evening(b)chronotypes (linear mixed model, ps >0.283).

The above analyses were based on a somewhat arbitrary assignment of "synchronous" times by the investigators, meaning that 6am-12pm was considered synchronous for morning types, and 6pm-12am was considered synchronous for evening types. Game plays at other times were not considered because they lay in a gray zone. However our extremely large dataset of game plays allowed us to examine cognitive performance across the 24-hour day. This revealed extremely interesting time-of-day effects on cognitive performance, which were affected by age (**Figure 6**, modified from *Richards et al., 2019, Fig. 6*) as well as features of the task (i.e. inhibitory vs. non-inhibitory trial, modified from *Richards et al., 2019, Fig. 5*).

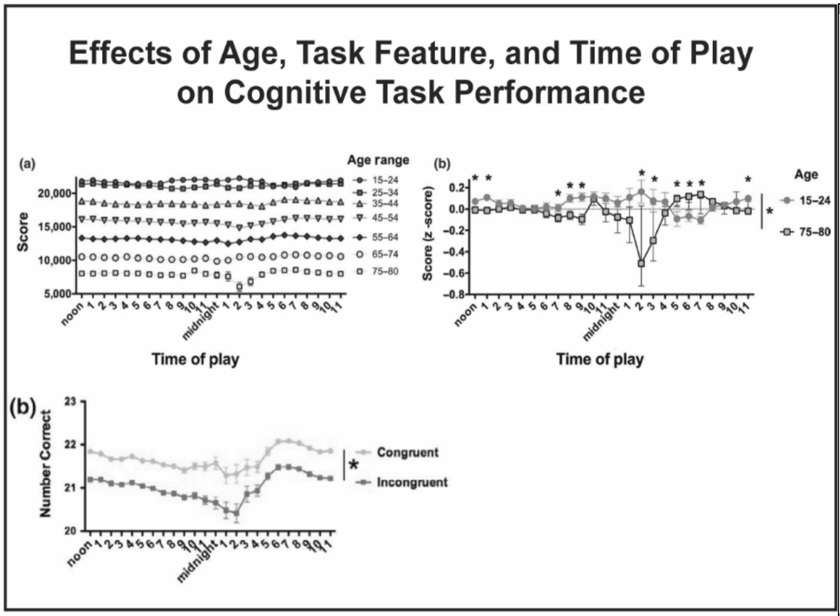

Figure 6. Assessment of time of play effects revealed a pronounced difference in performance between young and old participants when playing between midnight and 4 am (linear mixed model, covariate adjusted for education, * $p < 0.05$). Additionally, there was a greater decrease in performance for inhibitory (incongruent) task between midnight and 4 am (linear mixed model, covariate adjusted for age, education, and age by education * $p < 0.05$). *Modified from Richards et al., 2019.*

We were surprised to observe a pronounced age by time-of-day effect, wherein the youngest age group showed higher performance in the early night *despite the absence* of a chronotype effect. Presumably, these age effects are driven, at least in part, by the delayed chronotype which is thought to be characteristic of adolescence and early adulthood. As they stand, these data are suggestive that younger people are resilient to time-of-day effects independently of chronotype effects. We are currently working with our industry collaborator to redesign the subjective chronotype measure, given that limitations in the measure may have contributed to these negative findings with respect to chronotype.

While we did not observe a simple chronotype effect on performance (**Figure 4)**, we *did* identify an interaction effect for chronotype and deviation from usual sleep duration, providing evidence that research to unravel the complex relationships between sleep, chronotype, circadian and other variables in the prediction of cognitive performance is crucial (**Figure 7**, unpublished). For example, these analyses showed that morning chronotypes may be *less* vulnerable to the effects of negative deviation from their average sleep duration on cognitive performance. These observations deserve additional follow-up, especially with a larger variety of tasks and tasks of varying difficulty.

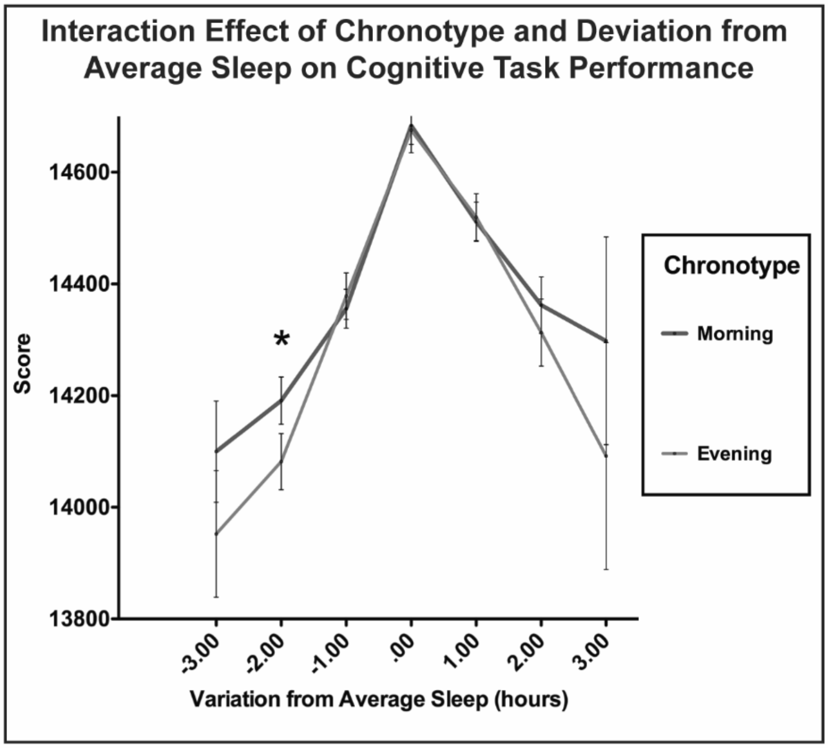

Figure 7. Effect of chronotype and deviation from habitual sleep duration on performance. Though we previously saw no overall effect of chronotype on performance, we assessed whether morning or evening chronotypes might perform differently depending on how far their prior nights' sleep duration was to their habitual sleep duration. We found a significant interaction between chronotype and deviation from average sleep, with evening chronotypes performing worse than morning chronotypes when getting less sleep than normal (linear mixed model, $p < 0.05$).

For Primary Aims 1 and 2, analysis of sleep and chronotype effects on *learning* did not yield the hypothesized effects. While we proposed to look at the first 10 gameplays in our aims, we had quality data to examine effects over the first 20 gameplays. As with our prior analyses, we utilized a linear mixed model approach. This approach does not require the same rigid assumptions of other repeated measures analyses (eg repeated measures analysis of variance). Namely, there is no independence assumption for repeated measures; instead the covariance between measures at different timepoints is explicitly modeled, allowing for more efficient and specific modeling. For our analyses of learning rate, we used a compound symmetry covariance matrix structure, and as in other analyses, covariance corrected for demographic information, including age, gender, education, and the age by education interaction (to account for the fact that younger participants may not have completed their education yet). The typical learning rate reflected a log-normal curve, and thus to linearize and normalize this shape, we tested our learning effects using both untransformed and log-transformed scales. While the effects of typical, average and prior-night sleep duration on cognitive performance were pronounced (*Richards et al., 2019, Fig. 2a*), the effects of prior night's sleep, typical sleep duration, and chronotype did *not* appear to substantively affect the trajectory of learning over time for the executive functioning task which we focused on (**Figure 8**). Significant age-related effects were evident in the initial learning (gameplay #1 to gameplay #2), and the age effects became less pronounced over subsequent gameplays. Sleep duration, in contrast to age, did not seem to affect the trajectory of learning, either early on or over time. In **Figure 8**, gameplay number is log-transformed to straighten the curve for interpretation purposes, depicting nearly parallel lines for change in performance over gameplay as a function of average sleep duration. This negative effect may be of interest in and of itself and we are preparing these findings for peer-reviewed publication.

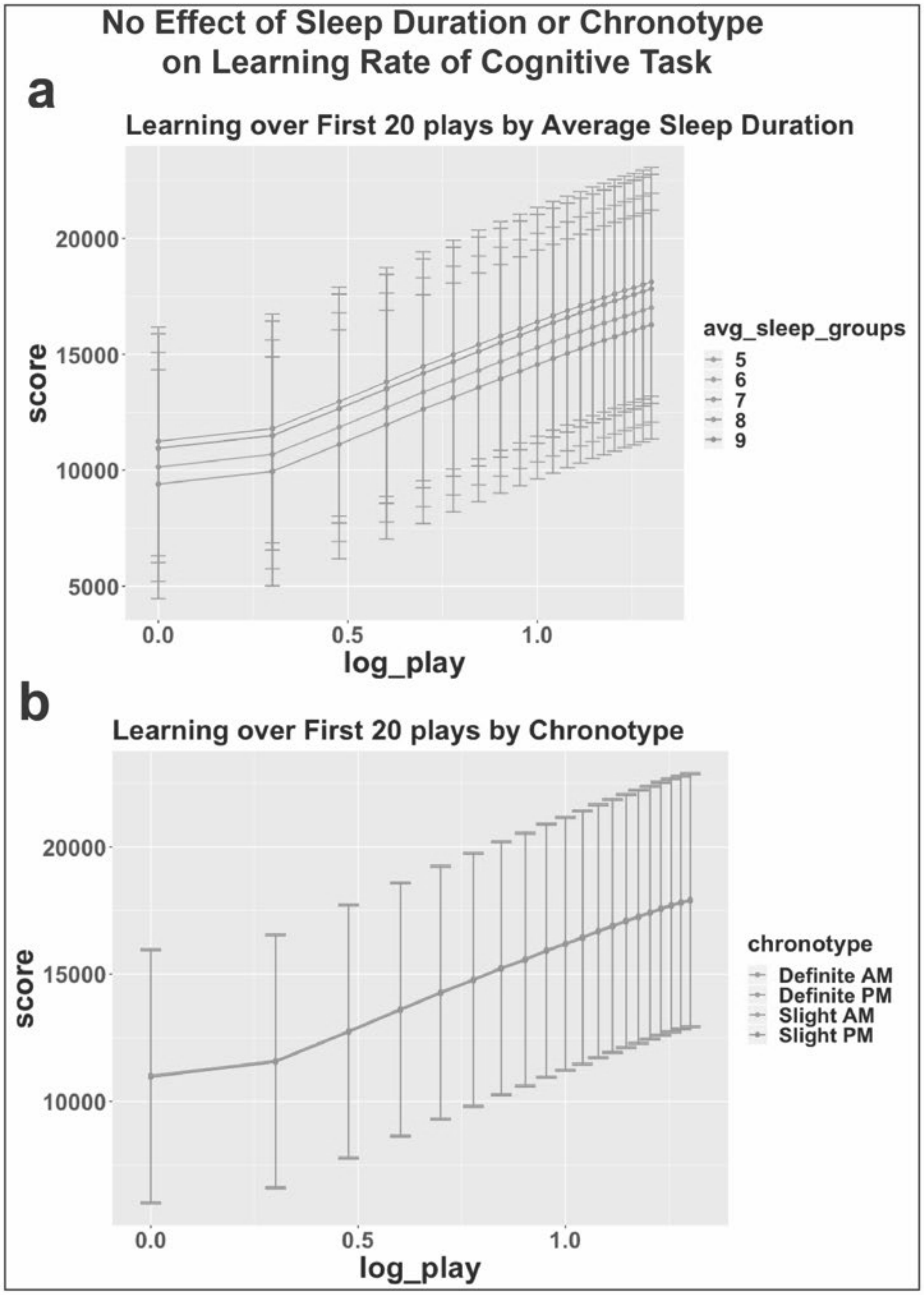

Figure 8. Assessment of performance over the first 20 plays of cognitive task revealed no effect of average sleep duration or chronotype on the learning rate. (linear mixed model, covariate adjusted for age, gender, education, and age by education, ps> 0.05.

Consistent with our negative finding with respect to chronotype synchrony (TTAC, Aim 2), analyses for **Aim 3**, focused on the interaction of chronotype synchrony with sleep duration, were unrevealing (not shown).

Our primary **Aim 4** sought to examine the effect of age in moderating the relationships between sleep duration, deviations from sleep duration, TTAC (synchrony) and cognitive performance. As expected, and has been well documented, age is the most important predictor of cognitive performance. One of our most interesting findings, as depicted in (**Figure 1 and Figure 2)**, is that the detrimental effects of *longer* sleep were equally or more pronounced in younger, as compared to older, individuals. Similarly, we also found that *deviation* from average sleep was expressed differently across age groups, with younger participants who average 6 hours of sleep showing a larger drop in performance when getting 2 or more hours sleep than their average compared to older players. (**Figure 9**).

Overall, we did find that shorter habitual sleep duration was associated with worse task performance in older participants as compared to younger participants (Figure 2). We saw no interaction between task-alignment or chronotype and age on performance (Figure 10; unpublished).

We further explored whether greater negative deviation from habitual sleep duration, and poor task-alignment with chronotype were associated with poor performance. We looked at prior night's sleep for 6-, 7- ,and 8-hour average sleepers and alignment to chronotype to determine if deviation from average sleep affects performance differently depending on whether players are playing at a time that aligns with their chronotype. We found that for morning chronotypes, performance was negatively affected by deviation from average sleep on asynchronous plays, but performance was not negatively affected by greater sleep than normal for synchronous plays (Figure 11; unpublished). These findings are not intuitive, and therefore we seek to examine these relationships further before dissemination.

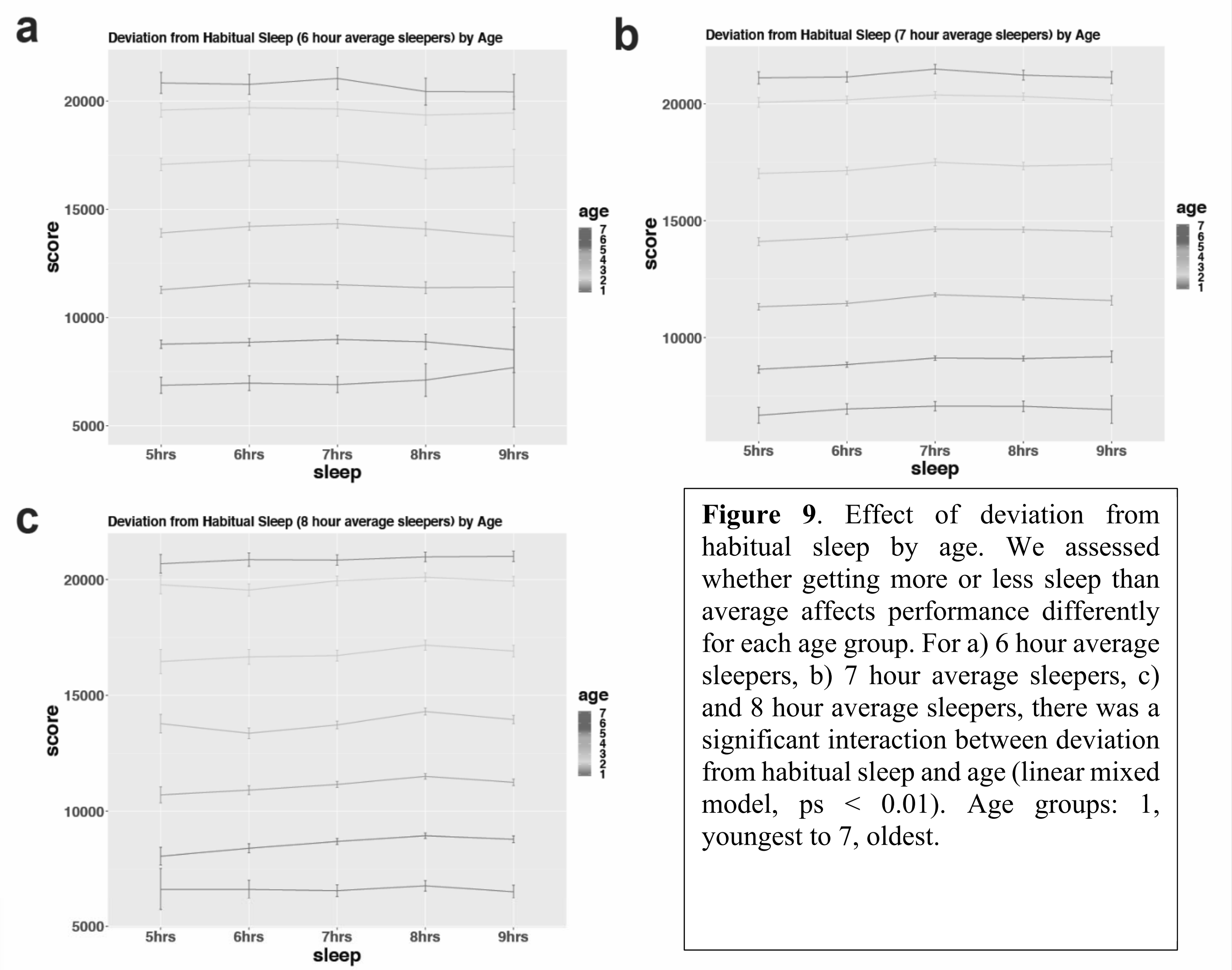

Figure 9. Effect of deviation from habitual sleep by age. We assessed whether getting more or less sleep than average affects performance differently for each age group. For a) 6 hour average sleepers, b) 7 hour average sleepers, c) and 8 hour average sleepers, there was a significant interaction between deviation from habitual sleep and age (linear mixed model, ps < 0.01). Age groups: 1, youngest to 7, oldest.

We proposed several exploratory analyses in our study. These were: 1. to determine whether greater variability in sleep duration negatively impacts performance on tasks of working memory, task-shifting, response inhibition and verbal fluency. Hypothesis E1: Greater variability in sleep duration will be associated with slower improvement in performance over 10 trials. 2. To examine the effects of gender, exercise, caffeine intake, alcohol intake, and self-reported mood on day of task performance as moderators of sleep duration and chronotype effects. 3. To examine the interactions of the primary variables (habitual sleep duration (HSD), deviation from habitual sleep duration, chronotype, degree of task-timing alignment with chronotype (TTAC score) and age), and exploratory variables (gender, lifestyle variables, and mood) on performance and/or improvement in performance on tasks of working memory, task-shifting, response inhibition and verbal fluency.

Analysis of variability in sleep duration was hampered by a limited range of sleep durations (only 5 options, including 5, 6, 7, 8 or 9 hours), resulting in absence of variability at the extremes of average sleep duration, greatest variability at 7 hours' sleep duration, and limited variability at 6 and 8 hours average sleep duration. We found that this problem biased our analyses and was too problematic for reasonable interpretation.

