Article published online: 2023-07-06

In the Hands of Hypnos: Associations between Sleep, Cognitive Performance and Financial Capacity in aMCI and Mild AD

Vaitsa Giannouli Magda Tsolaki

Department of Neurology, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece, Greece

Sleep Sci 2023;16:231–236.

Address for correspondence Vaitsa Giannouli, PhD, Aristotle University of Thessaloniki, School of Medicine, Thessaloniki, Greece, Greece (e-mail: giannouliv@hotmail.com; giannouliv@hotmail.com).

Abstract

Objective The aim of this monocentric observational study is to assess whether sleep disorders can predict financial capacity in single-and multiple-domain aMCI (amnestic Mild Cognitive Impairment), mild Alzheimer's Disease (AD), and healthy controls.

Methods Older participants from Northern Greece were examined with several neuropsychological tests, including Mini-Mental State Examination (MMSE), Geriatric Depression Scale (GDS-15), and the Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS). Sleep duration and quality were based on caregiver/family members' reports in the Sleep Disorders Inventory (SDI).

Results These preliminary findings coming from 147 participants indicate for the first time that apart from MMSE, complex cognitive functions, such as financial capacity may be also directly linked to the frequency of sleep-disturbed behaviours as indicated by SDI frequency questions, both in aMCI and mild AD.

Discussion An urgency for further investigation of the neglected sleep factor should be added in financial capacity assessment protocols.

Keywords
- Sleep
- Cognition
- Financial capacity
- aMCI
- mild AD

Introduction

Several studies support that a common finding in people with a diagnosis of Mild Cognitive Impairment (MCI) is the manifestation of sleep disturbances on self-report measures.[1] Patients with amnestic MCI (aMCI), a subtype of MCI when memory loss is the predominant symptom, exhibit primarily circumscribed declarative memory deficits, but still it is an open debate whether sleep is disrupted in the majority of aMCI and whether sleep disruptions contribute to memory impairment, although there is research supporting that sleep changes in aMCI patients contribute to memory impairments by interfering with sleep-dependent memory consolidation.[2] The role of sleep is not systematically investigated in amnestic single-domain MCI (aMCI-SD), the aMCI subtype in which memory is the only impairment, whereas the role of sleep remains confusing in amnestic multiple-domain MCI (aMCI-MD), the subtype that demonstrates impairment in memory and at least one other neuropsychological domain. On the other hand, the relationship between sleep and AD is well-reported, as sleep disturbances are typical symptoms of AD that may precede the other clinical signs of this neurodegenerative disease.[3]

Financial capacity is found to be impaired in vascular dementia,[4] AD,[5] Parkinson's Disease,[6] and aMCI.[7] Although it is considered as one of the complex instrumental activities of daily living,[8] for the first time this study aims to examine in both subtypes of aMCI (aMCI-SD and aMCI-MD), in mild AD

DOI https://doi.org/10.1055/s-0043-1770796.
ISSN 1984-0659.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

patients' as well as in controls, the influence of sleep quality-disturbances as reported by a third person (caregiver/family members) on the elder participants' actual financial capacity performance. Emphasis on aMCI and mild AD is given, as although these are considered two different and distinct diagnoses, aMCI is also considered a transition stage between normal aging and AD, with not a clearly established pattern of financial capacity deficits.[8]

Thus, the objective of this study is to examine sleep disorders and their possible influence on financial capacity performance in older adults with diagnoses of different neurocognitive disorders, including single-domain aMCI, multiple-domain aMCI, mild AD, and healthy controls by corroborating the obtained information by additionally examining their caregivers.

Material and Methods

Participants

In this monocentric observational study, the sample of enrolled participants comprised a total of 147 participants (112 females, 35 males) divided into four groups: 35 non-institutionalized mild AD, 41 single-domain aMCI patients, 41 multiple-domain aMCI patients, and 30 healthy controls (HC).

Procedure

Participants with mild AD and aMCI were recruited from the Memory and Dementia Outpatient Clinic in "G. Papanikolaou" General Hospital, Thessaloniki and controls were recruited from the community. Recruitment took place between June 2013-September 2015. This research has been approved by the Ethics Committee of Aristotle University of Thessaloniki (protocol 2.27/3/2013), and it is conformed to the provisions of the Declaration of Helsinki. Inclusion criteria for the study required that participants should be aged $\geq$65 years (in older to define this a homogeneous group of elderly participants), and have a diagnosis of mild AD or MCI according to the established guidelines from the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association Inc. (NINCDS-ADRDA) and the dementia criteria defined by DSM-V (as examined after the data collection).

