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COMMENTARY

# Are there sensitive age ranges at which disrupted sleep differentially affects cognition?

## Commentary on "Effects of age on the relationship between sleep quality and cognitive performance: Findings from the Human Connectome Project Aging Cohort" by Cohen *et al.*

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Age-related cognitive changes in healthy adults are well established in the scientific literature (Harada *et al.*, 2013; Salthouse, 2010). In simple terms, crystallized cognition, such as vocabulary or semantic knowledge obtained over the lifespan, tends to gradually increase over the life course. In contrast, fluid mental processes, such as processing speed, problem solving, and learning efficiency, demonstrate a near linear decline with age (Salthouse, 2010). Despite these robustly demonstrated trends, successful healthy aging tends to be the rule, not the exception, for most older adults (Salthouse, 2012). Even so, healthy cognitive aging may be negatively impacted by social, environmental, physical, and mental health factors. Sleep quality is one such variable with both short- and long-term interactive effects with aging and cognitive outcomes.

Sleep changes in both quality and quantity are common across the lifespan. Older adults tend to experience shorter overall sleep time, longer latency to sleep onset, and increased wake time after sleep onset (Ohayon *et al.*, 2004). Underlying sleep architecture also changes over time with older adults experiencing less deep sleep (Stages 3–4) and Rapid Eye Movement sleep on average, and spending more time in light sleep (Stages 1–2) (Neubauer, 1999). As individuals age, the innate circadian rhythm can also shift such that older individuals are more likely to experience advances in their circadian tendencies (Duffy *et al.*, 2015). Additionally, rates of certain sleep disorders such as insomnia, restless legs syndrome, periodic limb movement, and obstructive sleep apnea (OSA) increase with age (Cooke and Ancoli-Israel, 2011).

Multiple lines of research indicate that there are negative impacts of sleep deprivation on diverse neurocognitive domains including processing speed, decision making, executive functioning, and working memory (Alhola and Polo-Kantola, 2007; Durmer and Dinges, 2005). Mood and motor functioning, in addition to cognitive functions, are also negatively impacted by short-term sleep deprivation. Over time, negative effects of sleep loss can become cumulative (Goel *et al.*, 2009), though there are indications that individual differences in susceptibility to sleep loss affect the overall impact on functioning (Alhola and Polo-Kantola, 2007). Medical sleep disorders such as restless legs syndrome (RLS) and OSA result in similar short term effects on functioning. Long term effects of poor sleep quality and OSA have been associated with accelerated cognitive decline and increased risk of mild cognitive impairment (MCI) and dementia in later life, although the causal mechanisms are complex and not clearly understood (Bubu *et al.*, 2020; Dunietz *et al.*, 2021; Ercolano *et al.*, 2023; Wong and Lovier, 2023). One study (Lo *et al.*, 2014) demonstrated that for each hour of reduced sleep, healthy older adults showed year-over-year decrements in cognitive performance (0.67%) and increased ventricular expansion (0.59%). Untreated OSA in older adults has been associated with declines in cognition, particularly attention and executive functioning, and increased risk of dementia, likely due to intermittent hypoxia and sleep fragmentation, among other mechanisms (Bubu *et al.*, 2020; Ercolano *et al.*, 2023). Effective positive airway pressure treatment in older adults has been linked with a lower odds of MCI and dementia diagnoses (Bubu *et al.*, 2020; Dunietz *et al.*, 2021). While clear mechanistic/causal links are yet to be established, evidence suggests that corrective interventions to improve sleep across the lifespan confers a protective benefit to cognitive aging.