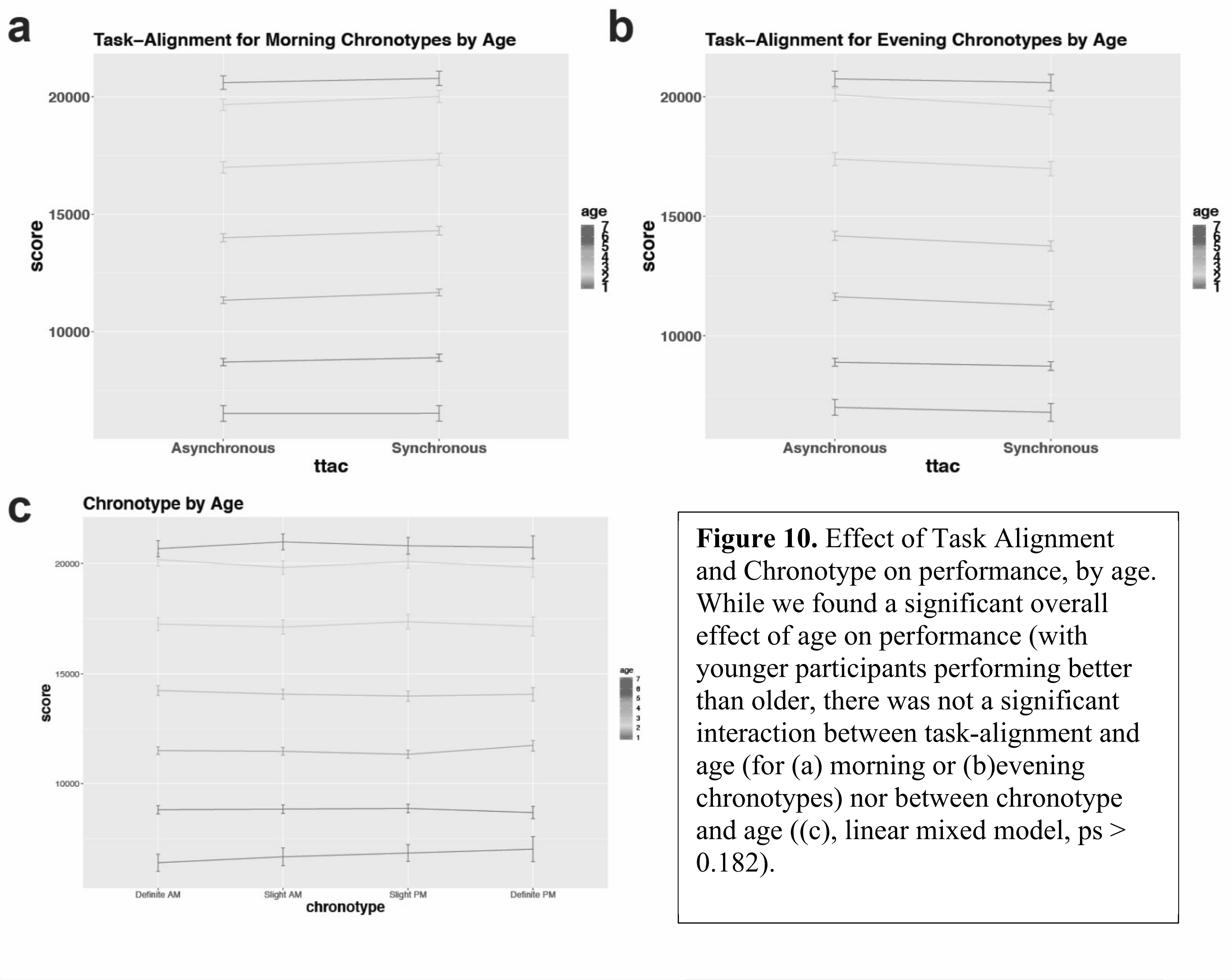

Figure 10. Effect of Task Alignment and Chronotype on performance, by age. While we found a significant overall effect of age on performance (with younger participants performing better than older, there was not a significant interaction between task-alignment and age (for (a) morning or (b)evening chronotypes) nor between chronotype and age ((c), linear mixed model, ps > 0.182).

We have begun to explore the possible differential effects of gender and sleep on performance. We found a main effect of gender, with males performing better overall. We found no significant differences by gender in the effects of chronotype or task-alignment on performance (**Figures 12 & 13**). Interestingly, we did find that for players with a habitual sleep duration of 7 hours, there was a significant interaction between gender and deviation from sleep, indicating females who got an average of 7 hours of sleep were more resilient than males to the effects of getting more sleep than normal, but were more vulnerable to negative deviation from average sleep.(**Figure 14**). Our plan is to continue to examine this question as cognitive tasks with sufficient sample sizes are generated, to enhance confidence in these findings prior to reporting these findings.

Sample size and data quality were not sufficiently satisfactory to perform rigorous exploratory analyses of lifestyle factors and mood on task performance and learning.

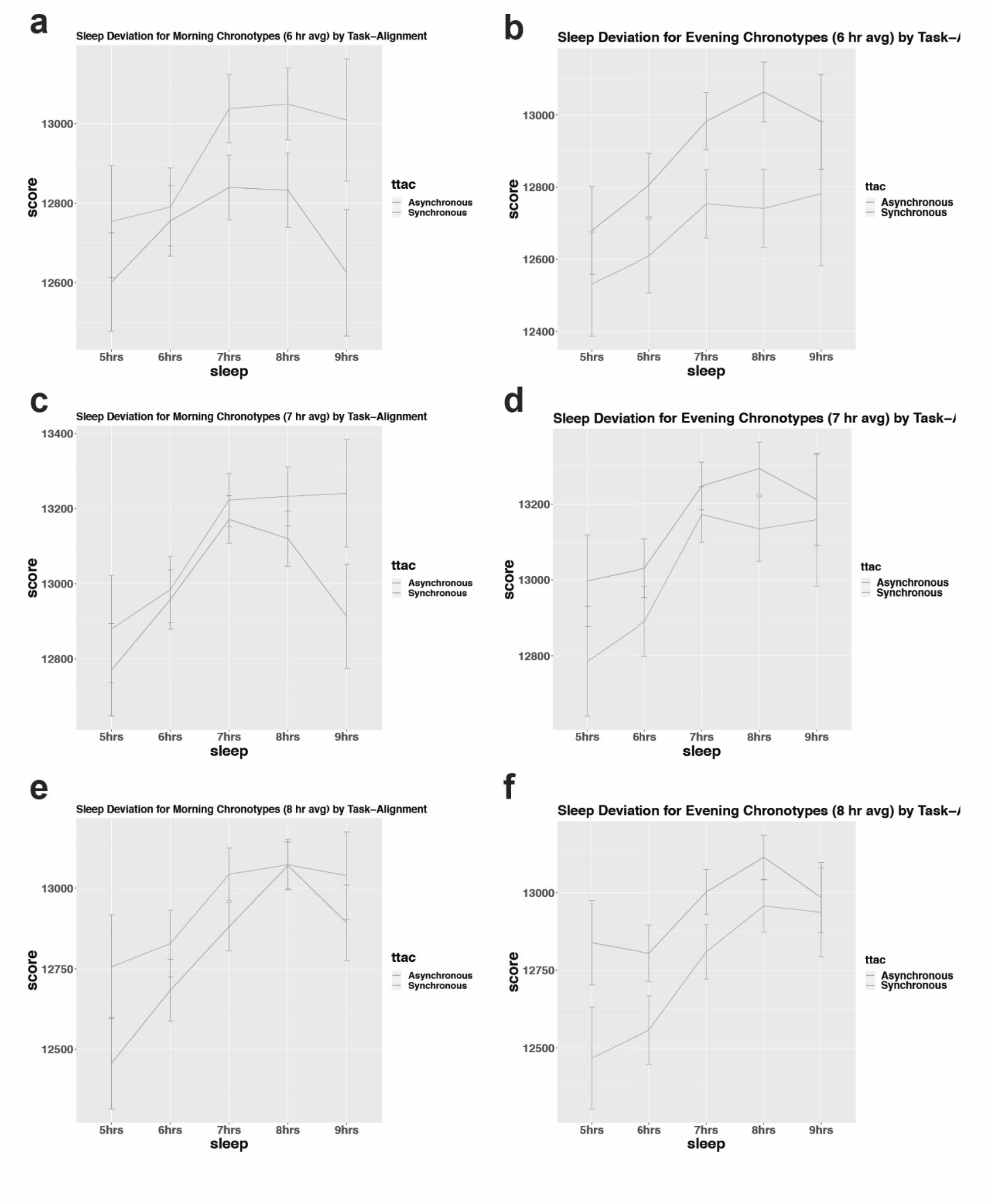

Figure 11. Effect of sleep deviation on performance by task-alignment for morning and evening chronotypes. We assessed whether deviation from habitual sleep duration affects performance differently depending on whether task was performed aligned to participants' chronotype (synchronous vs. asynchronous). We found significant interactions between deviation from sleep and task alignment for both morning (a,c,e) and evening (b,d,f) chronotypes across 6 (a,b), 7 (c,d), and 8(e,f) hour average sleepers (linear mixed model, ps < 0.05).

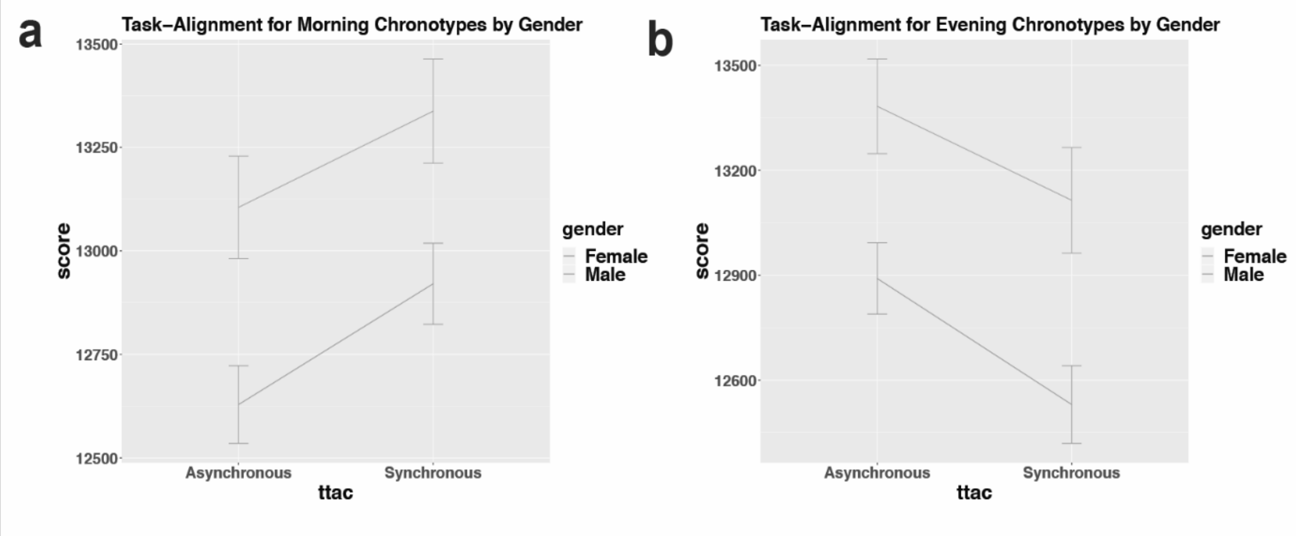

Figure 12. Effect of Task-Alignment on performance by gender. We tested whether game play aligned to chronotype (synchronous vs asynchronous) for morning or evening chronotypes is differentially expressed by gender. We found no significant interaction between task alignment and gender for either morning (a) or evening (b) chronotypes (linear mixed model, ps > 0.328).

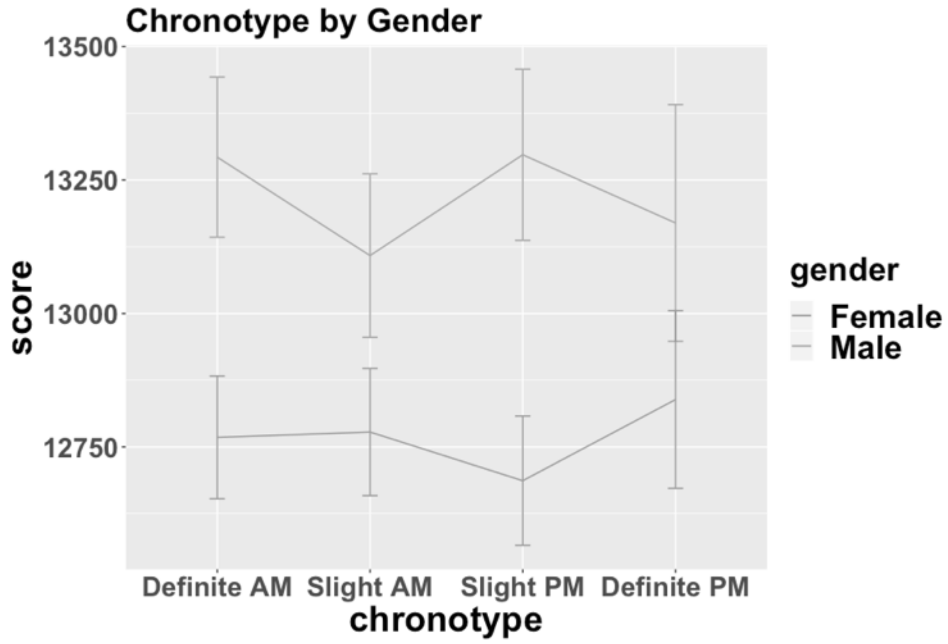

Figure 13. Effect of chronotype on performance by gender. We tested whether chronotype affects performance differently for each gender. Despite a trend in which performance diverges for each gender across chronotypes, there was no significant interaction between chronotype and gender (linear mixed model, p = 0.268).

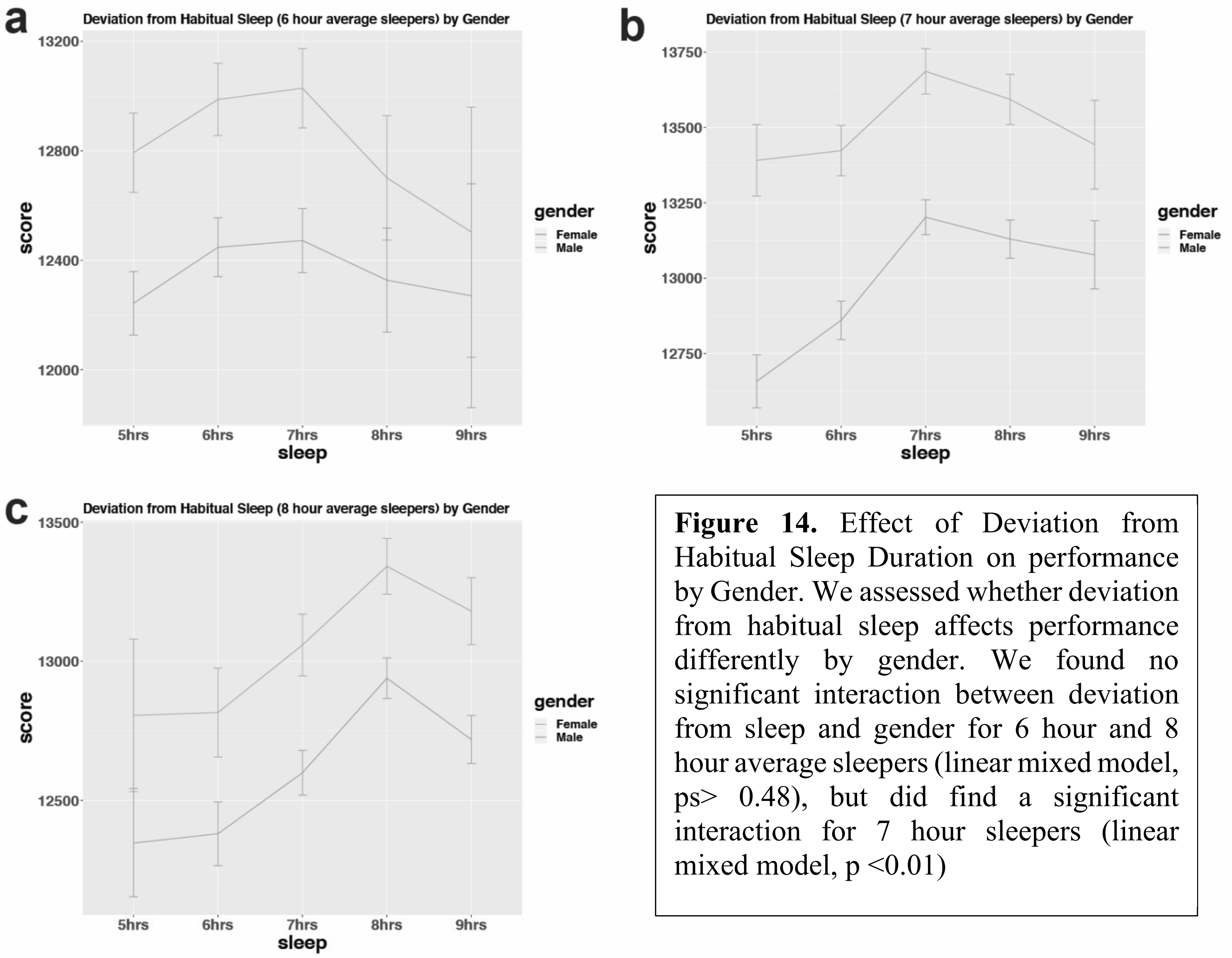

Figure 14. Effect of Deviation from Habitual Sleep Duration on performance by Gender. We assessed whether deviation from habitual sleep affects performance differently by gender. We found no significant interaction between deviation from sleep and gender for 6 hour and 8 hour average sleepers (linear mixed model, ps> 0.48), but did find a significant interaction for 7 hour sleepers (linear mixed model, p <0.01)

See:

Richards A, Inslicht SS, Metzler TJ, Mohlenhoff BS, Rao MN, O'Donovan A, Neylan TC. Sleep and Cognitive Performance from Teens to Old Age: More is not Better. Sleep. 2017 Jan 1;40(1) PMID: 28364476

Richards A, Kanady JC, Huie JR, Straus LD, Inslicht SS, Levihn-Coon A, Metzler TJ, Neylan TC. Work by Day and Sleep by Night, Don't Sleep too Little or too Much: Effects of Sleep Duration, Time of Day, and Circadian Synchrony on Flanker-Task Performance in Internet Braingame Users from Teens to Advanced Age. Journal of Sleep Research. PMID: 31631467

Richards A, Kanady J, Huie JR, Straus L, Inslicht S, Levihn-Coon A, Metzler T, Neylan TC. Effects of sleep duration, time of day, and synchrony with circadian preference on Flanker-Task Performance in Internet Braingame Users from Teens to Advanced Age. Conference Abstract. 2019 World Sleep Conference.