The exclusion criteria for all groups included other neurological or psychiatric illness (with an emphasis on the exclusion of depression as the influence of depressive symptomatology on financial capacity has been established in past research in AD and MCI [for a detailed report of the exclusion criteria see [5,6]). Regarding the exclusion of depressive symptomatology, the 15-item Geriatric Depression Scale was used using the culturally appropriate cut-off 6/7 point applied for diagnosing depression in older adults.[9] None of the participants had a score above this cutoff ($M_{GDS\text{-}15}$ =1.79, $SD_{GDS\text{-}15}$ =2.77).

Instruments

Participants received a comprehensive neuropsychological assessment and before entering the study, the four groups of older adults as well as their caregivers/family members provided informed consent to participate. Participants received neuropsychological assessment presented in detail in,[8] using among other neuropsychological tests one that is of paramount importance in the assessment protocols in Greek cultural settings, the Mini Mental State Examination (MMSE) for screening-assessing global cognitive functioning for which a higher score value is related to a higher level of general cognitive status (score range = 0–30 points, cut-off score for normal $\geq$26/30), along with the Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS).[8] LCPLTAS comprises 7 domains, namely basic monetary skills, cash transactions, bank statement management, bill payment, financial conceptual knowledge, financial decision making, and knowledge of personal assets.[8] A cutoff score has been proposed for the Greek older population (corresponding to maximum sensitivity and maximum specificity) with the scores 211 and 154 respectively.[8] The cut-off that optimizes both based on Youden's index is 200 (with range of scores 0 to 212 points).[8]

Additionally, all accompanying caregivers/family members (n = 98 adult children, n = 49 wives/husbands) completed The Sleep Disorders Inventory (SDI), which is an expanded version of one of the items of the Neuropsychiatric Inventory (NPI).[10] The same exclusion criteria, as in the case of elderly (e.g. a history of any psychiatric or neurological diagnosis), were applied to the caregivers/family members. The choice of third sources of information (caregivers/family members without psychiatric symptomatology, who lived with the older participants and slept near to the elderly in the last two weeks of the data collection) instead of self-reports made by the patients/participants is based on the fact that it has been found that older patients with neurocognitive disorders are influenced by overstimations/underestimations, while actigraphy or other sleep tracking was not possible as they attended a day care center. SDI describes the frequency and severity with an emphasis on data regarding only the sleep subscale pertaining to the frequency on a 4-point scale and severity on a 3-point scale of the behavior. Frequency ratings are relative to the past 2 weeks and present values such as 0 = not present, 1 = less than once per week, 2 = 1–2 times per week, 3 = several times per day but less than every day, 4 = once or more per day (every night). Severity ratings has values ranging from 0 = not present, 1 = mild, 2 = moderate, to 3 = marked. Finally, there caregiver distress ratings are also measured (how emotionally distressing is the behaviour?): 0 not at all; 1 = minimally, 2 = mildly, 3 = moderately, 4 = severely, and 5 = very severely/extremely.[10] The SDI is made up of the seven subquestions coming from the NPI sleep disturbance item. More specifically, the questions examine the following: «1) Difficulty falling asleep. 2) Getting up during the night (do not count if the subject gets up once or twice per night to go to the bathroom and quickly falls back to sleep). 3) Wandering, pacing or getting involved in inappropriate activities at night. 4) Awakening you during the night. 5) Awakening at night, dressing, and planning to go out, thinking that it is morning and time to start the day. 6) Awakening too early in the morning (earlier than is his/her

habit). 7) Sleeping excessively during the day».[10] Each of the subquestions represents a separate question with frequency, severity, and caregiver distress rated by the caregiver(s) with respect to the patient-participant for the 2 weeks prior to the neuropsychological assessment (see ►**Table 1** for mean scores per item and total scores).

Data Analysis

Data analysis was performed using the SPSS Statistical Program, version 24.0. Categorical variables were expressed by absolute frequency and quantitative variables by Means and Standard Deviation (SD). To study the correlation between variables, Pearson's as well as Spearman's correlation tests were used. Multivariate regressions were used to evaluate the determinants of LCPLTAS and MMSE. The tests were two-tailed and only applied if the assumptions were met, while values of $p < .05$ were considered statistically significant.

