



Featured Article

Sleep changes without medial temporal lobe or brain cortical changes in community-dwelling individuals with subjective cognitive decline

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Abstract

Introduction: Subjective cognitive decline (SCD) is a risk factor for mild cognitive impairment (MCI) and Alzheimer disease (AD). Although sleep has been shown to be altered in MCI and AD, little is known about sleep in SCD.

Methods: Seventy cognitively normal community-dwelling participants were classified as SCD (32) or controls (38) using the Subjective Cognitive Decline Questionnaire. Sleep was assessed using actigraphy and diaries. FreeSurfer was used for performing medial temporal lobes (MTLs) and brain cortical parcellation of 3T magnetic resonance images. Multiple regression models were used to assess the presence of sleep, MTL, or regional cortical differences between groups.

Results: Objective sleep was disrupted in SCD participants, which showed increased nighttime wakefulness and reduced sleep efficiency. No group differences emerged in subjective sleep or magnetic resonance imaging outcomes.

Discussion: Objective sleep resulted disrupted in community-dwelling SCD, without any subjective sleep or cortical change. Sleep assessment/intervention in SCD might help prevent/delay AD onset.

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Keywords:

Subjective cognitive decline; Sleep; Medial temporal lobe; MRI; Actigraphy; Alzheimer disease; Risk factors

1. Introduction

Alzheimer disease (AD) develops along a continuum that begins with a long, asymptomatic preclinical period (10–20 years), evolves into mild cognitive impairment (MCI), and culminates in clinical dementia [1]. Subjective cognitive decline (SCD), a state in which a subjectively perceived decline in cognition appears in the absence of an objective decline detected by neuropsychological tests, tends to occur at the late phase of preclinical AD and has been therefore recently proposed as a pre-MCI stage [2]. This preclinical condition has been studied for many decades

under a wide nomenclature (see [2]), but only recently the Subjective Cognitive Decline Initiative (SCD-I) working group defined international research criteria and established a common nomenclature for SCD [2]. Because this condition is very common among older adults and increases the risk for developing MCI and AD [3,4], many research studies have focused on SCD, trying to find a linkage between this condition and AD biomarkers.

The relationship between AD and sleep is increasingly apparent. Previous studies have demonstrated that sleep alterations, such as decreased total sleep time and sleep quality, increased nighttime wakefulness, and fragmented sleep are not only highly prevalent in MCI and AD patients [5–7] but also increase the risk for future cognitive decline when present in normal older adults [8,9]. Moreover, sleep

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influences not only cognition (for a review, see [10]) but also several cortical regions early affected by AD pathology, such as the medial temporal lobes (MTLs) [11,12] as well as other cortical regions [13]. The MTL consists of the hippocampus and its adjacent cortices (e.g., entorhinal, parahippocampal and perirhinal) [14]. Differently from other cortical areas, the hippocampal volume is a well-established and validated magnetic resonance imaging (MRI) marker of AD [15], allowing predictions about progression from MCI to AD (for a review, see [16]).

Previous studies have investigated changes in the MTL in SCD, MCI, and AD. Although MCI and AD patients show reliably reduced MTL thickness and volume [17–19], these findings are not as consistent in SCD, with some studies showing group differences between SCD and controls [20–27] and other failing to detect differences in MTL structures [20,27,28].

Few studies to date have assessed sleep in SCD and how it is related to MTL volume/thickness and/or other regional cortical changes. Therefore, the aims of the present study were as follows:

1. To compare objective (actigraphy) and subjective (diary) sleep pattern between community individuals with SCD and matched, noncomplainer controls. We hypothesized that individuals with SCD would show a more disrupted sleep pattern compared to controls.
2. To compare MTL volume/thickness and cortical thickness between SCD and controls. We hypothesized that SCD would display reduced hippocampal volume and/or MTL/cortical thickness compared to controls.
3. To determine if objective sleep outcomes correlated with MTL volume/thickness or regional cortical thickness. We hypothesized that worse sleep outcomes would correlate with reduced hippocampal volume and MTL/brain cortical thickness.

2. Methods

2.1. Participants

Seventy 50- to 76-year-old volunteers (all Caucasians, 48 females) were recruited through advertisements in the region of Abruzzo, Italy.

All participants underwent a screening interview that included a medical and neuropsychological assessment, an actigraphic sleep study, an objective apnea screening, and an MRI scan of the brain. Exclusion criteria were as follows: presence of MCI, dementia, or any other neurodegenerative and/or psychiatric disorders [29]; history of alcohol or any substance abuse [29]; shift working; international travels within the previous 6 months; use of psychotropic and/or sleep medications; diabetes; untreated systemic disorders (e.g., hypertension); vascular problems (detected on MRI FLAIR and/or during the medical anamnesis); usual MRI exclusion criteria; and abnormalities on MRI. None of the

participants self-reported having any sleep disorder (e.g., breathing-related sleep disorders, leg movement disorders).

Participants were assigned to the SCD or control group based on (1) the SCD research criteria [2] that are as follows: normal cognition on standardized cognitive tests accompanied by self-experienced decline in cognitive capacity in comparison with a previously status, unrelated to an acute event and/or another medical/psychiatric condition, and (2) their total score on the Subjective Cognitive decline Questionnaire (SCD-Q score ≥ 7 was classified as SCD, SCD-Q scores < 7 as controls) [30]. The SCD-Q is a novel validated questionnaire that assesses the presence of subjective cognitive decline. It consists of two parts (MyCog and TheirCog): MyCog is filled in by the subject, TheirCog by the subjects' informant. Both parts have identical 24 dichotomous (yes/no) questions assessing decline in memory, language, and executive functions within the last 2 years. The SCD-Q score for both MyCog and TheirCog ranges from 0 to 24, with higher scores associated with greater perceived cognitive changes (cutoff for being classified as SCD = 7). Considering that the confirmation of cognitive decline by an informant is no longer a core feature for SCD research criteria [2], we here used only the MyCog section. Both SCD and control participants underwent to a full neuropsychological assessment (see the following) and scored within normal ranges for age/education level.

Thirty-two (21 females) participants met criteria for SCD and 38 were included as controls (27 females) for the study. MRI was obtained on 61/70 participants (nine excluded due to contraindications).

All participants provided informed consent. The study was approved by the Institutional and Ethical Committee of the University "G. d'Annunzio" of Chieti-Pescara.

Characteristics of the sample are provided in Table 1.

2.2. Neuropsychological and behavioral assessment

All participants underwent a complete neuropsychological assessment. The Mini-Mental State Examination (MMSE) was used as a global cognitive test. Several tests were also used to investigate specific cognitive domains (the Rey's Auditory Verbal Learning Test and the Babcock Story Recall Test for verbal memory, the digit span forward for echoic memory, the Corsi Cube Test for short-term visuospatial memory, the Rey-Osterrieth Complex Figure Test copy and recall for visuospatial skills and long-term visuospatial memory, the Stroop Test, the Trail Making Test A and B for attentional-executive functions, and finally the semantic and phonemic fluency test for language).

The Geriatric Depression Scale (GDS) [31] and the State Trait Anxiety Inventory [32] were administered for measuring depressive and anxiety symptoms, respectively. Finally, the following subjective sleep questionnaires were administered: the Epworth Sleepiness Scale [33] to assess daytime sleepiness, the Pittsburgh Sleep Quality Index [34] to investigate habitual sleep quality, the Insomnia

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