The study by Cohen *et al.* (2023) attempts to bridge these areas of research by investigating whether sleep plays a moderating role in the effect of aging on cognitive performance. In particular, the authors strive to identify sensitive periods during which sleep disruptions may maximally impact cognition. To this end, the authors examined a large sample with ages ranging from 36.0 to 89.8 who were administered the Pittsburgh Sleep Quality Index (PSQI), the Crystallized Cognition Composite and Fluid Cognition Compositive from the NIH Toolbox, the Trail Making Test (TMT), and the Ray Auditory Verbal Learning Test (RAVLT). Poor sleep, as measured by the PSQI, was related to worse performance on TMT-B but not other cognitive measures. Linear age was associated with poorer performance on all cognitive measures except crystalized cognition, consistent with established trends in cognitive aging. The authors additionally found that there was an interaction effect between linear age and PSQI on crystallized cognition; there was also an interaction effect between quadratic age and PSQI on crystallized cognition and TMT-B scores. The authors posit that the age at which maximum impact of sleep on TMT-B and crystalized cognition can be determined based on these data.

Cohen *et al.* (2023)'s paper has strengths in their data collection including a large sample of diverse age as well as scores on multiple domains of cognitive functioning. The study has important limitations, however, that warrant cautious interpretation of the findings. The associations reported, while statistically significant, were not strong or consistent enough to definitively determine the age-specific risk of reduced sleep quality for cognitive performance without further testing and replication. Additionally, the PSQI, while a well-validated measure of sleep quality, offers us only a snapshot of sleep functioning ("in the past month") that may not reflect broader sleep quality over the lifespan given the high rates of individual sleep variability (Dillon *et al.*, 2015). This measure also fails to account for medical sleep disorders that may impact sleep in an aging population, such as OSA and RLS, that could independently contribute to variability on cognitive performance measures. The data in this study confirm previous findings that both age and sleep can be related to performance on cognitive measures and teases the possibility of unraveling the question of whether specific life stages are more sensitive to the effects of sleep on cognition. These data provide an excellent starting point in posing this question; however, future within-subject measures of sleep and cognition would be better positioned to provide additional insight into this phenomenon and control for the multiple associated variables affecting outcomes. This highlights the challenges of addressing the research question given the interrelatedness of all three areas of interest, and the lack of longitudinal data demonstrating change in sleep and cognition as it occurs.

The interaction effects across sleep quality, aging, and cognition will be familiar to readers of *International Psychogeriatrics*, including a recent thematic focus on the topic (Jeste, 2020). The study by Cohen *et al.* (2023) seeks to investigate the potential for sensitive age ranges in which sleep differentially affects cognition. A similar study of sleep quality in adults and older adults (Siddarth *et al.*, 2021), also published in *International Psychogeriatrics*, found that PSQI scores were significantly associated with higher rates of subjective memory complaints and lower performance on measures of sustained attention, but were not associated with other cognitive abilities, including TMT performance, simple attention, or memory. In contrast, the study by Cohen *et al.* (2023) found that main effects of PSQI scores were associated with worse performance on TMT Part B alone; in addition, they found a curvilinear interaction between PSQI and age on TMT Part B performance and both a linear and curvilinear interactions between PSQI and age on crystallized cognition. Taken together, the concurrent effects of sleep quality and age on adult cognition have yet to demonstrate a reliable pattern of findings, despite hinting at the possibility of sensitive age ranges at which disrupted sleep may differentially affect cognition. Other studies from *International Psychogeriatrics* underscore the importance of sleep and aging on cognition, such as Kohn *et al.* (2020), who found disrupted sleep to be a stronger predictor of concurrent cognitive impairment than measures of metabolic syndrome, cellular inflammation, and depression. Therefore, despite our caution on making inferences from the data presented by Cohen *et al.* (2023), the findings demonstrate a need for further research in this area.

Future research is needed to help to clarify the interacting effects across sleep quality, natural aging, and cognitive performance, and the possibility of circumscribed age ranges in which risks of sleep disruption have greater affects on cognition should be explored. Cohen *et al.* (2023) have provided initial exploratory findings that warrant further analysis through replication with more comprehensive analytical techniques to better differentiate several interrelated factors informing the impact of sleep quality on cognition over the life course. This is a worthwhile area of study that would advance our understanding of the utility of implementing sleep-specific interventions to curb the impacts of sleep quality on cognitive performance in specific age groups. Existing data, however, broadly reinforce the neuroprotective effects of sleep across the lifespan, indicating that maintenance of sleep quality is a worthwhile aim regardless of the existence of sensitive age ranges.

## Conflicts of interest

None.

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