What opportunities for training and professional development has the project provided?

This project contributed to Dr. Richards' (PI) attendance at the following professional development opportunities:

1) Attendance at the International Society for Traumatic Stress Studies November 2016 Annual Meeting.
2) Attendance at the Neuroscience School of Advanced Studies: Sleep and Cognition July 2017 Course.
3) Attendance at the Associated Professional Sleep Studies June 2018 Annual Meeting.

4) Attendance at the International Society for Traumatic Stress Studies November 2019 Annual Meeting.
5) Attendance at the Neuroscience School for Advanced Studies: Sleep and Circadian Rhythms May 2019 Course.
6) Attendance at the Associated Professional Sleep Studies September 2019 Annual Meeting.

How were the results disseminated to communities of interest?

Two peer-reviewed publications; 1 conference presentation. Findings with respect to sleep and learning are being prepared for submission.

What do you plan to do during the next reporting period to accomplish the goals?

N/A. We continue to work with our industry partner to identify the best datasets for ongoing analyses due to the great potential of these data to inform our understanding of sleep, circadian rhythm and cognition.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Our findings raise compelling questions about sleep need and optimal sleep duration with respect to cognitive functioning at different ages. These findings highlight the importance of further research on the relationship between sleep duration and cognitive performance across the full range of the age spectrum. They demonstrate the potential of large-scale internet data for gaining knowledge in this area.

What was the impact on other disciplines?

We expect findings from our research to have an impact on disciplines focused on cognition, learning and neurodegenerative diseases, such as neurology and geriatric medicine. We expect our findings to be relevant in operational environments in which there may be barriers to normal sleep durations and job schedules and in which optimizing cognitive performance in the context of unusual work hours is critical, such as in the military and in medical settings.

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

These findings are relevant to understanding the relationship to sleep duration and cognitive performance, and time of day and cognitive performance. Published findings have public health implications with respect to optimizing sleep duration.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change:

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

Initial delays in data acquisition have been described. Limitations in quantity or quality of data for some secondary predictor and/or outcome variables (i.e. lifestyle variables) limited the usefulness of those variables for additional analyses. We continue to collaborate with our industry partner to enhance the quality of these data so that they can contribute to future work.

Changes that had a significant impact on expenditures

Initial delays in initiating work has been described in prior reports. A no-cost extension allowed the investigators to pursue the work once initial delays were overcome.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

6. PRODUCTS:

Richards A, Inslicht SS, Metzler TJ, Mohlenhoff BS, Rao MN, O'Donovan A, Neylan TC.
Sleep and Cognitive Performance From Teens To Old Age: More Is Not Better. Sleep. 2017 Jan 1;40(1) PMID: 28364476

Richards A, Kanady JC, Huie JR, Straus LD, Inslicht SS, Levihn-Coon A, Metzler TJ, Neylan TC. Work by Day and Sleep by Night, Don't Sleep too Little or too Much: Effects of Sleep Duration, Time of Day, and Circadian Synchrony on Flanker-Task Performance in Internet Braingame Users from Teens to Advanced Age. Journal of Sleep Research 2019. PMID: 31631467

Richards A, Kanady J, Huie JR, Straus L, Inslicht S, Levihn-Coon A, Metzler T, Neylan TC. Effects of sleep duration, time of day, and synchrony with circadian preference on Flanker-Task Performance in Internet Braingame Users from Teens to Advanced Age. Conference Abstract. 2019 World Sleep Conference.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

What individuals have worked on the project?

Name:	Anne Richards, MD, MPH
Project Role:	Principal Investigator
Researcher Identifier:	N/A
Nearest Person Month Worked:	1.5
Contribution to Project:	Dr. Richards is the initiating investigator and has assumed the overall scientific and administrative responsibility for the project. She is taking the lead on study design, data quality control, data analysis, and preparation of results for dissemination.

Name:	Thomas Neylan, MD
Project Role:	Co-Investigator
Researcher Identifier:	N/A
Nearest Person Month Worked:	.36

Contribution to Project:	Dr. Neylan has collaborated closely with Dr. Richards to ensure data quality and integrity. He has provided expertise in sleep and cognitive data analysis and interpretation.

Name:	Thomas Metzler, M.S.
Project Role:	Statistician
Researcher Identifier:	N/A
Nearest Person Month Worked:	.5
Contribution to Project:	Mr. Metzler has played a lead role in working with Lumos Labs data scientists to identify the appropriate datasets and prepare datasets for analysis via data quality examination and cleaning. He now serves as a statistical consultant for the lead statistician on the project, Dr. Huie.

Name:	Russell Huie
Project Role:	Statistician
Researcher Identifier:	N/A
Nearest Person Month Worked:	3
Contribution to Project:	Dr. Huie has taken on the leading statistician role for the project, based on his extensive experience working with large-scale data. He has taken a lead role in writing code and implementing complex data analytic procedures for this project.

Name:	Christen Chapman
Project Role:	Lab Manager
Researcher Identifier:	N/A
Nearest Person Month Worked:	0.75
Contribution to Project:	Ms. Chapman has provided general lab management support for Dr. Richards and preparation of grants, manuscripts and technical report and supervision of other research staff. She has expertise in lab management and regulatory issues but is currently off-site therefore collaborates with on-site staff to support the study team.

Name:	Alaisa Emery
Project Role:	Research Assistant
Researcher Identifier:	N/A
Nearest Person Month Worked:	1
Contribution to Project:	Ms. Emery provided work in the area of data cleaning and data management support for the study, with supervision of PI and statistician, as well as support of Dr. Richards and Ms. Chapman in preparation of grant, manuscript and technical report preparation.

Name:	Sijing Ye
Project Role:	Research Assistant
Researcher Identifier:	N/A
Nearest Person Month Worked:	.5
Contribution to Project:	Ms. Ye has provided work in the area of data cleaning and data management support for the study, with supervision of PI and statistician, as well as support of Dr. Richards and Ms. Chapman in preparation of grant, manuscript and technical report preparation.

Name:	Andrew Levihn-Coon
Project Role:	Research Coordinator
Researcher Identifier:	N/A
Nearest Person Month Worked:	.75
Contribution to Project:	Mr. Levihn-Coon has provided general research coordination support for Dr. Richards and preparation of grants, manuscripts and technical report and supervision of other research staff.

Name:	Sara Rama
Project Role:	Research Assistant

Researcher Identifier:	N/A
Nearest Person Month Worked:	1
Contribution to Project:	Ms. Rama provided work in the area of data cleaning and data management support for the study, with supervision of PI and statistician, in preparation of grant, manuscript and technical report preparation.

Name:	Emily Staggs
Project Role:	Lab Manager
Researcher Identifier:	N/A
Nearest Person Month Worked:	.2
Contribution to Project:	Ms. Staggs has provided general lab management support for Dr. Richards and preparation of grants, manuscripts and technical report and supervision of other research staff.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

What other organizations were involved as partners?

Lumos Labs, for provision of data. There is no change to report.

8. SPECIAL REPORTING REQUIREMENTS:

COLLABORATIVE AWARDS:

Not applicable.

QUAD CHART:

Not applicable

9. APPENDICES:

Richards, A, Kanady, JC, Huie, JR, et al. Work by day and sleep by night, do not sleep too little or too much: Effects of sleep duration, time of day and circadian synchrony on flanker-task performance in internet brain-game users from teens to advanced age. *J Sleep Res*. 2019; 00:e12919. https://doi.org/10.1111/jsr.12919

Richards A, Inslicht SS, Metzler TJ, et al. Sleep and Cognitive Performance From Teens To Old Age: More Is Not Better. *Sleep*. 2017;40(1):zsw029. doi:10.1093/sleep/zsw029

Received: 26 April 2019 | Revised: 20 July 2019 | Accepted: 18 August 2019
DOI: 10.1111/jsr.12919

REGULAR RESEARCH PAPER

Journal of Sleep Research
ESRS

Work by day and sleep by night, do not sleep too little or too much: Effects of sleep duration, time of day and circadian synchrony on flanker-task performance in internet brain-game users from teens to advanced age

Anne Richards[1,2] | **Jennifer C. Kanady**[1,2] | **John Russell Huie**[1,2] | **Laura D. Straus**[1,2] | **Sabra S. Inslicht**[1,2] | **Andrew Levihn-Coon**[2] | **Thomas J. Metzler**[2] | **Thomas C. Neylan**[1,2]

[1]University of California, San Francisco, San Francisco, CA, USA

[2]San Francisco VA Medical Center, San Francisco, CA, USA

Correspondence
Anne Richards, San Francisco VA Medical Center, 4150 Clement Street, San Francisco, CA 94121, USA.
Email: anne.richards@ucsf.edu

Funding information
U.S. Department of Defense, Grant/Award Number: W81XWH-16-1-0259; U.S. Department of Veterans Affairs (VA); NIMH; University of California, San Francisco

Summary

Research elucidating the effects of sleep and circadian rhythm on cognitive performance is advancing, yet many important questions remain. Using flanker-task performance scores from a large internet sample (N = 48,881) with repeated measures of cognitive performance and linked prior-night self-reported sleep duration, we analysed the relationship between sleep duration, time of day of task performance, and chronotype synchrony with performance in participants aged 15–80 years. Results indicate a performance peak at 7 hr habitual sleep duration, and point to a variable effect of deviation from habitual sleep duration depending on users' habitual sleep duration and age. Time-of-day effects were notable for a steady decline in performance up until 01:00 hours–02:00 hours for the group as a whole, which was accounted for by nighttime deterioration on trials requiring inhibitory executive functioning, particularly in older subjects. Analyses did not demonstrate an advantage for playing in synchrony with self-identified chronotype. Results strengthen findings indicating an inverted U-shaped relationship between sleep duration and cognitive performance across a broad spectrum of age groups. These findings underscore the importance of daytime task performance for tasks requiring inhibitory function, especially in elderly people. Findings highlight the utility of large-scale internet data in contributing to sleep and circadian science.

KEYWORDS
age, chronotype, cognition, sleep, synchrony

1 | INTRODUCTION

The research literature on the effects of sleep duration on cognitive performance is growing. While recent recommendations by a panel of sleep experts indicate that adults should sleep at least 7 hr per night to optimize functioning and performance (Watson et al., 2015), several studies on sleep and cognitive performance indicate that there may be such a thing as *excess* sleep (Faubel et al., 2009; Ramos et al., 2013; Richards et al., 2017; Schmutte et al., 2007; Xu et al., 2011, 2014). For example, several studies with predominantly older age samples indicate that performance peaks at about 7 hr of sleep and/or declines at sleep durations beyond about 7 hr (Faubel et al., 2009; Xu et al., 2011, 2014). The association between longer sleep duration and declining cognitive performance has traditionally been attributed to unmeasured confounders, such as age-related medical co-morbidities. However, our prior findings indicated that

https://doi.org/10.1111/jsr.12919

decline in performance with increasing sleep duration was found in younger individuals as well, and that the decline in performance beyond 7 hr of sleep duration was even steeper in the younger, presumably healthier, subjects than in older subjects (Richards et al., 2017). Furthermore, most of the above-cited studies controlled for major medical co-morbidities and/or self-reported health status in their analyses demonstrating negative cognitive effects of long sleep (Ramos et al., 2013; Schmutte et al., 2007; Xu et al., 2011, 2014). Altogether, these studies raise some doubts regarding the traditional belief that "more sleep is better". Additional research across the age spectrum is clearly needed to better understand *how much sleep* constitutes *the right amount* of sleep, if such a "right" amount exists.

Complementing the research on sleep duration and cognition, there is a growing body of research on the effects of time of day on cognitive performance. Published research generally indicates that daytime performance is enhanced relative to nighttime performance (for a review, see Schmidt, Collette, Cajochen, & Peigneux, 2007). For example, studies have shown that performance on tasks of vigilance and sustained attention, as well as more complex tasks involving selective attention, divided attention or memory, deteriorate during the night and ameliorate starting in the early morning (Cajochen, Sat Bir, Wyatt, Czeisler, & Dijk, 1999; Doran, Van Dongen, & Dinges, 2001; Folkard & Monk, 1980; Graw, Kräuchi, Knoblauch, Wirz-Justice, & Cajochen, 2004; Santhi, Horowitz, Duffy, & Czeisler, 2007; Schmidt et al., 2007; Van Eekelen & Kerkhof, 2003; Wright, Hull, & Czeisler, 2002; Wyatt, Cecco, Czeisler, & Dijk, 1999). However, studies that compare cognitive performance at times more typically associated with wakefulness in humans provide a more complex picture. These studies demonstrate inconsistencies with respect to the existence of time-of-day effects, and/or the timing of peak performance within typical waking hours (Bonnefond, Rohmer, Hoeft, Muzet, & Tassi, 2003; Hidalgo et al., 2004; Kraemer et al., 2000; Valdez et al., 2005). Some (Folkard, Knauth, & Monk, 1976; Mikulincer, Babkoff, Caspy, & Sing, 1989), but not other (Monk et al., 1997; Wright et al., 2002) studies have suggested that working memory load affects the timing of peak performance (Cajochen et al., 1999; Hidalgo et al., 2004; Koulack, 1997). Performance on inhibition tasks appear to be sensitive to time of day and differ depending on the participant's age, with older adults performing better in the morning and younger adults performing better in the evening (West, Murphy, Armilio, Craik, & Stuss, 2002).

The published research on the synchrony effect in cognitive performance (i.e. improvement in performance when task performance time is aligned with chronotype) is small and, similar to studies of simple time of day, effects are again not entirely consistent across cognitive domains or studies (Barclay & Myachykov, 2017; Bennett, Petros, Johnson, & Ferraro, 2008; Hidalgo et al., 2004; Lara, Madrid, & Correa, 2014; Lehmann, Marks, & Hanstock, 2013; Matchock & Mordkoff, 2009; May & Hasher, 1998; Schmidt, Peigneux, Cajochen, & Collette, 2012). Overall, individuals seem to perform best when there is synchrony between chronotype and time of testing. The synchrony effect may be greater in older adults compared with younger adults (Lehmann et al., 2013; May & Hasher, 1998), and the age-related synchrony effect may be partially mediated by individual sleep schedules (Schmidt et al., 2012). A few studies have demonstrated a synchrony effect for inhibition tasks (May & Hasher, 1998), which may be more pronounced in older adults (May & Hasher, 2017). More research is clearly needed as the available research on synchrony effects is small and based on laboratory-based studies with few participants and limited ecological validity.

The goals of the current analysis were to examine sleep duration, time-of-day and synchrony effects on cognitive performance in a flanker-style task in a large sample of participants aged 15–80 years with repeated measures of sleep duration and cognitive performance collected on an internet-based cognitive training platform. We predicted: (a) performance would peak at 7-hr average sleep duration in the sample as a whole, and that this effect would be most pronounced in young to middle-aged individuals (defined here as ages 15–64 years); (b) daytime performance would be superior to nighttime performance in the group as a whole; (c) younger individuals would demonstrate enhanced performance in the evening relative to the morning, and older individuals would perform better in the morning relative to the evening; (d) a synchrony effect in which late chronotypes would perform better in the evening and early chronotypes would perform better in the morning relative to the evening; (e) time-of-day and synchrony effects would be more pronounced for trials requiring higher inhibitory control than non-inhibitory trials. We also performed exploratory analyses to determine whether intra-individual deviations from one's average sleep duration (both up and down) would be associated with declines in cognitive performance.

2 | METHODS

We used data collected from the Lumosity brain-game database collected between 1 July 2013 and 31 December 2017 for one game, called Lost in Migration, which is a flanker-style task. We selected this task because it assesses inhibitory/cognitive control functions, which have been demonstrated to be sensitive to time of day and/or circadian synchrony (Barclay & Myachykov, 2017; Matchock & Mordkoff, 2009; May & Hasher, 1998), and because of the magnitude of the sample size and linked cognitive performance scores available during the time-frame of data collection. Details of the platform are described in our and other published papers (Richards et al., 2017; Sternberg et al., 2013). First-time use of the platform does not require payment, but repeated use for the purposes of cognitive training requires registration. Data were included for all players aged 15–80 years whose data met inclusion criteria. Individuals aged 81 years and above were excluded due to small sample size. Inclusion criteria required: (a) at least 20 game plays over a 6-month period with at least 10 self-reported sleep durations prior to game play; (b) no prior use of Lost in Migration by the user (i.e. the analyses were based on the first 20 Lost in Migration game plays by each user); (c) exclusive use of keyboards for desktops or laptops, as opposed to tablets, smartphones or touch screens for all game plays; (d) English as the preferred language and language used by the platform. Analyses were performed based on the first 20 game plays for all users. Not all respondents provided chronotype information; chronotype analyses were limited to 18,664 participants. The final sample size was comprised of 48,881 users with 979,649 game plays and with 938,699 prior-night sleep duration reports.

3 | MEASURES

3.1 | Demographic information

Participants enter basic demographic information, including date of birth, gender and educational attainment at the time of registration. Age at the time of game play is calculated by the Lumosity software.

3.2 | Sleep duration

Our dataset includes participants' estimate of typical sleep duration, provided at the time of registration on the Lumosity platform, as well as their sleep duration reported just prior to game play and with respect to their last night's sleep. At registration, participants respond to the question "How much sleep do you typically get each night?" by selecting a sleep duration in number of hours with response options including: "≤ 4", "5–6", "7–8" or "9 or more". Sleep duration for the prior night (the night prior to any linked game play) is assessed each time participants log into Lumosity with the question: "How many hours did you sleep last night?". Response options include: ≤ 5, 6, 7, 8 or 9+ hr. The large sample and the repeated measures nature of the dataset allowed us to compare the predictive value of typical sleep duration (reported at one time-point), average sleep duration (based on the mean of ~20 prior-night sleep reports per subject), and prior-night sleep linked with a performance score, for cognitive performance.

3.3 | Chronotype

Chronotype, or circadian preference, was assessed at registration using one question: "What time of day are you most productive?" There were four possible response options, including "definitely morning", "more morning than evening", "more evening than morning", or "definitely evening".

3.4 | Time of game play

Time of game play was based on clock time in the time-zone of the IP address of the participant at registration.

3.5 | Circadian synchrony

To examine the relative advantage of different times of day for morning and evening chronotypes, and drawing from existing literature on circadian synchrony but in the absence of definitive guidance regarding specific advantageous times for either chronotype, performance during the 06:00 hours to 12:00 hours time-frame (defined as synchronous for morning types) was compared with the 18:00 hours to 00:00 hours time-frame (defined as synchronous for evening types).

