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Associations of objective and subjective sleep disturbance with cognitive function in older men with comorbid depression and insomnia

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ABSTRACT

Objectives: To examine whether poor objective and subjective sleep quality are differentially associated with cognitive function.
Design: Cross-sectional.
Setting: Participants were recruited from primary and secondary care, and directly from the community, in Sydney, Australia.
Participants: The sample consisted of 74 men 50 years and older (mean [SD], 58.4 [6.2] years), with comorbid depression and above-threshold insomnia symptoms, participating in a trial of online cognitive behavioral therapy for insomnia.
Measurements: Insomnia severity and depression severity were assessed via self-report. Objective sleep efficiency and duration were measured using actigraphy. Objective cognitive function was measured using 3 subtests of a computerized neuropsychological battery.
Results: Poor objective sleep efficiency was associated with slower reaction time ($r = -0.249$, $P = .033$) and poorer executive functioning (odds ratio, 4.14; 95% confidence interval, 1.35-12.69), but not memory. These associations remained after adjusting for age, education, depression severity, cardiovascular risk, and medication. Subjective sleep quality was not related to cognitive function.
Conclusions: Among older men with depression and insomnia, objectively measured poor sleep efficiency may be associated with worse cognitive function, independent of depression severity. Objective poor sleep may be underpinned by neurobiological correlates distinct from those underlying subjective poor sleep and depression, and represent a potentially effective modifiable mechanism in interventions to improve cognitive functioning in this population. This supports the use of objective measures of sleep in diagnostic assessments and care.
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Introduction

For people with a range of mental disorders, cognitive functioning is associated with quality of life.[1,2] Both depression and insomnia are related to impairment in some cognitive domains,[3,4] for example, memory and executive function. This suggests that those with the commonly seen comorbidity of these 2 conditions may experience particular cognitive dysfunction.

Cognitive functioning in insomnia

A recent meta-analysis of 24 studies investigating cognitive function in adults with insomnia found impairments of small-to-moderate magnitude in working memory, episodic memory, some facets of executive functioning, and self-reported impairment in cognitive functioning compared with those without insomnia.[3] Some evidence suggests that gender may moderate the insomnia-cognition relationships, with

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men being particularly susceptible to cognitive impairment.[5] Greater subjective insomnia severity may also be related to worse cognitive impairment among those with insomnia, although related research is scarce and inconclusive.[6,7]

Subjective vs objective sleep disturbance

The diagnosis of insomnia is based on subjective sleep-related complaints. Therefore, possible differences in cognitive function between those with insomnia with objectively identified poor sleep, and those with objectively "normal" sleep (paradoxical insomnia), have rarely been addressed.[8,9] Those with insomnia and short sleep duration have been found to show impairment in processing speed, set switching, and visual memory, relative to healthy controls and those with paradoxical insomnia.[10]

Cognitive functioning and sleep disturbance in depression

Impaired cognitive function is also observed in depression[4,11] and is related to broader functional outcomes such as disability[12] and employment.[3] Greater depression severity is associated with greater cognitive impairment.[14] Furthermore, such impairment is a risk marker for chronicity of depression[15] and progression to dementia[11] in middle-aged and older adults.

In addition to sharing an association with cognitive impairment, sleep disturbance and depression have a bidirectional longitudinal association,[16] with each being a risk for the other. In the few published studies investigating whether sleep problems relate independently to cognitive functioning in depression, sleep disturbance has generally been assessed subjectively: for example, in depressed older adults, self-reported late insomnia was associated with worse cognitive function independent of depression severity.[17] In the one study measuring sleep objectively (via actigraphy), in a clinical sample of older patients with mild depressive symptoms, objectively poor sleep (ie, sleep efficiency and time awake after sleep onset) was independently associated with slowed processing speed, and poorer verbal fluency, memory, and executive functioning.[18] As depression and insomnia are also predictive of future cognitive decline,[11,19] it is of particular interest to determine what modifiable factors underpin cognitive function in populations experiencing this common comorbidity. We aimed to test the hypotheses that the severity of objective and/or subjective sleep disturbance is associated with cognitive function in older men with comorbid depression and insomnia, and that this association is robust to adjustment for potential confounding, including depression severity.[14]

