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Research report

Sleep disturbance relates to neuropsychological functioning in late-life depression

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ABSTRACT

Background: Sleep–wake disturbance in older people is a risk factor for depression onset and recurrence. The aim of this study was to determine if objective sleep–wake disturbance in late-life depression relates to neuropsychological functioning.
Methods: Forty-four older patients with a lifetime history of major depression and 22 control participants underwent psychiatric, medical and neuropsychological assessments. Participants completed self-report sleep measures, sleep diaries and wore wrist actigraphy for two weeks. Outcome measures included sleep latency, the number and duration of nocturnal awakenings and the overall sleep efficiency.
Results: Patients with depression had a greater duration of nocturnal awakenings and poorer sleep efficiency, in comparison to control participants. Sleep disturbance in patients was associated with greater depression severity and later ages of depression onset. It also related to poorer psychomotor speed, poorer verbal and visual learning, poorer semantic fluency as well as poorer performance on tests of executive functioning. These relationships largely remained significant after controlling for depression and estimated apnoea severity.
Limitations: This sample had only mild levels of depression severity and results require replication in patients with moderate to severe depression. The inclusion of polysomnography and circadian markers would be useful to delineate the specific features of sleep–wake disturbance that are critical to cognitive performance.
Conclusions: Sleep–wake disturbance in older patients with depression is related to neuropsychological functioning and to later ages of illness onset. This study suggests that common neurobiological changes may underpin these disease features, which may, in turn, warrant early identification and management.

1. Introduction

Depression in older people is associated with neuropsychological deficits in the fronto-subcortical circuitry including psychomotor speed, executive functioning, learning and memory (Naismith et al., 2003, 2006). Of concern, these deficits often persist despite antidepressant treatment (Devanand et al., 2003) or adequate symptom resolution (Dahabra et al., 1998) and are predictive of poor prognosis including progression to dementia (Steffens et al., 2007). There is therefore a need to identify modifiable risk factors for cognitive decline and in this regard, sleep and circadian (sleep–wake) disturbance may be relevant.

A convergence of literature now highlights the critical role of sleep for mood, cognition, overnight memory consolidation and neurogenesis (Meerlo et al., 2009; see review by Naismith et al.,

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2011). Indeed, clinical and community based data suggests that sleep disturbance is a risk factor for depression onset and recurrence in older people (Buysse, 2004; Cho et al., 2008), and in healthy older people sleep disturbance is associated with cognitive decline both cross-sectionally (Oosterman et al., 2009) and longitudinally (Cricco et al., 2001). In clinical samples with late-life depression, insomnia is a common complaint. It may be manifested by difficulties falling asleep, frequent nocturnal awakenings, and early morning wakefulness (Benca and Peterson, 2008; Buysse, 2004) and may also be predictive of treatment resistance (Dew et al., 1997). More recent studies in patients with moderate to severe depression have suggested a link between late insomnia (i.e., early morning awakening) and reduced performance on tests of memory and semantic fluency (Naismith et al., 2009b). Late insomnia has also been associated with later ages of depression onset (Naismith et al., 2009b), a clinical feature that often reflects underlying cerebrovascular disease (Hickie et al., 1995). Overall, this research suggests that sleep–wake disturbance, cognitive decline and late-life depression may share common neurobiological underpinnings. However, to-date, no known studies have used objective measures to specifically examine these inter-relationships.

Actigraphy is an acceptable objective method of measuring sleep–wake disturbance. This technology utilises an accelerometer to measure movement during the day and the sleep (rest) interval and is preferential to using self-report measures, particularly for older people with cognitive impairment (Ancoli-Israel et al., 2003; Riemersma-van der Lek et al., 2008). It also does not require the lengthy and costly laboratory-based polysomnographic assessments, which impose a need to adapt to an unfamiliar sleeping environment. In other areas of ageing and neurodegenerative research, this technology has variously been used to examine the sleep–wake system and such studies have shown that actigraphy-defined sleep disturbance is related to cognitive performance (Naismith et al., 2010b; Oosterman et al., 2009), depression severity (Naismith et al., 2010b), symptoms of rapid eye movement sleep behaviour disorder (Naismith et al., 2010c) and is sensitive to circadian-based interventions (Riemersma-van der Lek et al., 2008). Thus, this appears to be a viable method for exploring potential associations between sleep disturbance and underlying disease features (Ancoli-Israel et al., 2003).