3.6 | Flanker-task (cognitive) performance

Lost in Migration is a flanker-style task that presents a series of arrangements of small flying birds, identical except in the direction of orientation of flight (either leftward, rightward, upward or downward). Participants are required to selectively attend to a visual target (the central bird within the flock) and provide a response using the arrow keys on a keyboard with respect to the orientation of the target object while ignoring visual distractors (the target bird will be flanked by birds pointing in the same or different direction). The task lasts a fixed 45 s. Configurations of target and flanker

FIGURE 1 Screenshots of flanker-task arrangement. Two screenshots of flanker-task configurations in the Lumosity Lost in Migration task

birds were generated dynamically during each game play using the same probability distributions: on average, the target bird's orientation matched that of the flankers on 50% of trials; the remaining 50% of trials was divided evenly between configurations in which the flankers were oriented 90°, 180° or 270° from the orientation of the target. Figure 1 provides a picture of a sample arrangement. Multiple variations of flanker-style tasks have been used in cognitive neuroscience research, and the Lumosity task reflects a more animated version of the traditional task.

3.7 | Statistical analysis

The raw Lumosity game score was used as the primary outcome measure for the task. While there are many potential outcome measures for flanker tasks, as in our prior report, we used the Lumosity game score as the outcome measure because it incorporates both speed and accuracy. Secondarily, we examined effects for response time and percent correct for both congruent trials (trials in which the target bird is oriented in the same direction as flanking birds) and incongruent trials (trials in which the target bird is oriented in a different direction from flanking birds), given that several published studies on time-of-day and circadian-synchrony effects examine these outcomes (May & Hasher, 1998, 2017; West et al., 2002). Effects on invariant variables (those that do not change over time in this analysis, such as age, chronotype, biological sex) were tested using analysis of variance (ANOVA). All repeated measure effects were tested using a linear mixed model, with plays for each participant treated as a nested repeated measure. Gender, age, education level, as well as the age by education level interaction were treated as covariates, except for when the effects of age or gender were explicitly tested. In all analyses, participant and intercept were treated as random factors. Where appropriate, post hoc analyses of group differences were performed using the estimated marginal means, and a Bonferroni correction for multiple comparisons. Statistical significance was determined at an alpha level of .05. Analyses were performed in SPSS v.24 (IBM).

4 | RESULTS

4.1 | Demographic, sleep and chronotype characteristics of the sample

The demographic, sleep duration and chronotype information of the sample are presented in Table 1. The sample was predominantly female (63.1%), and the mean age was 54.08 years (*SD* = 15.85; see Figure S1 for a breakdown of the sample by age group). Educational attainment varied widely, with the median education level being a bachelor's degree. Similar to our prior published paper using a Lumosity dataset, the small number of participants in the “other” category for education (*n* = 1,150) were presumed to have a low education due to relatively poor age- and gender-adjusted performance (statistically indistinguishable from the lowest performing group, which was also the least educated).

TABLE 1 Demographic, sleep and chronotype characteristics of the sample

		Mean ± *SD*
Age		54.09 (15.85)
	%	***n***
Gender		
Female	63.1	30,856
Male	36.9	18,016
Education level		
Other/unknown	2.4	1,150
Some high school	2.6	1,249
High school	12.4	6,042
Some college	20.3	9,936
Associate degree	3.3	1,622
Bachelor's degree	30.2	14,770
Professional degree	7.2	3,537
Master's degree	18.5	9,067
PhD	3.1	1,622
Chronotype (*N* = 18,647)		
Definitely morning	30.2	5,640
Slightly morning	28.5	5,317
Slightly evening	27.0	5,037
Definitely evening	14.2	2,653
Typical sleep duration (per baseline report; *N* = 19,301)		
4 or fewer hours	4.6	884
5–6 hr	42.3	8,156
7–8 hr	46.6	8,996
9 or more hours	6.6	1,265

The median subjective habitual sleep duration category (typical sleep duration reported at baseline) was 7–8 hr, and did not vary by age. The median *prior-night's* sleep duration was 7 hr. This varied slightly with age, with the median for 15–24 year olds at 8 hr. There was no effect of age (ANOVA, *p* = .829) or gender (Pearson chi-square = 1.36, *p* = .715) on subjective sleep duration category.

With respect to our measure of subjective chronotype, 18,664 participants (38% of total sample) reported a subjective chronotype (Table 1). There was no statistically significant difference in age across chronotype (*p* = .236), with the mean age for each chronotype ranging from 53.9 (Definitely Evening) to 53.6 (Slightly Evening) years of age. The greater number of female participants was also seen across all chronotypes as well (all chronotypes had a greater number of female participants). Figure S2 includes a breakdown of average sleep duration and chronotype, separately, across age groups.

4.2 | Sleep duration and flanker-task performance

Analysis of the sleep duration–performance relationship using average sleep duration calculated from each participant's prior-night

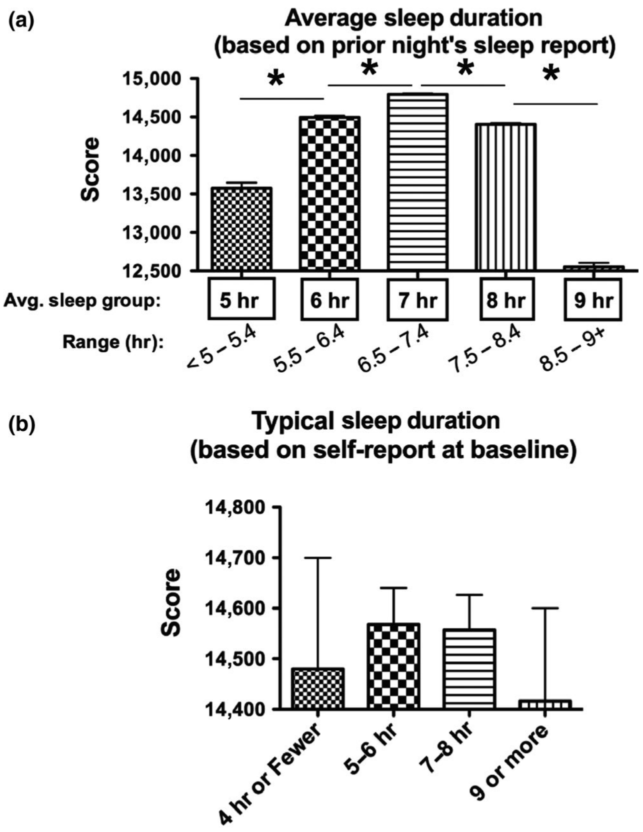

FIGURE 2 Predicting performance score from self-reported sleep duration. Self-reported sleep duration was measured in two ways: (a) within-subject average of ~20 prior-night sleep reports; and (b) single self-report of typical sleep duration reported prior to first game play. Error bars represent 95% confidence intervals

self-reported sleep duration and performance indicates a pronounced inverted U-shaped relationship between sleep duration and age-, education- and gender-adjusted performance, with a peak at 7 hr self-reported sleep duration (linear mixed model, main effect of average prior-night sleep duration on performance, $p < .01$ significant quadratic polynomial contrast, $p < .05$; Figure 2a). Post hoc pairwise comparisons of group mean differences (with Bonferroni correction for multiple comparisons) revealed that all adjacent sleep duration groups were significantly different from all others ($p < .05$). In contrast, the sleep duration–performance relationship using the one-time sleep duration report provided at registration also indicates an inverted U-shaped relationship between sleep duration and cognitive task performance, but no statistically significant differences in performance score (linear mixed model, main effect of one-time sleep duration on performance, $p = .59$; Figure 2b). Of note, because only a subsample of participants had baseline "typical" sleep duration reports, repeating the analysis with the repeated measures of sleep duration and cognitive task performance in that subsample demonstrated a statistically significant inverted U-shaped relationship analogous to that seen with the complete sample (not shown).

We then examined how the effect of sleep duration on cognitive task performance differed across age groups (Figure 3). Consistent with existing knowledge about age and cognitive performance, we found a pronounced stratification of performance by age, with performance deteriorating markedly with advancing age across all sleep durations (linear mixed model, main effect of age on performance, $p < .01$; sleep × age-bin interaction, $p < .00$; Figure 3a). Furthermore, there was a significant sleep by age-bin interaction (linear mixed model, $p < .00$). This finding suggests that, while all age groups showed peak performance at 7 hr *average* sleep duration (Figure 3a), there is a possible age difference in the slope of decline associated with sleeping less or more than 7 hr on average. In further exploration of this significant interaction, we performed piecewise linear regression of each age group on either side of the average sleep curve (< 7 hr and > 7 hr), to determine if there was a significant age-dependent difference in the slope of the performance deficits. We found that the performance deficit from shorter average sleep durations (< 7 hr) was significantly greater for older individuals (65–80 years old), while the performance deficit from *extended* average sleep durations (> 7 hr) was significantly greater in younger age groups (15–34 years old; *post hoc* comparisons of regression slopes by age, $p < .05$; Figure 3b).

In subsequent exploratory analysis of sleep duration and cognitive task performance, we examined how within-subject prior-night deviation from one's average sleep duration as derived from ~20

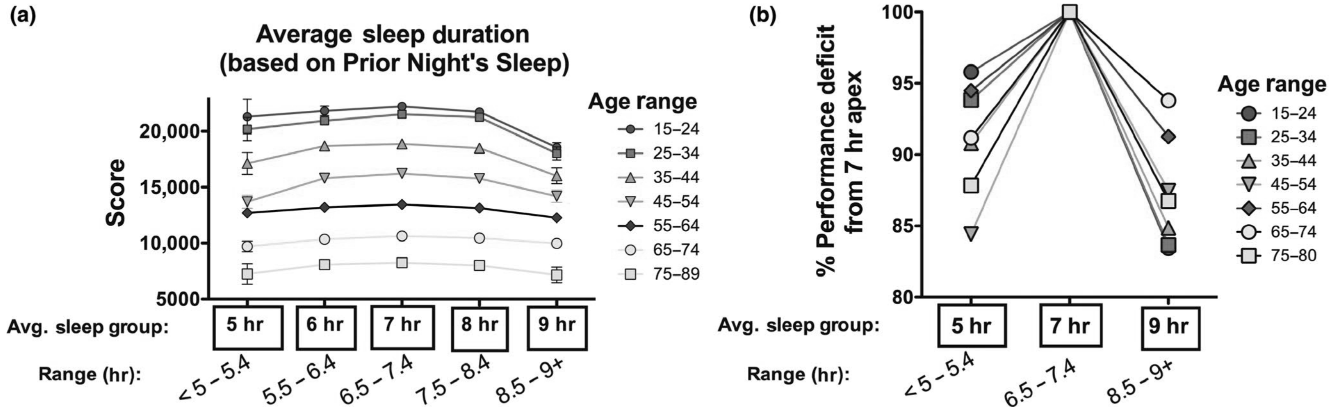

FIGURE 3 Relationship of performance score to average sleep duration by age. (a) Scores at average sleep durations, across age ranges. (b) Performance deterioration with variations from 7-hr average sleep duration across age groups. Error bars represent 95% confidence intervals

self-reports affected next-day cognitive performance. This analysis revealed an overall significant interaction between average sleep duration and variation from average sleep on performance ($p < .01$), indicating that the impact of deviation on performance depended on one's average sleep duration. To further explore this interaction, we tested the effect of prior-night's sleep on performance for each average sleep duration group. Most notably, 7-hr average sleepers performed significantly better overall than other groups and showed statistically significant decrements in performance if their prior-night's sleep value varied from their 7-hr average. Similarly, 8-hr average sleepers performed best at 8 hr, and showed statistically significant decrements above and below their average sleep duration. On the other hand, 6-hr average sleepers improved significantly with 7 hr of prior-night sleep. Interestingly, extreme short and long sleepers showed statistically significant improvements with a 1-hr sleep increase (for 5-hr sleepers) or sleep decrease (for 9+-hour sleepers), but no clear deterioration or improvement in performance with additional deviations (Figure 4).

4.3 | Time of play and performance

Overall, there was a main effect of time of day on score (linear mixed model, significant linear and quadratic contrasts, $p < .05$), with players performing best between 06:00 hours and 12:00 hours, with the nadir in performance occurring between 01:00 hours and 02:00 hours (Figure 5a). We also found a main effect of time-of-day on the number of correct responses, number of tries, percent correct, and response time across time-of-day (linear mixed model, $p < .01$; Figure 5b–e). Likewise, there were main effects of congruent and incongruent trials on performance, as well as a significant interaction between time of day and trial type (congruent versus incongruent; linear mixed model, $p < .01$). Interestingly, these findings demonstrate that the nighttime decline in percent correct is attributable to worsening performance on trials requiring response inhibition (Figure 5d).

Examination of time of play by age group demonstrated an overall stratification of age groups on flanker-task performance across time (Figure 6a). A linear mixed model revealed significant main effects of both time-of-day and age on performance (as shown in Figures 3 and 5). Interestingly, there was also a significant age by time-of-day interaction effect (linear mixed model, $p < .01$).

To further explore this significant interaction, we normalized scores (z-score) for the youngest and oldest age bins to compare their relative changes in performance over time. The results in Figure 6b illustrate a significant difference in relative performance (linear mixed model, $p < .05$) in the 02:00 hours–03:00 hours range

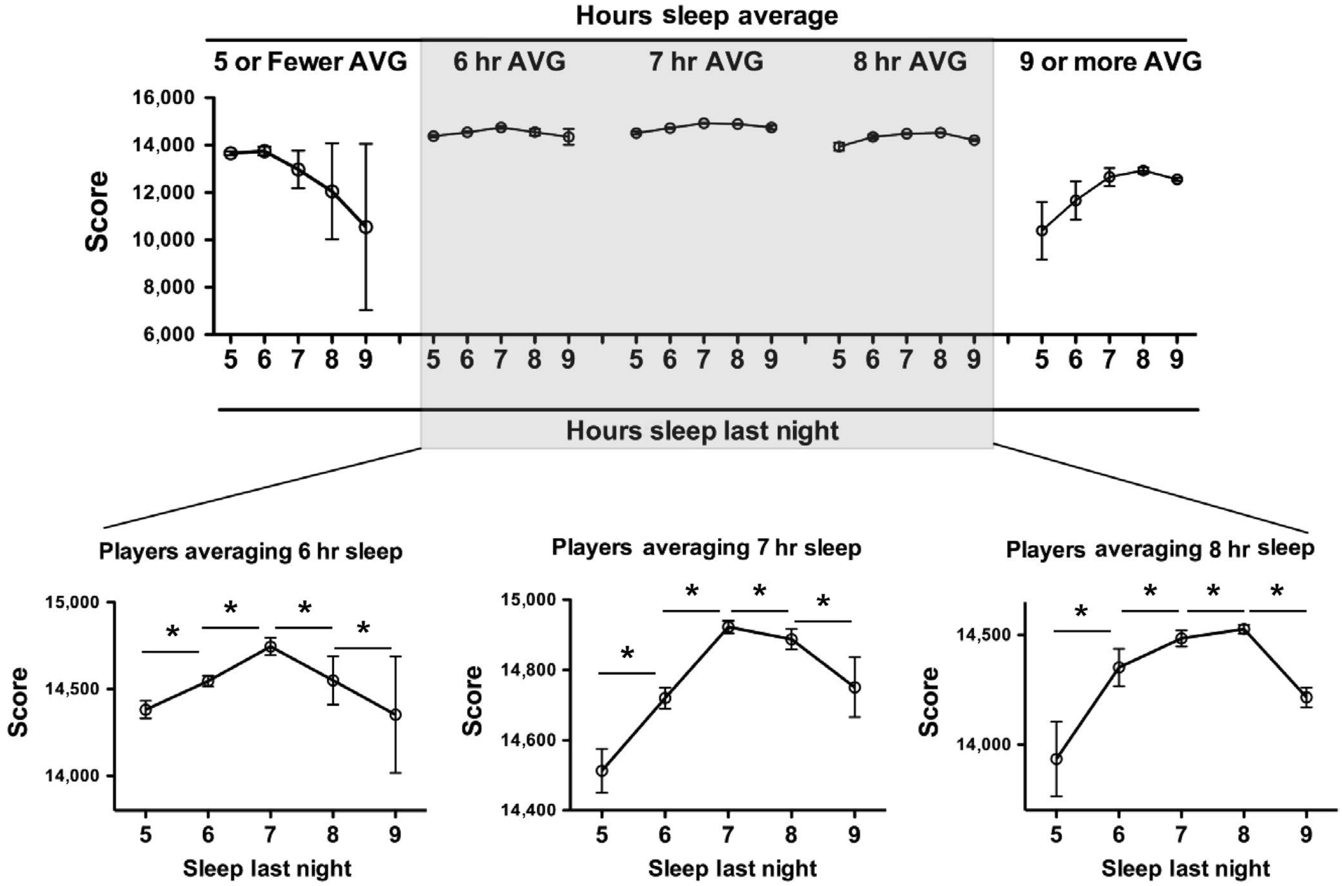

FIGURE 4 Within-subject changes in performance when deviating from average sleep. Scores based on prior-night's sleep, grouped by average sleep. Magnification of the 6-hr, 7-hr and 8-hr average sleep groups (green box) illustrates the performance deficit when participants slept more or less than their own average. Error bars represent 95% confidence intervals

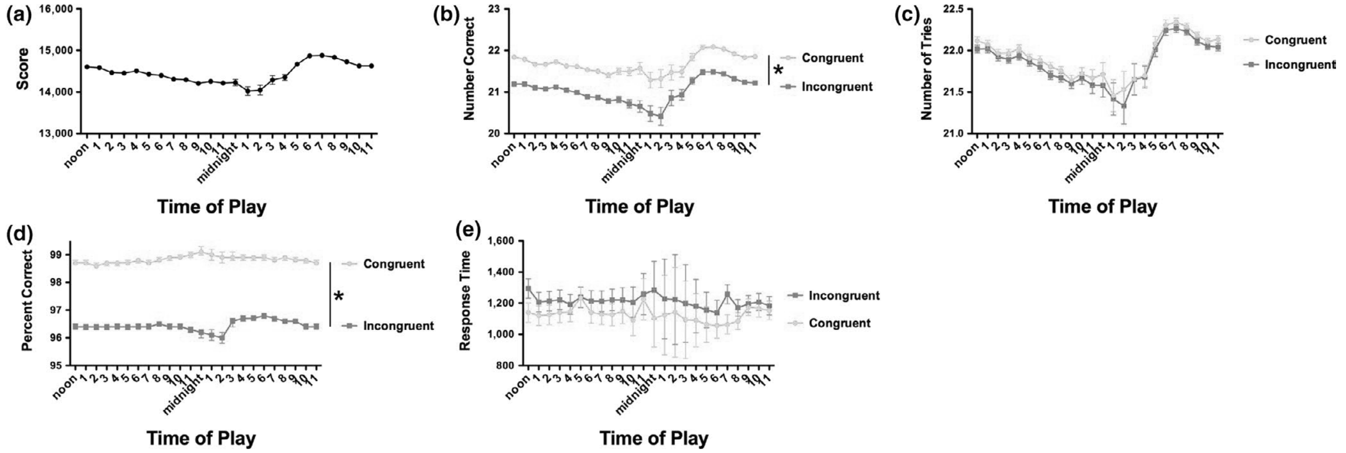

FIGURE 5 Performance score by time-of-day. (a) Mean scores for each time at which a game was played. Differences in performance across time of play for congruent and incongruent trials indicated by (b) number correct, (c) number of trials, (d) percent correct, and (e) response time. Error bars represent 95% confidence intervals

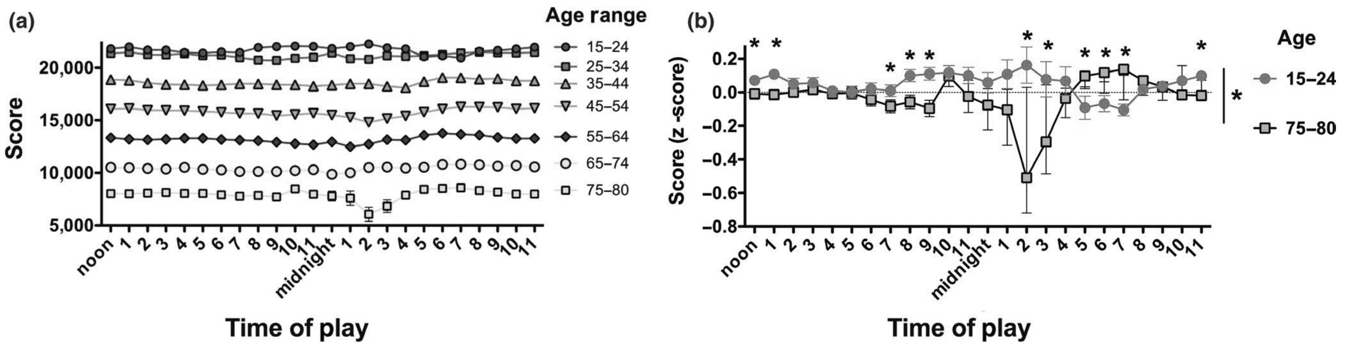

FIGURE 6 Time-of-day effects on performance by age group. (a) The breakdown of performance scores across time when grouped by age. (b) Performance across time for the youngest and oldest age groups. A normalized score (z-score) was calculated and plotted in order to best illustrate variations from the relative mean for each age group. Error bars represent 95% confidence intervals

between these age groups, indicating that performance drops at this time for the oldest age group (75–80 relative to performance in the youngest age group 15–24; Figure 6b), which actually improves during the early evening and nighttime interval. Figure 6b also indicates a relative benefit of early evening performance in the youngest age group as compared with the oldest age group and, in contrast, a relative benefit of early morning performance in the oldest age group as compared with the youngest age group.