Participants and methods

Participants

Men 50 years and older were recruited from the community and local primary and secondary care providers to participate in a randomized controlled trial of an online intervention for insomnia in depression.[20] This was the result of a specific male depression clinical research funding stream. One hundred fifty-six potential participants initially completed an online and telephone screening process. For inclusion, they were required to score at least 8 on the Quick Inventory of Depressive Symptomatology Self Report[21] and 8 on the Insomnia Severity Index (ISI),[22] not meet the criteria for restless leg syndrome using the Cambridge-Hopkins RLS short-form diagnostic questionnaire,[23] and not be at high risk for sleep apnea assessed by the Berlin Questionnaire.[24] Other exclusion criteria included a history of (hypo)manic episodes, current substance dependence, rotating shift work with overnight shifts, or recent transmeridian travel with insufficient time to adjust. After this initial screening process, participants underwent a clinical assessment with a psychiatrist and, for inclusion, were required to meet *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) criteria for a current major depressive episode and/or dysthymia using the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders for *DSM-IV*,[25] and score at least 24 on the Mini Mental State Examination,[26] indicating unlikely dementia. Eighty-seven were randomized into the trial. See Fig. 1 consort diagram for exclusion figures.

Measures

Demographics: Primary, secondary, and tertiary educational history was converted into years of (full-time) education.

Cardiovascular disease was ascertained as self-reported treated heart or cardiovascular disease.

Depressive symptoms: Depressive symptom severity was assessed using the Centre for Epidemiologic Studies Depression Scale (CES-D),[27] a standard, validated, 20-item self-report measure of depressive symptoms, with a range of 0-60.

Subjective sleep disturbance: The ISI is a validated 7-item questionnaire assessing the severity of early, middle, and late insomnia, as well as concern and worry attributed to insomnia symptoms.[22] Responses on a 5-point Likert scale are summed to obtain an insomnia severity score.

Objective sleep disturbance: Ambulatory sleep assessment was conducted for up to 2 weeks using either Actiwatch 2 or Actiwatch Spectrum devices (Philips Respironics, Murrysville, PA), which have been shown to be commensurable.[28] Sleep estimates were obtained using a medium sensitivity threshold with 10 minutes of immobility for sleep onset, in conjunction with manual scoring.[29] Electronic sleep diaries aided in the scoring process, which requires an accurate estimation of bed and rise time. If diary entries were available for at least 5 nights during the monitoring period, only nights with diary entries were analyzed. If fewer than 5 diary entries were completed, all valid nights of actigraphy recording were included. Sleep efficiency (time asleep/time in bed) and total sleep duration were calculated by computing a weighted average such that weekday estimates accounted for 5 of 7 of the total value and weekend estimates the remainder. In line with previous practice[10] and based on nonlinearity and strength of associations with cognitive function in the current sample, objective poor sleep efficiency was defined as average nightly sleep efficiency of less than 80% and objective short sleep duration as less than 6 hours of average total sleep time.

Cognitive functioning: The Cambridge Neuropsychological Test Automated Battery (CANTAB) is a computerized neuropsychological test battery.[30] The parallel versions of the reaction time inventory (RTI; 5-choice; an assessment of mental processing speed and reaction time), intra-extra dimensional set shift (IED; an assessment of set-shifting—an executive function), and paired associates learning (PAL; a measure of visual memory) were assessed. The cognitive functions these tasks assess show impairment in both insomnia and depression.[3,4] Variables of interest included reaction time in milliseconds for the RTI (5-choice trial), IED total errors, and PAL errors (6-shapes trial). Scores from failed test attempts are incomparable with those of completers and were excluded from the analysis. During neuropsychological assessment, participants were also asked about recent cognitive complaints (clarified as referring to problems with memory, attention, concentration, or things of that nature), as is commonly done in clinical practice as a screen. Responses were coded yes (1) or no (0) to provide a simple binary measure of subjective cognitive impairment.

Procedure

After the screening and written informed consent process, assessment was conducted over 2 visits. At visit 1, a psychiatrist conducted a

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