Results

The age of the participants ranged from 65 to 89 years ($M = 69.34$, $SD = 5.34$). There were four groups: 1) thirty-five Greek older adults with a diagnosis of non-institutionalized mild AD (21 women; Mage = 68.48, SD = 2.55; Myears of education = 10.00, SD = 3.74), 2) forty-one single-domain aMCI patients (31 women; Mage =70.51, SD = 5.57; Myears of education = 9.80, SD = 3.98), 3) forty-one multiple-domain aMCI patients (37 women; Mage = 69.80, SD = 5.75; Myears of education = 9.17, SD = 4.38), and 4) thirty healthy controls (HC) (23 women; Mage = 68.10, SD = 6.55; Myears of education = 8.30, SD = 4.48).

Participants consisting the abovementioned 4 groups were similar for age [$F(3, 146) = 1.617$, $p = .188$], gender $\chi^2(1) = 3.506$, $p = .061$, and years of education [$F(3, 146) = 1.114$, $p = .346$].

Pearson's correlations between MMSE and Sleep Severity total score ($r = -.477$, $p < .0001$), MMSE and Sleep Frequency ($r = -.515$, $p < .0001$), and MMSE and Sleep Distress ($r = -.572$, $p < .0001$), were all statistically significant. These correlations were also confirmed by nonparametric Spearman's rho correlations (given that sleep measurements can be measured on an ordinal scale): MMSE and Sleep Severity total score ($r_s = -.222$, $p = .011$), MMSE and Sleep Frequency ($r_s = -.346$, $p < .0001$), and MMSE and Sleep Distress ($r_s = -.257$, $p = .002$), were all statistically significant. In addition to that, regression with total scores for Sleep Severity, Sleep Frequency, Sleep Distress, MMSE, age, and education (in years) as predictors of LCLPTAS are presented. Age and education were included (as both have been found to relate to MMSE and LCPLTAS performance). The same regression was performed for MMSE as dependent variable.

Linear Regression model, "Enter" method indicated that MMSE and Total Sleep Frequency predicted the older participants' LCPLTAS scores ($R = .598$; $R^2 = .358$, $p < .001$)

Table 1 Mean scores Mini Mental State Examination (MMSE), Legal Capacity for Property Law Transactions Assessment Scale (LCPLTAS), and for each of the items for Sleep Frequency, Sleep Severity, and Sleep Distress.

Tests and questions	Diagnosis	Mean	SD
MMSE	aMCI-SD	27.63	1.29
	aMCI-MD	26.39	1.44
	HC	29.13	.43
	mild AD	23.06	3.77
LCPTLAS	aMCI-SD	180.18	29.73
	aMCI-MD	145.65	72.18
	HC	210.70	1.78
	mild AD	103.25	16.30
Sleep 1 Frequency	aMCI-SD	.65	.48
	aMCI-MD	.64	.48
	HC	.63	.49
	mild AD	1.28	.45
Sleep 2 Frequency	aMCI-SD	.62	.49
	aMCI-MD	.64	.48
	HC	.66	.47
	mild AD	1.28	.45
Sleep 3 Frequency	aMCI-SD	.70	.46
	aMCI-MD	.63	.48
	HC	.70	.46
	mild AD	1.25	.44
Sleep 4 Frequency	aMCI-SD	.15	.36
	aMCI-MD	.22	.42
	HC	.06	.25
	mild AD	1.17	.51
Sleep 5 Frequency	aMCI-SD	.30	.46
	aMCI-MD	.54	.50
	HC	.36	.49
	mild AD	1.29	.57
Sleep 6 Frequency	aMCI-SD	.27	.45
	aMCI-MD	.38	.49
	HC	.26	.44
	mild AD	1.17	.51
Sleep 7 Frequency	aMCI-SD	.72	.45
	aMCI-MD	.41	.49
	HC	.73	.44
	mild AD	1.14	.42

(*Continued*)

Table 1 (*Continued*)