4.4 | The synchrony effect in cognitive performance

Examination of the synchrony effect on flanker-task performance demonstrated that, contrary to our expectations, all chronotypes demonstrated a remarkably consistent pattern of performance across the 24-hr day, indicating better performance in the early part of the day, a steady decline in performance starting in the late afternoon, and a nadir in performance between 01:00 hours and 03:00 hours (Figure 7a). A linear mixed model revealed no main effect of chronotype on performance, nor a chronotype by time-of-day interaction (linear mixed model, $p > .05$). Additionally, there was no clear evidence of a shift in the clock time of peak or nadir for the performance curves with shift in chronotype. (At most, visual inspection of the curves in Figure 7, *when excluding slight PM chronotypes*, indicates a progressively later nadir in performance when moving from definite AM, to slight AM, to definite PM chronotypes.) Post hoc analyses also did not display a clear pattern of performance time by chronotype: the mode game play times were 08:03 hours for definite AM, 11:11 hours for slight AM, slight PM 10:55 hours, and 09:08 hours for definite PM players (not shown). Comparison of performance for definite AM and definite PM chronotypes at synchronous versus asynchronous times (using a prior definition of synchrony) indeed demonstrated that all participants performed better in the morning (i.e. synchronous for morning types and asynchronous for evening types; Figure 7b).

5 | DISCUSSION

The above analyses on sleep duration, time-of-day and synchrony effects on flanker-task performance across a broad age range demonstrate multiple compelling findings with respect to sleep and circadian effects on cognition. Our findings largely confirmed our first hypothesis, that performance would peak at 7-hr average, and that this effect would be most pronounced in younger individuals.

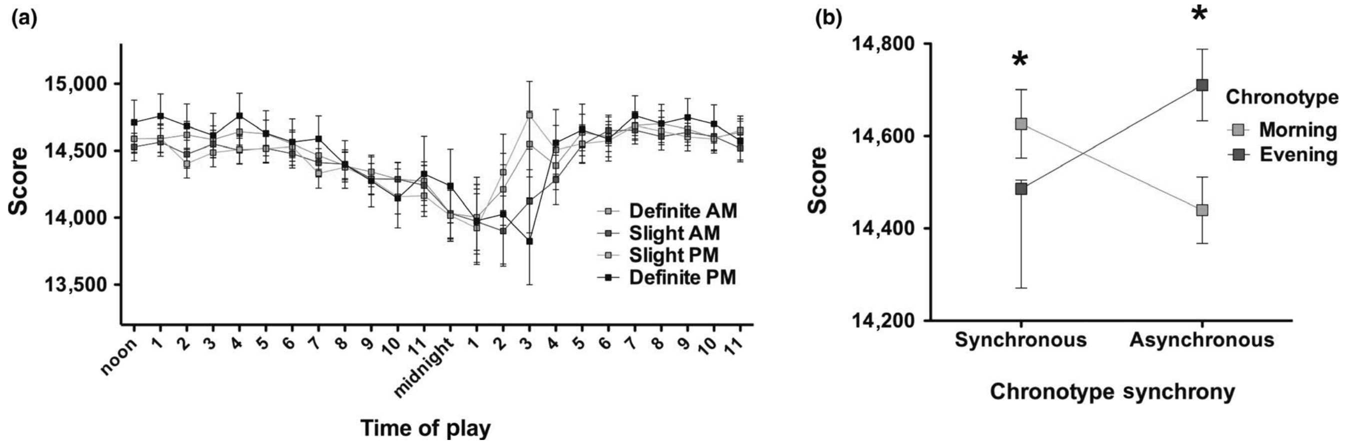

FIGURE 7 Time-of-day effects and synchrony effects by chronotype. (a) Performance across time of day when grouped by chronotype. (b) Performance grouped by synchronous (playing during preferable time of day based on chronotype) and asynchronous (playing outside one's preferable time of day based on chronotype). Error bars represent 95% confidence intervals, $^{*}p < .05$

Indeed, 7-hr average sleep duration, when calculated based on nearly 20 prior-night sleep duration self-reports, was associated with peak performance in the group as a whole as well as in all 10-year age groups examined separately. These findings are particularly intriguing as they run counter to the traditional belief that adolescents and young adults require more sleep for optimal functioning than other age groups. In fact, recent guidelines indicate that up to 9 hr of sleep may be indicated for healthy adolescents, while these data indicate that even 8 hr of average sleep is associated with a worsening of performance in the sample as a whole.

Our findings on sleep duration are also compelling because they indicate that 7-hr average sleep may be a marker for optimal cognitive functioning. Our exploratory analyses clearly demonstrated that 7-hr habitual sleepers performed better than individuals with other average sleep durations, and that prior-night deviations (either up or down) in individuals with other average sleep durations could not compensate for the benefits of 7-hr average sleep duration. For example, while 8-hr average sleepers perform best at 8-hr average sleep, 7-hr average sleepers still perform statistically significantly better than 8-hr average sleepers with 8 hr of sleep on the night prior to game play (Figure 4). And while 6-hr average sleepers performed better at 7 hr than at 6 hr of sleep, their performance at 7 hr was inferior to peak performance of 7-hr sleepers at 7 hr prior-night sleep duration. Additionally, while extreme short and long average sleepers were shown to benefit from a 1-hr deviation up (for short sleepers) or down (for long sleepers), their performance was generally inferior to 6–8 hr average sleepers and there was no indication that further deviation would significantly enhance performance.

Our findings with respect to sleep duration also demonstrate the advantages of large-scale repeated measures data for examining the relationships of interest. Many epidemiological studies rely on a single-item measure of typical sleep duration collected at a single time-point. Using the single-item assessment of "typical" sleep duration resulted in a statistically non-significant effect despite the large sample.

With respect to time-of-day effects, our findings were largely consistent with our hypotheses. The magnitude of performance scores enabled us to demonstrate a clear pattern of performance change over the 24-hr day. While performance in the group as a whole was highest in the morning and early afternoon, it gradually deteriorated in the late afternoon, and reached a nadir at about 01:00 hours–02:00 hours. This finding is intriguing given our current understanding of the biological regulators of sleep and arousal, known as process S, or the homeostatic process, and process C, the circadian process. While process S results in an increasing drive for sleep over the course of the day, it has been proposed that the circadian arousal signal strengthens over the course of the day and reaches its peak just prior to the dim-light melatonin onset in the evening, thus counteracting the homeostatic drive towards increased drowsiness and maintaining a steady level of alertness, and indirectly of cognitive functioning, until bedtime. Our data, in all but the youngest participants, show that while performance remains high and fairly steady from morning until the late afternoon, performance begins to gradually and steadily deteriorate starting in the late afternoon and reaches its nadir at 01:00 hours–02:00 hours. Thus, our data conflict with the idea that circadian arousal mechanisms fully compensate for rising homeostatic pressures in the latter part of the day.

Notwithstanding the pronounced time-of-day pattern seen in the group as a whole, a striking contrast was revealed when breaking the sample down by 10-year age group. Fifteen to 24-year-olds demonstrate an increase in performance in the night hours that was not seen in any other age group. This youth effect contrasted starkly with the effect in the oldest age group (75–80 year olds) who demonstrated the sharpest decline in performance at night. This finding is partly consistent with our understanding of circadian rhythm changes with development and aging: a circadian phase delay seems to emerge in adolescence and dissipates thereafter. On the other hand, while one might expect a relative maintenance of performance into the evening and night in adolescents and young adults, the improvement above daytime performance at late night is surprising, given that homeostatic forces resulting in deterioration over the day would be expected to counter circadian alerting signals as the day progresses.

Although the age-related time-of-day effect might be thought to be related to circadian rhythm differences between the youngest and oldest participants, the above data do not demonstrate the expected synchrony effect on performance across chronotypes. There were no clear differences in the time-of-day patterns for performance, and both evening and morning chronotypes clearly performed better in the morning. Furthermore, we did not detect a benefit for performance of incongruent (inhibitory) trials relative to congruent trials, contrasting with some research reporting a synchrony effect for tests of executive inhibitory functioning (May, 1999; Yoon & May, 1999).

Despite the absence of synchrony effects, our data clearly demonstrated that time-of-day effects were accounted for by deterioration in performance for the more difficult incongruent (inhibitory) trials. Other research has indicated that tasks requiring greater executive control may be more vulnerable to time-of-day effects than simpler tasks (Schmidt et al., 2007), and these data are consistent with this.

While this dataset provides many valuable insights, it has limitations. These data were not collected specifically for research, and the sample, despite its impressive magnitude, is not a representative sample of the population. Additionally, single-item, self-report items were utilized to assess sleep duration and subjective chronotype. While similar to those used in several epidemiological studies, they may insufficiently characterize the variable of interest. The chronotype variable, which assesses subjective daytime period of optimal productivity, rather than circadian *preference* per se, may be particularly limited in capturing subjective chronotype. It is possible that this limitation explains discrepancies between the chronotype and age effects, as one would expect the time-of-day effects for youth versus elderly would parallel the time-of-day effects of owls versus larks. Future studies would benefit from an improved measure of subjective chronotype.

Additionally, these analyses could not account for effects of building homeostatic sleep pressure (i.e. fatigue and drowsiness) on cognition, as the timing of the last sleep episode relative to the time of game play was not available. The available data also did not include information on naps, nor information about whether nighttime game plays occurred after an initial sleep period. We found it curious that the nadir in performance occurred earlier than what would be expected based on our knowledge of human temperature rhythms (i.e. 03:00 hours or 04:00 hours). It is possible that some individuals playing in the night after a period of sleep, even if brief, may have pulled the performance scores up in the 03:00 hours–04:00 hours period. Finally, it should also be noted that the IP address for plays subsequent to registration was not tracked. Therefore it is conceivable that time of play is incorrect where players may have registered using an IP address in a time-zone that differed from later game plays. Finally, information on health and lifestyle, such as caffeine or substance use, that might affect sleep and/or cognition were also not available for these analyses. While access to such data would be highly advantageous, plausible explanations for their significant contribution to unexpected findings are difficult to come by in this large sample.

In conclusion, these analyses demonstrate subtle but reliable and compelling findings about sleep duration and time-of-day effects on cognition, and ways in which age moderates these effects. In particular, adolescents and young adults have some advantages for maintaining cognitive performance in the late hours of the night. Further research is key for better understanding sleep and circadian factors impacting cognitive performance, and to understand participant and task characteristics that contribute to these effects.

AUTHOR CONTRIBUTIONS

AR is the principal investigator on the study, and took the lead in design, analysis, interpretation and manuscript preparation. JCK participated in interpretation of findings and manuscript preparation. JRH performed statistical analyses for the manuscript and participated in manuscript preparation. LDS contributed to interpretation of findings and manuscript preparation. SSI contributed to interpretation of findings and manuscript preparation. ALC participated in manuscript preparation. TJM served as senior statistician and provided consultation for statistical analyses based on his experience working with our industry data provider's data. TCN contributed significantly to design, analysis, interpretation and manuscript preparation.

CONFLICTS OF INTEREST

AR has consulted for Jazz Pharmaceuticals. She receives research grant funding from the University of California, San Francisco, the US Department of Veterans Affairs (VA), and the US Department of Defense (DoD). She reports no financial or other conflicts of interest with respect to the current manuscript. TN has consulted for Genentech and Jazz Pharmaceuticals, has received study medication from Actelion and Glaxo-Smith Kline for federally funded grants, and received grant funding from NIMH, DoD and VA. He reports no financial or other conflicts of interest with respect to the current manuscript. SI has received study medication from Merck for a federally funded study, and has received grant funding from VA, DoD and UCSF. None of these activities are related to the current study. All other authors have reported no potential financial conflicts of interest. Our industry partner has provided the raw data for these analyses free of charge, and with no restrictions on the analysis or interpretation of results.

ORCID

Anne Richards https://orcid.org/0000-0002-8814-2278

REFERENCES

Barclay, N. L., & Myachykov, A. (2017). Sustained wakefulness and visual attention: Moderation by chronotype. *Experimental Brain Research*, *235*(1), 57–68. https://doi.org/10.1007/s00221-016-4772-8

Bennett, C. L., Petros, T. V., Johnson, M., & Ferraro, F. R. (2008). Individual differences in the influence of time of day on executive functions. *American Journal of Psychology*, *121*(3), 349–361. https://doi.org/10.2307/20445471

Bonnefond, A., Rohmer, O., Hoeft, A., Muzet, A., & Tassi, P. (2003). Interaction of age with time of day and mental load in different cognitive tasks. *Perceptual and Motor Skills*, *96*(3 Pt 2), 1223–1236. https://doi.org/10.2466/pms.96.3.1223-1236

Cajochen, C., Sat Bir, S. K., Wyatt, J. K., Czeisler, C. A., & Dijk, D.-J. (1999). EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, *277*(3), 640–649. https://doi.org/10.1152/ajpregu.1999.277.3.r640

Doran, S. M., Van Dongen, H. P., & Dinges, D. F. (2001). Sustained attention performance during sleep deprivation: Evidence of state instability. *Archives Italiennes de Biologie*, *139*(3), 253.

Faubel, R., Lopez-Garcia, E., Guallar-Castillon, P., Graciani, A., Banegas, J. R., & Rodriguez-Artalejo, F. (2009). Usual sleep duration and cognitive function in older adults in Spain. *Journal of Sleep Research*, *18*(4), 427–435. https://doi.org/10.1111/j.1365-2869.2009.00759.x

Folkard, S., Knauth, P., & Monk, T. H. (1976). The effect of memory load on the circadian variation in performance efficiency under a rapidly rotating shift system. *Ergonomics*, *19*(4), 479–488. https://doi.org/10.1080/00140137608931559

Folkard, S., & Monk, T. H. (1980). Circadian rhythms in human memory. *British Journal of Psychology*, *71*(2), 295–307. https://doi.org/10.1111/j.2044-8295.1980.tb01746.x

Graw, P., Kräuchi, K., Knoblauch, V., Wirz-Justice, A., & Cajochen, C. (2004). Circadian and wake-dependent modulation of fastest and slowest reaction times during the psychomotor vigilance task. *Physiology and Behavior*, *80*(5), 695–701. https://doi.org/10.1016/j.physbeh.2003.12.004

Hidalgo, M. P., Zanette, C. B., Pedrotti, M., Souza, C. M., Nunes, P. V., & Chaves, M. L. (2004). Performance of chronotypes on memory tests during the morning and the evening shifts. *Psychological Reports*, *95*(1), 75–85. https://doi.org/10.2466/pr0.95.1.75-85

Koulack, D. (1997). Recognition memory, circadian rhythms, and sleep. *Perceptual and Motor Skills*, *85*(1), 99–104. https://doi.org/10.2466/pms.1997.85.1.99

Kraemer, S., Danker-Hopfe, H., Dorn, H., Schmidt, A., Ehlert, I., & Herrmann, W. M. (2000). Time-of-day variations of indicators of attention: Performance, physiologic parameters, and self-assessment of sleepiness. *Biological Psychiatry*, *48*(11), 1069–1080. https://doi.org/10.1016/s0006-3223(00)00908-2

Lara, T., Madrid, J. A., & Correa, A. (2014). The vigilance decrement in executive function is attenuated when individual chronotypes perform at their optimal time of day. *PLoS ONE*, *9*(2), e88820. https://doi.org/10.1371/journal.pone.0088820

Lehmann, C. A., Marks, A. D., & Hanstock, T. L. (2013). Age and synchrony effects in performance on the Rey Auditory Verbal Learning Test. *International Psychogeriatrics*, *25*(4), 657–665. https://doi.org/10.1017/s1041610212002013

Matchock, R. L., & Mordkoff, J. T. (2009). Chronotype and time-of-day influences on the alerting, orienting, and executive components of attention. *Experimental Brain Research*, *192*(2), 189–198. https://doi.org/10.1007/s00221-008-1567-6

May, C. P. (1999). Synchrony effects in cognition: The costs and a benefit. *Psychonomic Bulletin & Review*, *6*(1), 142–147. https://doi.org/10.3758/bf03210822