This study aimed to determine if actigraphy-defined sleep disturbance is associated with neuropsychological functioning and other clinical features in older patients with a lifetime history of depression. We hypothesised that patients with depression would exhibit greater sleep disturbance than a control group. In accordance with the widely held notion that aberrant fronto-subcortical circuitry underpins major depression and its associated cognitive deficits (Naismith et al., 2009b, 2010a), we further hypothesised that sleep–wake disturbance would be associated with poorer performance on neuropsychological tests that probe fronto-subcortical circuitry, as well as with clinical features including later ages of depression onset.

2. Methods

2.1. Sample

Forty-four participants (age range = 46 to 86 years) meeting criteria for lifetime major depressive disorder were recruited from specialist psychiatry clinics at the Brain & Mind Research Institute, Sydney. Participants were required to be over the age of 45 years and to be stabilised on medication prior to referral. *Exclusion criteria* were: history of stroke; neurological disorder; head injury with loss of consciousness ≥30-minutes; medical condition known to affect cognition (e.g. cancer); other psychiatric illness; Mini-Mental State Examination Score (MMSE)<24 (DePaulo and Folstein, 1978) and/or diagnosis of dementia. Twenty-two control participants (age range = 45 to 68 years) were recruited from the community via local advertisements and were screened according to inclusion and exclusion criteria as well as for history of affective disorder. A full medical history was conducted and included screening for suspected sleep apnoea. Patients also completed the Multivariable Apnea Prediction Index (MAP), an objective measure that takes into account age, gender, and body mass index in addition to physiological measures (Maislin et al., 1995). The MAP predicts the likelihood of having an apnoea–hypopnoea index of greater than 10 events per hour and at a cut-score of 0.5, has excellent predictive capacity for detecting apnoea. According to this score, 11 patients and two controls had suspected sleep apnoea. All participants were required to have adequate English communication skills for neuropsychological assessment, and be willing to wear an actigraphy watch and complete sleep diaries for two weeks. This research was approved by the Human Research Ethics Committee of the University of Sydney. Written informed consent was obtained from all participants.

2.2. Measures

2.2.1. Psychiatric

An Old Age Psychiatrist performed a structured clinical assessment to derive clinical history including psychiatric history, age of depression onset and medication use. Medical burden was recorded using the Cumulative Illness Rating Scale, geriatric version (Miller and Towers, 1991). The affective component of the Structured Clinical Interview for DSM-IV-R Disorders (First et al., 1996) was performed to confirm lifetime and current depression diagnosis. While for descriptive purposes, depression severity was rated using the Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1960), the 30-item Geriatric Depression Scale (GDS) was used for analyses due to the minimal number of somatic items in this scale (Yesavage et al., 1982; score range = 1 to 30). Twenty-four participants had early-onset and 20 patients had late-onset depression (i.e., age of onset after 50 years) and 18 participants met DSM-IV criteria for current major depression at the time of testing. Twenty-five participants were taking antidepressant medications, including twenty who took newer generation antidepressants and five who used tricyclics. Four patients were taking mood stabilisers and three were taking a low dose atypical antipsychotic (Quetiapine). Two patients were taking benzodiazepines regularly and one patient used sedative hypnotics on a *prn* basis.

2.2.2. Cognitive

A neuropsychologist administered a standardised battery of tests that were chosen for their sensitivity to neuropsychological deficits in affective disorders (Naismith et al., 2003,