May, C. P., & Hasher, L. (1998). Synchrony effects in inhibitory control over thought and action. *Journal of Experimental Psychology: Human Perception and Performance*, *24*(2), 363–379. https://doi.org/10.1037/0096-1523.24.2.363

May, C. P., & Hasher, L. (2017). Synchrony affects performance for older but not younger neutral-type adults. *Timing Time Percept*, *5*(2), 129–148. https://doi.org/10.1163/22134468-00002087

Mikulincer, M., Babkoff, H., Caspy, T., & Sing, H. (1989). The effects of 72 hours of sleep loss on psychological variables. *British Journal of Psychology*, *80*(Pt 2), 145–162. https://doi.org/10.1111/j.2044-8295.1989.tb02309.x

Monk, T., Buysse, D., Reynolds Iii, C., Berga, S., Jarrett, D., Begley, A. M. Y., & Kupfer, D. (1997). Circadian rhythms in human performance and mood under constant conditions. *Journal of Sleep Research*, *6*(1), 9–18. https://doi.org/10.1046/j.1365-2869.1997.00023.x

Ramos, A. R., Dong, C., Elkind, M. S., Boden-Albala, B., Sacco, R. L., Rundek, T., & Wright, C. B. (2013). Association between sleep duration and the mini-mental score: The Northern Manhattan study. *Journal of Clinical Sleep Medicine*, *9*(7), 669–673. https://doi.org/10.5664/jcsm.2834

Richards, A., Inslicht, S. S., Metzler, T. J., Mohlenhoff, B. S., Rao, M. N., O'Donovan, A., & Neylan, T. C. (2017). Sleep and cognitive performance from teens to old age: More is not better. *Sleep*, *40*(1), https://doi.org/10.1093/sleep/zsw029

Santhi, N., Horowitz, T. S., Duffy, J. F., & Czeisler, C. A. (2007). Acute sleep deprivation and circadian misalignment associated with transition onto the first night of work impairs visual selective attention. *PLoS ONE*, *2*(11), e1233. https://doi.org/10.1371/journal.pone.0001233

Schmidt, C., Collette, F., Cajochen, C., & Peigneux, P. (2007). A time to think: Circadian rhythms in human cognition. *Cognitive Neuropsychology*, *24*(7), 755–789. https://doi.org/10.1080/02643290701754158

Schmidt, C., Peigneux, P., Cajochen, C., & Collette, F. (2012). Adapting test timing to the sleep-wake schedule: Effects on diurnal neurobehavioral performance changes in young evening and older morning chronotypes. *Chronobiology International*, *29*(4), 482–490. https://doi.org/10.3109/07420528.2012.658984

Schmutte, T., Harris, S., Levin, R., Zweig, R., Katz, M., & Lipton, R. (2007). The relation between cognitive functioning and self-reported sleep complaints in nondemented older adults: Results from the Bronx aging study. *Behavioral Sleep Medicine*, *5*(1), 39–56. https://doi.org/10.1080/15402000709336725

Sternberg, D. A., Ballard, K., Hardy, J. L., Katz, B., Doraiswamy, P. M., & Scanlon, M. (2013). The largest human cognitive performance dataset reveals insights into the effects of lifestyle factors and aging. *Frontiers in Human Neuroscience*, *7*, 292. https://doi.org/10.3389/fnhum.2013.00292

Valdez, P., Ramírez, C., García, A., Talamantes, J., Armijo, P., & Borrani, J. (2005). Circadian rhythms in components of attention. *Biological Rhythm Research*, *36*(1–2), 57–65. https://doi.org/10.1080/09291010400028633

van Eekelen, A. P. J., & Kerkhof, G. A. (2003). No interference of task complexity with circadian rhythmicity in a constant routine protocol. *Ergonomics*, *46*(15), 1578–1593. https://doi.org/10.1080/0014013031000121598

Watson, N. F., Badr, M. S., Belenky, G., Bliwise, D. L., Buxton, O. M., Buysse, D., & Tasali, E. (2015). Joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society on the recommended amount of sleep for a healthy adult: Methodology and discussion. *Sleep*, *38*(8), 1161–1183. https://doi.org/10.5665/sleep.4886

West, R., Murphy, K. J., Armilio, M. L., Craik, F. I. M., & Stuss, D. T. (2002). Effects of time of day on age differences in working memory. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *57*(1), P3–P10. https://doi.org/10.1093/geronb/57.1.p3

Wright, K. P. Jr, Hull, J. T., & Czeisler, C. A. (2002). Relationship between alertness, performance, and body temperature in humans. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, *283*(6), 1370–1377. https://doi.org/10.1152/ajpregu.00205.2002

Wyatt, J. K., Cecco, A. R.-D., Czeisler, C. A., & Dijk, D.-J. (1999). Circadian temperature and melatonin rhythms, sleep, and neurobehavioral function in humans living on a 20-h day. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, *277*(4), 1152–1163. https://doi.org/10.1152/ajpregu.1999.277.4.r1152

Xu, L., Jiang, C. Q., Lam, T. H., Liu, B., Jin, Y. L., Zhu, T., & Thomas, G. N. (2011). Short or long sleep duration is associated with memory impairment in older Chinese: The Guangzhou Biobank Cohort Study. *Sleep*, *34*(5), 575–580. https://doi.org/10.1093/sleep/34.5.575

Xu, L., Jiang, C. Q., Lam, T. H., Zhang, W. S., Cherny, S. S., Thomas, G. N., & Cheng, K. K. (2014). Sleep duration and memory in the elderly Chinese: Longitudinal analysis of the Guangzhou Biobank Cohort Study. *Sleep*, *37*(11), 1737–1744. https://doi.org/10.5665/sleep.4162

Yoon, C., & May, C. (1999). Aging, circadian arousal patterns, and cognition. In N. Schwarz, D. Park, B. Knauper, & S. Sudman (Eds), *Cognitive aging: A primer* (pp. 151–170). New York, NY: Psychology Press.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.s1S2

How to cite this article: Richards A, Kanady JC, Huie JR, et al. Work by day and sleep by night, do not sleep too little or too much: Effects of sleep duration, time of day and circadian synchrony on flanker-task performance in internet brain-game users from teens to advanced age. *J Sleep Res*. 2019;00:e12919. https://doi.org/10.1111/jsr.12919 pii: zsw0 http://dx.doi.org/10.10 3/sleep/zsw0

ORIGINAL ARTICLE

Sleep and Cognitive Performance From Teens To Old Age: More Is Not Better

Anne Richards, MD, MPH[1,] ; Sabra S. Inslicht, PhD[1,] ; Thomas J. Metzler, MS ; Brian S. Mohlenhoff, MD[1,] ; Madhu N. Rao, MD[1]; Aoife O'Donovan, PhD[1,] ; Thomas C. Neylan, MD[1,]

[1]*University of California, San Francisco, CA;* [2]*San Francisco VA Medical Center, San Francisco, CA*

Objectives: To determine the interaction of age and habitual sleep duration in predicting cognitive performance in a large sample of participants aged 15 to 8 years.

Methods: This study is a cross-sectional analysis of performance data gathered between January 01 and September 013. First-time players (*N* = 51 8 3) of three internet cognitive training games measuring processing speed, working memory, visuospatial memory, and arithmetic participated in the study.

Results: Performance was based on a measure of speed and accuracy for each game. The relationship between performance and self-reported habitual sleep duration was examined in the sample as a whole and across 10-year age groups starting at age 15 and ending at 75 and older. Performance peaked at 7 h of sleep duration for all three games in the sample as a whole, and the decrements in performance for sleep durations greater than 7 h were either comparable or greater in the youngest as compared to the oldest age groups.

Conclusions: These findings challenge the hypothesis that deteriorating cognitive performance with long sleep duration is driven by medical comorbidities associated with aging. Further, these data are consistent with an optimal dose model of sleep and suggest that the model for the homeostatic recovery of cognitive function as a function of sleep duration should incorporate a curvilinear decline with longer duration sleep, indicating that there may be a cost to increased sleep. Replication and further research is essential for clarifying the sleep duration–cognition relationship in youth and adults of all ages.

Keywords: Sleep duration, cognitive performance, aging, adolescence.

Statement of Significance

While most studies are consistent in finding that short sleep durations are problematic, little research has focused on the effects of long sleep durations. The assumptions that long sleep durations are better for functioning and that associations detected between longer sleep durations and poor functioning found in some studies must be attributable to medical or other unmeasured confounders, are reflected in current recommendations regarding sleep duration. Recent clinical guidelines recommend that healthy adults obtain at least 7 hours of habitual sleep and that or more hours may be appropriate in young adults. The current study focused on sleep duration and cognitive performance in a large internet-based sample of cognitive-training-game players aged 15–8 . This study found a reliable peak in performance at 7 hours' sleep duration in all 3 games examined in all but the oldest age categories, with deteriorations in performance beyond the peak equal or more steep in the youngest as compared to older age groups. These findings run counter to existing assumptions, especially with respect to younger individuals. Further research is necessary to further understand how sleep duration affects cognitive functioning across the lifespan.

INTRODUCTION

There is a growing interest in the role of sleep and sleep duration on cognitive functioning across the lifespan. With respect to younger age groups, research is motivated by evidence that chronic sleep deprivation is pervasive and associated with poorer school performance and increased risk-taking behavior.[1–3] For example, two systematic reviews of research on sleep and functioning in school-aged children and/or adolescents provide convincing evidence that low sleep duration is associated with lower school performance and increases in risk-taking behavior, such as substance use.[1,2] The threshold of sleep duration below which less sleep is associated with loss of performance has ranged across studies from 6 h,[4] to approximately 7 h[5,6]; to as much as 8 h.[7] Nonetheless, the sleep variables and the duration thresholds that define sleep duration as "low" vary across studies, making it difficult to compare findings and confidently conclude what sleep durations are problematic. In elderly populations, studies with fairly large sample sizes also indicate that inadequate or poor quality sleep contributes to cognitive dysfunction.[8–10] Using validated measures of cognitive performance, such as the Delayed Word Recall Test (DWRT), digit span tasks, verbal fluency tests, and/or the Mini-Mental State Examination (MMSE), these studies demonstrated that scores were significantly lower in subjects reporting sleep durations of 3–4 h as compared to sleep durations of 7–8 h,[8] ≤5 h as compared to 7 h,[10] or <6 h as compared to 6–9 h.[9] Xu and colleagues identified a significant trend in the sleep duration–cognitive performance relationship, demonstrating a dose–response relationship between sleep duration and improved performance from 3 to 7 h of sleep duration.[8]

Although there is sizeable evidence indicating that inadequate sleep contributes to cognitive deficits,[1–7] less is known about the relationship of long sleep duration and cognitive performance across the lifespan. A growing body of research in older-age subjects indicates that habitual sleep duration in excess of 7 to 9 h may be associated with decreased cognitive performance.[8,9,11–13] In one of the studies described above, Xu et al. identified an inverted U-shaped relationship between sleep duration and MMSE score which peaked at 7 h.[8] While the change in score across sleep durations was small (mean MMSE exam scores ranged from 26.6 to 27.3 across sleep durations), the trend was highly statistically significant and controlled for a number of demographic and health factors that are often thought to contribute to both sleep duration and cognition. Despite this, the association between longer sleep duration and poorer functioning, including cognitive performance, has generally been attributed to unmeasured confounding factors such as medical comorbidities that independently degrade cognition, rather than an indication that excess sleep is independently detrimental to cognitive function.[9] In contrast to research in older-age subjects, research on the topic of sleep duration and cognition in youth is focused primarily on the effects of sleep deprivation, and has generally concluded that children and adolescents would benefit from an increase in habitual sleep duration above 7 h for optimal functioning.[3] The potential consequences of excess sleep have not been explored. Based on existing epidemiological research and a small body of experimental research on individuals aged 18–60 years, the most recent clinical guidelines recommend that healthy adults obtain at least 7 or more h of habitual sleep and that 9 or more h may be appropriate in young adults.[14] It is generally recommended that adolescents sleep 8 h at the very least.[3]

To better understand the interaction of age and habitual sleep duration on predicting cognitive functioning, we analyzed data from three large samples of Lumosity brain game users on tasks of working memory, short-term visuospatial memory, and arithmetic, respectively. Although we expected age and education to be the strongest predictors of performance, as has been widely demonstrated in the literature,[15–18] we hypothesized that (1) short sleep duration would be associated with worse task performance (in all age groups); (2) peak performance would occur at longer habitual sleep duration in younger subjects as compared to older subjects; and (3) performance would degrade more rapidly with sleep durations beyond the peak in older as compared to younger participants.

METHODS

We used data collected by the Lumosity brain game database between January 2012 and September 2013 for three games, Speed Match, Memory Matrix, and Raindrops, focused on working memory/processing speed, short-term visuospatial memory, and basic arithmetic, respectively. Lumosity is an online brain training program that consists of tasks invoking processing speed, memory, problem solving and other cognitive skills. First-time use of the platform does not require payment, but repeated use for the purposes of training requires a paid registration. Additional details on the Lumosity platform and tasks have been published elsewhere.[19] Data were included for all players greater than or equal to 15 years of age at the time of play. All data were derived from a player's first use of the game so as to eliminate practice effects. Only data for participants whose preferred language was English, and who used keyboards for desktops or laptops (as opposed to tablets, smartphones, and touchscreens), were included. Data for participants with scores of zero were excluded. Zero scores are clear outliers on each of the tasks and are likely to result from participants beginning a game but not responding to the questions. These excluded responses constituted 0.10% of the data for Speed Match, 0.01% for Memory Matrix, and 2.27% for Raindrops. After removing zero scores, we computed the standard deviation of the scores for each game (after log transformation to normalize the distributions) and further removed scores that were above or below 4 *SD* from the mean. These exceptionally long or short play durations are likely to result from participants starting a game but not actively playing. This resulted in an additional 1541 participants being dropped from Raindrops (0.66% of the sample) and 124 participants dropped from Speed Match (0.02% of sample). Play duration was not available for Memory Matrix. The total number of players in the analysis sample was 512 823. Of these, 42.6% completed all three games, 44.5% completed two games, and 12.8% completed only one game.

To maximize the sample size for each game, data for each game were analyzed separately. Sample size for each game are as follows: Speed Match: *N* = 499 273; Memory Matrix: *N* = 447 665; and Raindrops: *N* = 231 658.

Measures

Demographic Information

At time of registration on the Lumosity website, users entered basic demographic information, including date of birth, gender, and educational attainment. Age at time of each game play is calculated by the Lumosity software.

Sleep Duration

Information about habitual sleep duration was obtained at registration. Participants answered the question "How much sleep do you typically get each night?" by selecting a sleep duration in "number of hours" ranging from "less than 4 h," then increasing integrally from 4 to 10 h, and ending with "more than 10 h" as the final option.

Speed Match

Speed Match is a simple test of working memory and processing speed and is a version of the 1-back test. Players are shown a variety of colored shapes in sequence and are required to indicate, using a keyboard stroke, whether each presented shape is the same as or different from the previously presented shape. Users are instructed to respond to as many trials as they can within the task's duration, which is 45 s. *n*-Back tasks, among which the 1-back is the simplest, are used widely in clinical and research settings as a measure of working memory.[20–23] Neuroimaging studies provide evidence for a consistent pattern of activation of frontal and parietal cortical regions by various versions of the *n*-back tasks,[22] providing support that the 1-back task can effectively measure simple working memory despite slight variations in task stimuli and duration.

Memory Matrix

Memory Matrix is a measure of visuospatial working memory in which participants are briefly presented with a pattern of squares on a grid, which they must reproduce on an empty grid using keyboard strokes. Participants complete 12 grids, or trials, with the complexity increasing with each successful trial or decreasing with each failed trial according to a predefined algorithm. There is no time limit for completion of the task. This computer-based test is based on a validated measure of visual memory, the Visual Patterns Test (VPT) used in research and clinical settings.[24,25] While the Lumosity version of the task is not the same as the official VPT, the task is designed according to rules that are considered important for visual working memory assessments, such as the use of patterns that cannot easily be coded verbally.[25] Researchers studying visual working memory have frequently modified matrix-based visual working memory tasks based on specific study aims and study populations.[24,26] They have the common feature of addressing the important question regarding how much can be remembered and are generally designed to be reliable and easy to use.[24]

Raindrops

Raindrops is a measure of calculations, in which participants are presented with a series of raindrops containing simple arithmetic problems at the top of their screen. Participants must enter numerical solutions using the keypad before each of the raindrops reaches the bottom of the screen. The concentration of raindrops on the screen and the complexity of the problems increase gradually over time (and therefore as a consequence of successful problem solving) according to a predefined algorithm, such that players must complete harder and harder problems at an increasingly fast pace to prevent game termination. The game ends once three raindrops have hit the ground. Raindrops is similar to other tasks used in neuroscience research on arithmetic.[27,28] While it is not a formally validated measure of cognitive function, its straightforward design lends it face validity as a measure of speeded, simple mathematical problem solving.

Statistical Analysis

The game score for each task was used as a measure of performance. The Lumosity scoring algorithm awards increasing numbers of points for each correct response as performance level increases, as a means to enhance motivation. Consequently, the score distributions are approximately exponential, with extreme right-skew. In order to normalize the distributions and to linearize the scoring scales, all performance score data were natural-log transformed prior to analysis. Samples were categorized into 10-year age groups with 15- to 24-year olds at one extreme and >75-year olds at the other extreme to examine the relationship of performance to sleep duration across age categories. Analyses of performance by habitual sleep duration across age groups controlled for gender and education level. Because higher education contributed to performance, and because education is naturally confounded with age in a sample that includes young people who haven't completed their education, we used the following method to adjust the log scores for education in each game: We noted that education levels were stable in age groups above 35, so we constructed regression models to predict performance scores from education level in the 35 and older participants only. We then used the regression coefficients to adjust log scores for education level for participants in all age groups. Thus scores for each participant in each age group, including the youngest group, were adjusted for estimated effects of education level derived from age groups above 35, in which age and education were not confounded.

We also noted a confound between age and gender, with women tending to be older (median age 34.1, interquartile range [IQR] 22.1–50.5) than men (median age 28.2, IQR 20.9–44.2). We therefore further adjusted the scores for gender by constructing regression models to predict education-adjusted scores from gender, age group, and gender by age group interactions, to allow for varying gender differences across age groups. We used the gender and gender by age group interaction parameters to adjust scores for gender within each age group. Education- and gender-adjusted log scores were then used for all subsequent analyses.

RESULTS

The demographic and sleep duration characteristics of the sample of participants playing at least one game are presented in Table 1. The sample was predominantly female (64%), and the mean age of the participant population was 35.8 (16.3) years.

Table 1—Demographic and Sleep Characteristics of the Sample of Subjects With Scores on at Least One Game.

	***n*/% *N* = 512 823**	**Self-reported sleep duration *M* (*SD*)**
Gender		
Male	186 577 (36.4)	6.9 (1.4)
Female	326 245 (63.6)	6.9 (1.4)
Age (years)		
15–24	183 664 (35.8)	7.2 (1.5)
25–34	100 988 (19.7)	6.9 (1.4)
35–44	71 830 (14.0)	6.7 (1.4)
45–54	75 819 (14.8)	6.7 (1.3)
55–64	54 136 (10.6)	6.8 (1.3)
65–74	21 263 (4.2)	6.9 (1.3)
75–89	5123 (1.0)	7.0 (1.3)
Education level		
Other	20 374 (4.0)	7.0 (1.6)
Some HS	35 272 (6.9)	6.9 (1.6)
HS diploma	106 430 (20.8)	7.0 (1.5)
Some college	125 865 (24.5)	6.8 (1.5)
Associate degree	33 118 (6.5)	6.8 (1.4)
Bachelor's degree	101 804 (19.9)	6.9 (1.3)
Master's degree	46 721 (9.1)	7.0 (1.2)
PhD/Professional	43 239 (8.4)	7.0 (1.3)

Due to the large sample size, all pairwise comparisons of mean sleep duration for gender, age, and education level are statistically significant, even when effect sizes are negligible.

Because of the small size of the sample of participants between the ages of 85 and 89, these participants were combined with the 75- to 84-year age category for purposes of data analysis. Table 1 provides a profile of subsample size and sleep characteristics for the gender, age, and education level categories. The youngest age group comprised the largest age category, containing 35.8% of the sample and the oldest age group contained only 1% of sample, but nonetheless represents over 5000 participants. There was a broad range of education categories, with the median education being some college. The "other" education category represented only 4% of the sample and although little information is known about this sample's educational attainment, the assumption that it represents individuals with less than a high school education is consistent with this group's relatively low age- and gender-adjusted performance as compared to other groups. Age, gender, and education were very similarly distributed in the three games, with gender and education categories equal across games to the nearest 1 percentage point and mean age equal within 0.3 years.

The mean subjective habitual sleep duration approximated 7 h of sleep for all demographic categories, with 15- to 24-year olds reporting a mean of 7.2 h and middle-aged individuals in

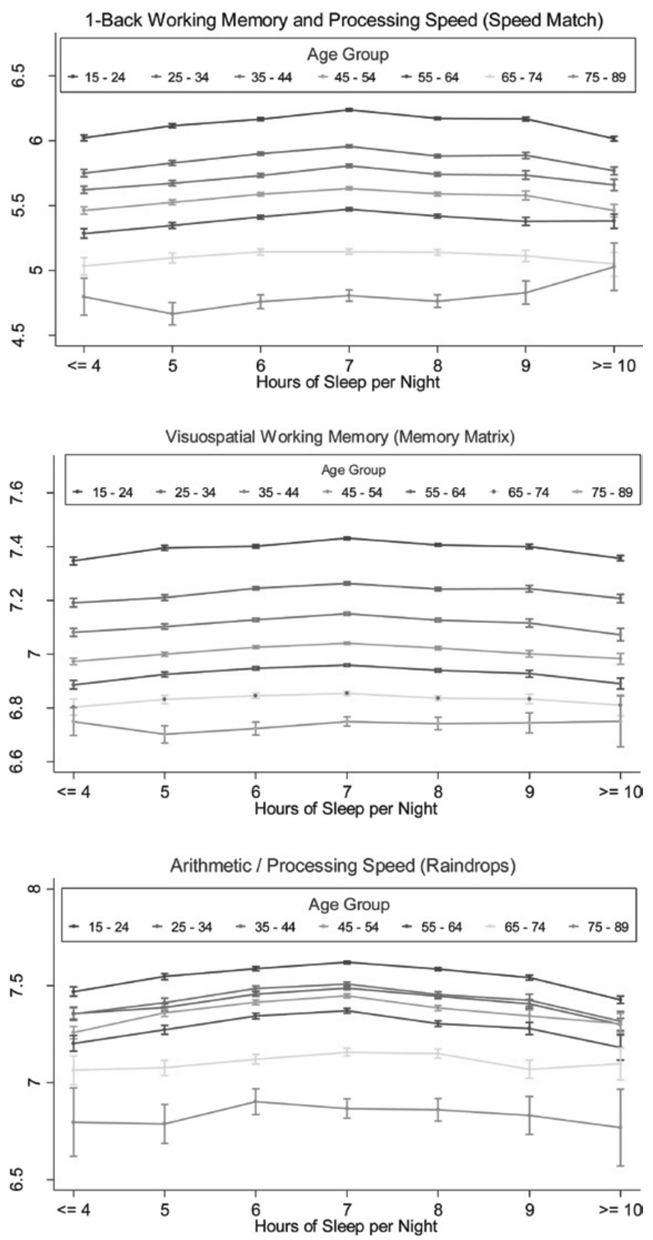

Figure 1—The three panels depict the relationship of mean-adjusted log score and self-reported habitual sleep duration by 10-year age category for working memory/processing speed (Speed Match; *N* = 499 273), visuospatial working memory (Memory Matrix; *N* = 447 665), and speeded arithmetic (Raindrops; *N* =231 658). Due to small sample size in the 85- to 89-year-old category, this group was combined with the 75- to 84-year-old category. Error bars represent 95% confidence intervals.

the 35- to 44-year and 45- to 54-year categories demonstrating the shortest sleep duration (Table 1). A more detailed breakdown of the sample by age and sleep duration is provided in Supplementary Table 1.

For the group as a whole, peak performance occurred at 7 h of sleep in all games, and the difference in performance at 7-h sleep duration was statistically significantly higher than performance at both 6-h and 8-h sleep duration. When the sample was broken down by 10-year age category, a similar pattern in the relationship between performance and sleep duration was found. Figure 1A–C depicts the relationship between task performance and sleep duration for all three brain games for all age categories. In addition to a predictable age-related decline in cognitive performance, these graphs reveal a consistent inverted u-shaped curve for the relationship between performance and sleep duration in younger and middle-aged age groups in all three games. Furthermore, peak performance occurred reliably at 7-h self-reported habitual sleep time for all three games for all age groups in which this inverted u-shaped relationship was present. This curve appears to flatten out in older age groups, such that the peak at 7 h is less discernible in 65- to 74-year olds and absent in 75- to 89-year olds.

Given the consistency of the peak in performance at 7-h sleep duration in most age groups and the flattening of the curves in older age groups on visual inspection, we estimated linear slopes for change in performance for each hour change in sleep duration for both sides of the curve (i.e., between <4 and 7 h and between 7 h and >10 h), in order to determine whether rates of change in performance to and beyond the peak of 7-h sleep duration varied with age category in a statistically significant manner. Although performance in each age group is not perfectly linear with sleep duration on either side of the curve, the linear slope provides an approximate measure of steepness of the sleep–performance relationship that is more easily interpretable than a more complex nonlinear characterization. We modeled the flattening of the curves in terms of the sleep duration by age interaction in linear mixed models. Although results were subtle, we found evidence supporting a flattening of the slope with age on the left side of the curve (<4–7 h) as well as on the right side of the curve (7–10+ h). On the lower end of sleep durations (<4–7 h), analysis of linear trend for change in slope indicated less improvement in performance for each hour increase in habitual sleep duration up to 7 h in older age groups as compared to younger groups, for two of the three cognitive tasks. The flattening, with age, of the lower half of the curve observed in Figure 1 was statistically significant for Speed Match and Memory Matrix ($p < .01$) but not for Raindrops ($p = .16$). For sleep durations beyond 7 h, the flattening of the slope was significant only for Speed Match ($p < .001$). This indicates that there is a greater degradation in performance for each additional hour of sleep in younger people than in the oldest age groups for Speed Match, but not significantly in the other two tasks ($p > .50$). Figure 2A depicts the effect of each additional hour of sleep from <4 up to 7 h on performance in the Speed Match task. Figure 2B depicts the effect of each additional hour of sleep longer than 7 h. The slope coefficient in the oldest age group in Figure 2B appears positive, but the wide confidence interval overlaps with zero.

Given the unexpected finding that performance peaked at 7-h sleep duration, even in the youngest age group which was expected to require more sleep, we performed a post-hoc analysis to examine these relationships more closely in adolescents as compared to young adults, with the expectation that peak performance would be associated with a longer sleep duration at least in the adolescent age category. Figure 3 demonstrates that the difference in performance between 15- to 19-year olds and 20- to 24-year olds was comparable in magnitude to that found between 10-year age groups across the sample. With respect to the relationship with sleep, and contrary to expectations, 15- to 19-year olds also demonstrated peak performance at 7-h sleep duration, with a decline in performance

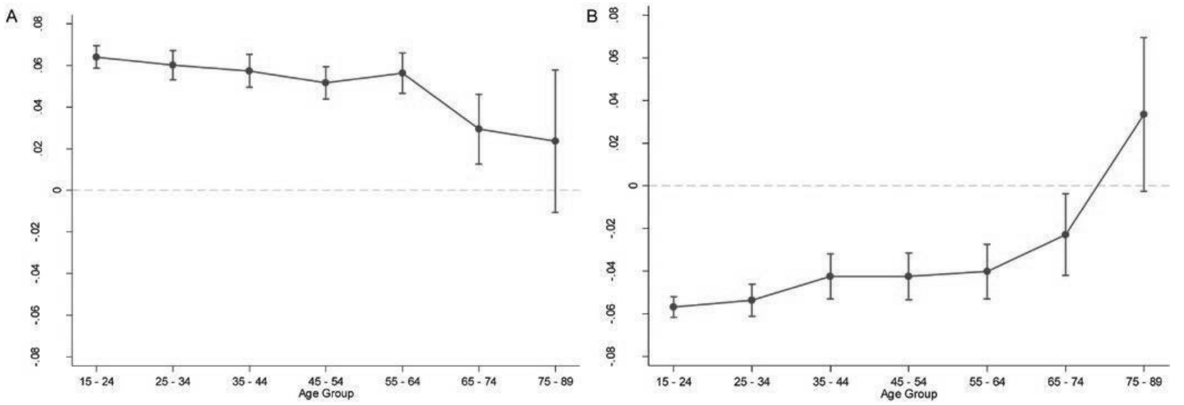

Figure 2—Performance change per hour of increased sleep duration from <4 to 7 h (A) and for 7 h to 10+ h (B) for the working memory/processing speed task (Speed Match; *N* = 499 273). In Panel A, more positive values indicate a greater gain in performance for each additional hour of sleep in the <4 to 7 h range. In Panel B, more negative values indicate a greater loss in performance for each additional hour of sleep in the 7–10+ h range. All age groups except the oldest demonstrated a statistically significant negative change in performance, while the oldest age group had a broad confidence interval that overlapped with a zero slope. Error bars represent 95% confidence intervals.

beyond that peak comparable (Speed Match (p = .175)) or greater (Memory Matrix (p = .002) and Raindrops (p = .009)) than that seen in 20- to 24-year olds. For sleep durations between <4 and 7 h of sleep, the benefits of increasing number of hours of sleep were numerically, but not statistically, greater in the 15- to 19-year olds as compared to the 20- to 24-year olds (Speed Match (p = .866), Memory Matrix (p = .065), and Raindrops (p = .482)).

Analysis of gender-specific effects indicated a main effect for gender on game performance, with males performing modestly better than women on all three tasks, but no consistent age by gender by sleep interaction effects.

DISCUSSION

These present findings demonstrate a reliable peak in cognitive performance at 7 h of self-reported habitual sleep duration in the group as a whole and, when the sample is broken into age categories, in all except the oldest two age categories in all three cognitive tasks. While this effect is small, it is remarkably consistent across younger and middle-aged age groups and is reliably reproduced in different tasks.

For the group as a whole, these data support existing evidence that short sleep durations (most commonly defined in the literature as sleep durations falling below the 6- to 9-h range) are detrimental to cognitive functioning.[8,9,29] While the detrimental effect of short sleep durations was not evident in the two oldest age groups, the smaller number of these older individuals at each sleep duration may mask any potential effects of sleep duration. Although various studies of sleep and cognitive functioning in older individuals do indicate worse performance at shorter habitual sleep duration,[8,9] it is important to note that some studies did not find this effect, even when multiple potential confounding factors were taken into account.[11–13] It is also important to note that most of the large-scale studies of sleep and performance on cognitive tasks have been conducted in middle-age and elderly subjects.[30,31] Studies in youth tend to focus on the relationship of sleep duration and school performance, or other behaviors that may be indirect evidence of suboptimal cognitive functioning, such as risk-taking behaviors. Further research is therefore crucial for better understanding the effects of short sleep duration on various aspects of cognitive performance in all age groups.

Contrary to our hypothesis that peak performance would occur at higher sleep durations in younger as compared to older participants, these data clearly indicate that performance peaks at 7-h sleep duration for all age groups between 15 and 65 years. A peak is less discernible in the 65- to 75-year olds, and not at all evident in the 75- to 89-year olds. Several studies provide evidence that middle-aged and older individuals tend to over-report sleep duration as compared to objective measures of sleep,[32–34] although factors that contribute to (e.g., age, gender, and cognitive status) or moderate such overestimations (e.g., objective sleep duration) differ across studies. Nonetheless, an overestimation would be consistent with evidence that total sleep time (measured objectively) decreases with age decreases with age[35], and to a greater degree than we observed in our study. Given this possibility, it is plausible that the peaks of the sleep duration–performance curves (Figure 1) are artificially shifted to the right as individuals become older and that true peak performance occurs more solidly to the left of 7-h sleep duration. Such a shift would not, however, have a self-evident impact on the slope of the curve we saw, nor would it alter the unexpected shape of the sleep duration–performance curves in younger participants. There is limited research comparing subjective and objective sleep measures in adolescents,[36,37] but we are not aware of literature suggesting that adolescents underestimate sleep time and that average sleep times and/or sleep times associated with peak performance are therefore biased toward being too low in our sample.

There is no research of which we are aware that indicates that teens or young adults might experience decrements in cognitive performance as a result of excess habitual sleep duration. The majority of previous research in youth has been focused on the detrimental consequences of sleep loss.[1–3,30] In contrast,

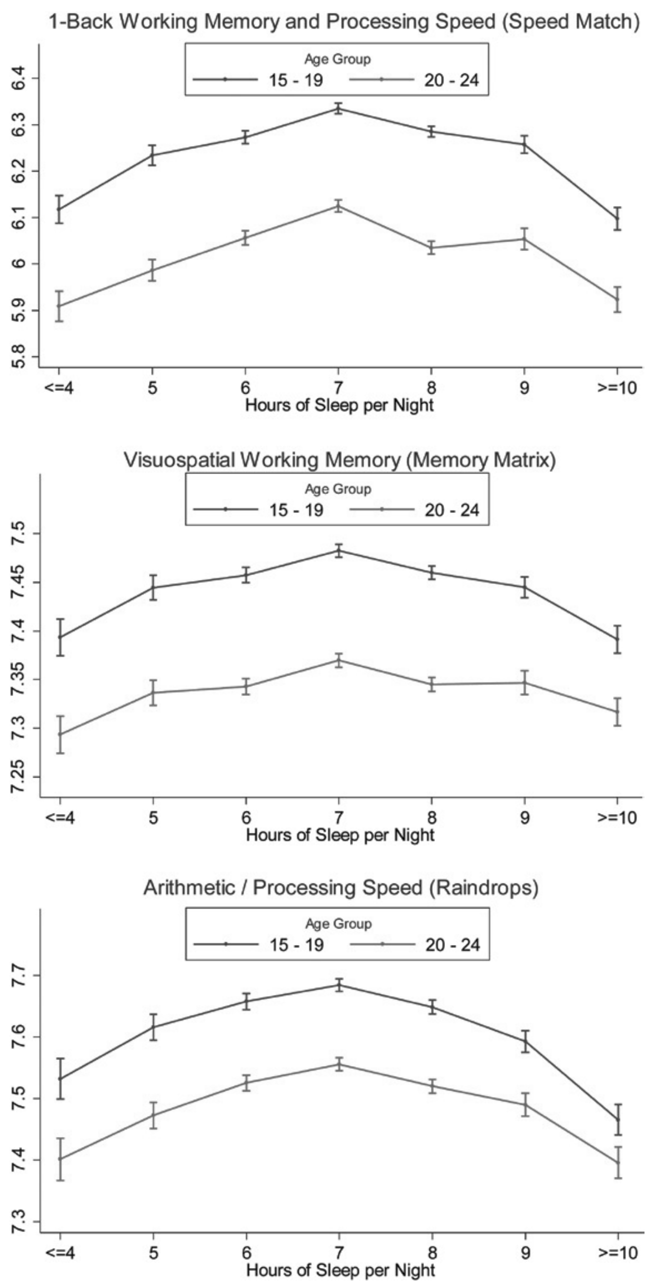

Figure 3—The three panels depict the relationship of mean-adjusted log score and self-reported habitual sleep duration for 15- to 19-year olds (blue curve) and 20- to 24-year olds (red curve) for working memory/processing speed (Speed Match; *N* = 179 031, including 96 927 15- to 19-year olds and 82 104 20- to 24-year olds), visuospatial working memory (Memory Matrix; *N* = 157 618, including 84 598 15- to 19-year olds and 73 020 20- to 24-year olds), and speeded arithmetic (Raindrops; *N* = 82 915, including 44 092 15- to 19-year olds and 38 823 20- to 24-year olds). Error bars represent 95% confidence intervals.

our findings are more consistent with an "optimal dose model" of sleep, as described by Marshall and colleagues, which proposes that a specified amount of sleep is required for optimal health and functioning and that more or less of it is detrimental.[38] As was recently explained by a consensus panel of experts in sleep research and clinical sleep medicine, while a biological mechanism by which "excess" sleep could be detrimental has not been uncovered, this relationship would be consistent with many biological systems.[14]

The association we saw between long sleep durations and cognitive performance decline in young participants raises questions about the argument that the decline in performance associated with increasing habitual sleep duration is attributable to the confounding factors of increased age-related medical comorbidities. While several recent research studies of older adult samples have demonstrated associations between worsening cognitive performance and increasing sleep,[8,9,11–13] the traditional argument has been that age-related medical comorbidities lead to both increased sleep need and worsening cognitive performance.[9] If this were the case, one would expect the slope of the decline from peak performance at 7 h to longer sleep durations to be flatter in the younger age groups, in which medical comorbidities are presumably low, or at the very least lower than they are in the older age groups in our sample. Analyses of the linear slopes in the present dataset indicate the opposite; younger participants demonstrated a steeper decline in one task and indistinguishable decline in performance in the other tasks for each additional hour of sleep beyond 7 h.

Could there be other, unmeasured confounding factors that could affect our most surprising findings, which were that performance peaked at a mere 7-h sleep duration in the youngest groups and that performance declined reliably at longer sleep durations? It may be worth considering the possibility that intrinsic features of the cognitive task, such as emotional content, might moderate some of the relationships that we found. This would be different from subject-related features such as the age-related medical comorbidities that we have discussed previously. Adolescents are undergoing a period of profound social-emotional development, and more sleep may be required for emotional homeostasis during these years. Ample research has demonstrated that sleep is important for emotional processing and recalibration.[39] School-related cognitive performance, and solid judgment in the context of teen driving and substance use, for example, which are the types of cognitive performance outcomes most often examined in large-scale research on sleep in youth, may be inextricably influenced by social-emotional pressures generated by peers, parents, and society. These may create moderating variables in the sleep–cognition relationship that may be absent in the context of internet-based activities (potentially devoid of such emotional loads). While this proposal is speculative, and while such a possibility does not undermine the findings described here with respect to emotionally neutral tasks, future research is essential to further understand this and other potential influences on the sleep duration and cognitive performance relationship in youth, and across the lifespan.

The current data may support the momentum to refocus research and public health attention to other problematic aspects of sleep in adolescents. For example, it may be the timing of sleep, which may be misaligned with the delayed chronotype that many adolescents temporarily develop, rather than the duration of sleep, that needs to be addressed in teens and young adults.[3,40,41] In post-hoc analyses using a subset of scores for which time of game play was available, we found significant effects of time of play on performance for Speed

Match and Raindrops (p values < .0001), but did not find time of play by sleep duration by age group effects on performance. Chronotype information was not available for this dataset. As much as possible, future analyses should take into account the timing of sleep, timing of task performance, and chronotype when examining sleep duration–cognition relationships.

The great strength of these findings is that they are derived from an unparalleled sample size and represent an impressive range of ages. This generates the statistical power to examine the relationship between cognitive performance and small changes in habitual sleep duration and identify a small, but precise, relationship between sleep duration and cognitive performance. The finding that peak performance consistently occurs at 7 h in all but the oldest two age groups raises intriguing questions about sleep homeostasis. Is 7 h of habitual sleep duration optimal for cognitive recovery and functioning? This peak at 7 h is consistent with recent studies demonstrating a similar curvilinear relationship between sleep duration and cognitive performance in older populations,[8,19] but the consideration of its implications for sleep regulation has been limited by the assumption that confounding factors such as medical comorbidities must explain the decline in performance with increasing sleep duration. Future research may benefit from examining this more closely in young and middle-aged samples.

Because this is a cross-sectional study, a major question that this study cannot answer is what the 7-h sleep duration for peak performance implies for people at an individual level. Does this mean that all individuals would benefit by extending or reducing, in the case of long sleepers, their sleep duration to 7 h? This goes against the evidence that sleep need varies across individuals, and there is no one-size-fits-all for optimal sleep duration. On the other hand, it may be worth entertaining the possibility that a 7-h sleep need is a correlate, or marker, of optimal sleep regulatory health. That is, it is possible that individuals who need and achieve 7 h habitual sleep duration have the biological substrate to optimize the physiological recovery functions of sleep, including those related to cognitive functioning. Recent genetics research has identified genes that have independent effects on the timing and duration of sleep, but which may have coordinated roles with respect to achieving the physiological functions of sleep.[42,43] There may be a genetic make-up, then, that promotes optimal cognitive functioning through independent and interacting effects on circadian rhythmicity, sleep duration, and the cognitive recovery functions of sleep and that is reflected in a 7-h sleep duration. Some researchers have also proposed that efficient sleep may reflect an all-around neural efficiency that may be reflected in cognitive performance.[44] Future analyses using repeated measures of sleep and cognitive performance, with sophisticated approaches to controlling for practice effects, will be crucial in addressing the implications of these findings for understanding the relationship of acute and chronic sleep duration with cognitive function.

Despite the many strengths of this dataset, it is important to acknowledge several limitations. Due to protections to privacy for participants who engaged in brain games, factors such as health status could not be considered in the present analyses. Future research should take advantage of the large-scale recruitment potential afforded by the internet and include demographic, health, and lifestyle information to maximize the ability to control for a range of factors that impact cognitive performance. Nonetheless, it is unlikely that the decline in performance with increasing sleep duration is explained by health factors alone, as has been suggested, simply because this relationship is strong, if not stronger, in the younger age groups where health problems would be expected to be lower than in older age groups. Additionally, other reports that demonstrated a similar relationship between increasing sleep duration and worsening cognitive performance controlled for some of these factors (e.g., depression and Alzheimer's disease) and still found significant results.[8,13] It is possible, however, that older brain game users may be healthier in many respects than their non-internet using counterparts.[45]

An obvious limitation of the data is that information on habitual sleep duration is based on a one-item self-report measure. Although this is not ideal, single-question assessments of sleep duration have been used in most epidemiologic studies of sleep and health outcomes and more objective measures of sleep are prohibitive on a large scale.[46–50] All the studies we cite examining the sleep duration–cognitive task performance relationship use single-question measures of sleep duration, although some studies explicitly incorporate nap time into the question regarding sleep duration,[10,11] while others do not.[8,9,12,13] Although naptime is a feature that may distinguish sleep patterns in the elderly people from that in other age groups, this difference does not explain the long sleep duration effects on cognitive performance in the above-mentioned studies on elderly participants. Hopefully, future studies will be able to parse the role of naps out further. Additionally, because teens and young adults may be particularly prone to social jetlag, which is marked by short weekday sleep durations accompanied with longer weekend "recovery" sleep, it is possible that the young participants' self-reported sleep duration underestimates average sleep duration. Such an underestimate could artificially shift the curve to the left in younger age groups. When possible, future studies should consider whether self-reported sleep duration and task performance information was obtained on weekdays or weekends and/or ensure that estimates include all 7 days of the week.

With respect to the measures of cognitive performance, the Lumosity games are based on standardized cognitive tests (Speed Match and Memory Matrix) and basic arithmetic (Raindrops). They are also designed to be visually appealing and engaging to an internet audience. While it would be preferable to use tasks that have been validated against standardized measures of processing speed, working memory, visuospatial memory, and arithmetic skill, the scientific research demonstrates that *n*-back tests and grid-based visuospatial memory tasks are frequently modified across studies but that they generally function consistently in assessing the main domains of interest. Furthermore, the game scores vary as would be expected as a function of education and age, the largest predictors of cognitive performance, which increases our confidence in the reliability of our findings. While the scores are generated using an algorithm resulting in a nonlinear increase in score with higher performance, our findings were consistent with findings previously reported for a similar dataset using simpler outcomes such as number correct or memory thresholds.[19] We chose the overall score as the outcome because of its consistency with previously reported findings and because it reflects a more global measure of performance encompassing both speed and accuracy of performance. Finally, because performance on all these tasks requires the ability to manipulate a computer keyboard, it is important to consider the degree to which performance reflects motor speed and coordination, all factors which are known to decline with age.[51] Regardless, the impact of sleep on these functions would also be evidence of sleep's effect on neural function, albeit of a different type. Additionally, it may be important to note that these tasks can be considered to be mild (Speed Match and Memory Matrix) to moderate (Raindrops) in complexity and that the sleep duration–performance relationships may have behaved differently with more complex tasks. It will be important for future research to determine whether task complexity moderates sleep duration–performance relationships and the impact of age on these relationships. Finally, while elderly individuals are increasingly savvy with the use of computers and the internet, it is possible that decreased skill and experience with computers, and computer- and internet-based tasks, resulted in an artificial downward shift in cognitive performance with increasing age. While very possible, this would not create a shift in peak cognitive performance relative to reported sleep duration.

In conclusion, our findings indicate a subtle but reliable inverted u-shaped relationship between self-reported habitual sleep duration and cognitive performance in a large sample of internet brain game users. These findings shift the focus of the role of sleep duration in predicting performance from older to younger age groups. Given the current concerns about sleep duration in younger people, further research is crucial to better understand sleep timing and duration effects in this age group. The internet may be a viable and effective strategy for studying this population. Further research is also crucial to examine mechanisms whereby increasing sleep may have negative effects on outcome.

REFERENCES

1. Shochat T, Cohen-Zion M, Tzischinsky O. Functional consequences of inadequate sleep in adolescents: a systematic review. Sleep Med Rev. 2014; 18(1): 75–87.
2. Dewald JF, Meijer AM, Oort FJ, Kerkhof GA, Bogels SM. The influence of sleep quality, sleep duration and sleepiness on school performance in children and adolescents: a meta-analytic review. Sleep Med Rev. 2010; 14(3): 179–189.
3. Owens J; Adolescent Sleep Working Group, Committee on Adolescence. Insufficient sleep in adolescents and young adults: an update on causes and consequences. Pediatrics. 2014; 134(3):e921–e932.
4. Roberts RE, Roberts CR, Duong HT. Sleepless in adolescence: prospective data on sleep deprivation, health and functioning. J Adolesc. 2009; 32(5): 1045–1057.
5. Wolfson AR, Carskadon MA. Sleep schedules and daytime functioning in adolescents. Child Dev. 1998; 69(41): 875–887.
6. Chung KF, Cheung MM. Sleep-wake patterns and sleep disturbance among Hong Kong Chinese adolescents. Sleep. 2008; 31(2): 185–194.
7. McKnight-Eily LR, Eaton DK, et al. Relationships between hours of sleep and health-risk behaviors in US adolescent students. Prev Med. 2011; 53(4-5): 271–273.
8. Xu L, Jiang CQ, Lam TH, et al. Short or long sleep duration is associated with memory impairment in older Chinese: the Guangzhou Biobank Cohort Study. Sleep. 2011; 34(5): 575–580.
9. Gildner TE, Liebert MA, Kowal P, Chatterji S, Snodgrass JJ. Associations between sleep duration, sleep quality, and cognitive test performance among older adults from six middle income countries: results from the Study on Global Ageing and Adult Health (SAGE). J Clin Sleep Med. 2014; 10: 613–621.
10. Xu L, Jiang CQ, Lam TH, et al. Sleep duration and memory in the elderly Chinese: longitudinal analysis of the Guangzhou Biobank Cohort Study. Sleep. 2014; 37(11): 1737–1744.
11. Faubel R, Lopez-Garcia E, Guallar-Castillon P, Graciani A, Banegas JR, Rodriguez-Artalejo F. Usual sleep duration and cognitive function in older adults in Spain. J Sleep Res. 2009; 18(4): 427–435.
12. Ramos AR, Dong C, Elkind MS, et al. Association between sleep duration and the mini-mental score: the Northern Manhattan study. J Clin Sleep Med. 2013; 9(7): 669–673.
13. Schmutte T, Harris S, Levin R, Zweig R, Katz M, Lipton R. The relation between cognitive functioning and self-reported sleep complaints in nondemented older adults: results from the Bronx aging study. Behav Sleep Med. 2007; 5: 39–56.
14. Watson NF, Badr MS, Belenky G, et al. Recommended amount of sleep for a healthy adult: a joint consensus statement of the American academy of sleep medicine and sleep research society. Sleep. 2015; 38: 843–844.
15. Park DC, Lautenschlager G, Hedden T, Davidson NS, Smith AD, Smith PK. Models of visuospatial and verbal memory across the adult life span. Psychol Aging. 2002; 17(2): 299–320.
16. Barnes DE, Tager IB, Satariano WA, Yaffe K. The relationship between literacy and cognition in well-educated elders. J Gerontol A Biol Sci Med Sci. 2004; 59(4): 390–395.
17. Heaton R, Ryan L, Grant I, Matthews CG. Demographic influences on neuropsychological test performance. In: Grant IAK, ed. Neuropsychological Assessment of Neuropsychiatric Disorders. New York: Oxford University Press; 1996: 141–163.
18. Salthouse TA. Selective review of cognitive aging. J Int Neuropsychol Soc. 2010; 16(5): 754–760.
19. Sternberg DA, Ballard K, Hardy JL, Katz B, Doraiswamy PM, Scanlon M. The largest human cognitive performance dataset reveals insights into the effects of lifestyle factors and aging. Front Hum Neurosci. 2013; 7: 292.
20. Wilhelm O, Hildebrandt A, Oberauer K. What is working memory capacity, and how can we measure it? Front Psychol. 2013; 4: 433.
21. Kirchner WK. Age differences in short-term retention of rapidly changing information. J Exp Psychol. 1958; 55(4): 352–358.
22. Owen AM, McMillan KM, Laird AR, Bullmore E. N-back working memory paradigm: a meta-analysis of normative functional neuroimaging studies. Hum Brain Mapp. 2005; 25(1): 46–59.
23. Cansino S, Hernández-Ramos E, Estrada-Manilla C, et al. The decline of verbal and visuospatial working memory across the adult life span. Age (Dordr). 2013; 35: 2283–302.
24. Wilson JTL, Scott JH, Power KG. Developmental differences in the span of visual memory for pattern. Brit J Dev Psychol. 1987; 5: 249–255.
25. Della Sala S, Gray C, Baddeley A, Wilson L. The Visual Patterns Test: A New Test of Short-Term Visual Recall. Feltham, Suffolk: Thames Valley Test Company; 1997.
26. Ichikawa S. Measurement of visual memory span by means of the recall of dot-in-matrix patterns. Behav Res Methods Instrument. 1982; 14: 309–313.
27. Pauli P, McClelland JL, Seidenberg MS, Patterson KE. Extensive practice in mental arithmetic and practice transfer over a ten-month retention interval Math Cogn. 1998; 4: 21–46.
28. Delazer M, Domahs F, Bartha L, et al. Learning complex arithmetic—an fMRI study. Brain Res Cogn Brain Res. 2003; 18(1): 76–88.
29. Tworoger SS, Lee S, Schernhammer ES, Grodstein F. The association of self-reported sleep duration, difficulty sleeping, and snoring with cognitive function in older women. Alzheimer Dis Assoc Disord. 2006; 20: 41–8.
30. Benitez A, Gunstad J. Poor sleep quality diminishes cognitive functioning independent of depression and anxiety in healthy young adults. Clin Neuropsychol. 2012; 26(2): 214–23.
31. Scullin MK, Bliwise DL. Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. Perspect Psychol Sci. 2015; 10(1): 97–137.
32. Silva GE, Goodwin JL, Sherrill DL, et al. Relationship between reported and measured sleep times: the sleep heart health study (SHHS). J Clin Sleep Med. 2007; 3: 622–630.

33. Van Den Berg JF, Van Rooij FJ, Vos H, et al. Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. J Sleep Res. 2008; 17: 295–302.
34. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? Epidemiology. 2008; 19(6): 838–845.
35. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep. 2004; 27: 1255–1273.
36. Wolfson AR, Carskadon MA, Acebo C, et al. Evidence for the validity of a sleep habits survey for adolescents. Sleep. 2003; 26(2): 213–216.
37. Short MA, Gradisar M, Lack LC, Wright HR, Chatburn A. Estimating adolescent sleep patterns: parent reports versus adolescent self-report surveys, sleep diaries, and actigraphy. Nat Sci Sleep. 2013; 5:23–26.
38. Marshall NS, Glozier N, Grunstein RR. Is sleep duration related to obesity? A critical review of the epidemiological evidence. Sleep Med Rev. 2008; 12(4): 289–98.
39. Goldstein AN, Walker MP. The role of sleep in emotional brain function. Annu Rev Clin Psychol. 2014; 10: 679–708.
40. Carskadon MA, Acebo C, Jenni OG. Regulation of adolescent sleep: implications for behavior. Ann NY Acad Sci. 2004; 1021: 276–291.
41. Colrain IM, Baker FC. Changes in sleep as a function of adolescent development. Neuropsychol Rev. 2011; 21(1): 5–21.
42. Hallows WC, Ptáček LJ, Fu YH. Solving the mystery of human sleep schedules one mutation at a time. Crit Rev Biochem Mol Biol. 2013; 48: 465–475.
43. Kurien PA, Chong SY, Ptáček LJ, Fu YH. Sick and tired: how molecular regulators of human sleep schedules and duration impact immune function. Curr Opin Neurobiol. 2013; 23: 873–879.
44. Geiger A, Achermann P, Jenni OG. Association between sleep duration and intelligence scores in healthy children. Dev Psychol. 2010; 46: 949–954.
45. Xavier AJ, d'Orsi E, Wardle J, Demakakos P, Smith SG, von Wagner C. Internet use and cancer-preventive behaviors in older adults: findings from a longitudinal cohort study. Cancer Epidemiol Biomarkers Prev. 2013; 22: 2066–2074.
46. Kurina LM, McClintock MK, Chen JH, Waite LJ, Thisted RA, Lauderdale DS. Sleep duration and all-cause mortality: a critical review of measurement and associations. Ann Epidemiol. 2013; 23(4): 361–370.
47. Ford ES, Cunningham TJ, Croft JB. Trends in self-reported sleep duration among US adults from 1985 to 2012. Sleep. 2015; 38(5): 829–832.
48. Krueger PM, Friedman EM. Sleep duration in the United States: a cross-sectional population-based study. Am J Epidemiol. 2009; 169(9): 1052–1063.
49. Maslowsky J, Ozer EJ. Developmental trends in sleep duration in adolescence and young adulthood: evidence from a national United States sample. J Adolesc Health. 2014; 54: 691–697.
50. Fang SC, Subramanian SV, Piccolo R, et al. Geographic variations in sleep duration: a multilevel analysis from the Boston Area Community Health (BACH) Survey. J Epidemiol Community Health. 2015; 69(1): 63–69.
51. Vandervoort AA. Aging of the human neuromuscular system. Muscle Nerve. 2002; 25(1): 17–25.

SUPPLEMENTARY MATERIAL

Supplementary Material is available at *SLEEP* online.

FUNDING

Work on this project was funded in part by grants to Dr. Richards from the U.S. Department of Veteran Affairs (1IK2CX000871-01A2) and the U.S. Department of Defense (W81XWH-16-1-0259).

ACKNOWLEDGMENTS

We gratefully acknowledge Lumosity, Inc, including Daniel Sternberg, Director of Data Science, for the provision of the data to the investigators free of charge and with no restrictions on how the data were analyzed or interpreted.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication October, 2015
Submitted in final revised form June, 2016
Accepted for publication August, 2016
Address correspondence to: Anne Richards, MD, MPH, San Francisco VA Medical Center, 4150 Clement Street, San Francisco, CA 94121. Telephone: 415-221-4810, ext: 23312; Fax: 415-750-6921; Email: anne.richards@ucsf.edu

DISCLOSURE STATEMENT

This was not an industry supported study. Dr. Neylan has consulted for Genentech, and received study medication from Actelion for a study funded by the Department of Defense, Glaxo-Smith Kline for a study funded by the Department of Veterans Affairs. All other authors have reported no financial conflicts of interest.