Tests and questions	Diagnosis	Mean	SD
Total Sleep Frequency	aMCI-SD	3.46	1.07
	aMCI-MD	3.54	1.39
	HC	3.41	1.15
	mild AD	8.58	2.01
Sleep 1 Severity	aMCI-SD	.90	.30
	aMCI-MD	.65	.48
	HC	.86	.34
	mild AD	1.20	.40
Sleep 2 Severity	aMCI-SD	.68	.47
	aMCI-MD	.38	.49
	HC	.70	.46
	mild AD	1.08	.37
Sleep 3 Severity	aMCI-SD	.12	.33
	aMCI-MD	.20	.40
	HC	.17	.38
	mild AD	1.17	.45
Sleep 4 Severity	aMCI-SD	.67	.47
	aMCI-MD	.38	.49
	HC	.75	.43
	mild AD	2.78	.73
Sleep 5 Severity	aMCI-SD	.65	.48
	aMCI-MD	.44	.50
	HC	.73	.44
	mild AD	2.60	.69
Sleep 6 Severity	aMCI-SD	.12	.33
	aMCI-MD	.15	.36
	HC	.10	.30
	mild AD	2.54	.81
Sleep 7 Severity	aMCI-SD	.65	.48
	aMCI-MD	.46	.50
	HC	.73	.44
	mild AD	2.71	.62
Total Sleep Severity	aMCI-SD	3.86	1.69
	aMCI-MD	2.78	2.20
	HC	4.25	1.64
	mild AD	14.03	2.49
Sleep 1 Distress	aMCI-SD	.67	.47
	aMCI-MD	.39	.49
	HC	.73	.44
	mild AD	2.97	.82
Sleep 2 Distress	aMCI-SD	.35	.48
	aMCI-MD	.51	.50
	HC	.23	.43
	mild AD	2.68	1.02
Sleep 3 Distress	aMCI-SD	.65	.48
	aMCI-MD	.41	.49
	HC	.63	.49
	mild AD	2.60	.77
Sleep 4 Distress	aMCI-SD	.07	.26
	aMCI-MD	.25	.44
	HC	.10	.30
	mild AD	2.60	.65
Sleep 5 Distress	aMCI-SD	.71	.45
	aMCI-MD	.53	.50
	HC	.76	.43
	mild AD	2.80	.86
Sleep 6 Distress	aMCI-SD	.97	.15
	aMCI-MD	.79	.40
	HC	.93	.25
	mild AD	2.51	.78
Sleep 7 Distress	aMCI-SD	.20	.40
	aMCI-MD	.13	.34
	HC	.16	.37
	mild AD	.42	.65
Total Sleep Distress	aMCI-SD	3.64	1.13
	aMCI-MD	3.00	1.78
	HC	3.58	.98
	mild AD	16.60	3.90

Note: amnestic single-domain MCI (aMCI-SD); amnestic multiple-domain MCI (aMCI-MD); Healthy Controls (HC); mild Alzheimer's Disease (mild AD).

(►**Table 2**). Additionally linear Regression model indicated that Total Sleep Severity and Total Sleep Distress predicted the MMSE scores of the patients ($R = .639$; $R^2 = .408$, $p < .001$) (►**Table 2**).

Discussion

Sleep should be regarded as one among other factors that must be included in assessment protocols of financial capacity. Declarative or explicit memory is devoted to processing

Table 2. Results of Enter method multiple regression analyses for Total Sleep Frequency, Total Sleep Severity, Total Sleep Distress, and relevant demographic factors (i.e., age, education) predicting MMSE and LCPLTAS.

Variables	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
(Constant)	29.988	2.898		10.347	<.001
Total Sleep Distress	-.593	.119	-1.199	-4.992	<.001
Total Sleep Frequency	-.286	.171	-.251	-1.673	.097
Total Sleep Severity	.521	.159	.859	3.277	.001
Age	-.017	.039	-.032	-.448	.655
Education (in years)	-.020	.052	-.028	-.387	.700
Dependent Variable: Mini-Mental State Examination (MMSE)					
Variables	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**p**
	B	**Std. Error**	**Beta**		
(Constant)	45.048	77.591		.581	.563
Total Sleep Distress	-2.497	2.546	-.277	-.981	.329
Total Sleep Frequency	-8.375	3.337	-.401	-2.510	.013
Total Sleep Severity	3.515	3.231	.317	1.088	.279
Age	.176	.755	.018	.234	.816
Education (in years)	-.153	1.008	-.012	-.152	.879
MMSE	5.507	1.784	.301	3.088	.003
Dependent Variable: Legal Capacity for Property Law Transactions Assessment Scale (LCPTLAS)					

of names, dates, places, facts, and events,[8] all of which are necessary for financial decision-making. Severity and Distress are predictors of MMSE performance, but only the reported Total Sleep Frequency score seems to predict financial capacity. This negative coefficient suggests that as the independent variable increases (the frequency of sleep disturbances), the dependent variable tends to decrease (financial capacity).

The above confirm previous findings for a noticeable financial incapacity in mild AD (lower than 2.5 SDs performance on LCPLTAS compared to normal),[8,11–13] but also both aMCI subtypes show deficits compared to controls.[8,14–17] An interesting finding is that statistically significant differences exist in LCPLTAS performance between aMCI-SD (who show higher financial capacity) and aMCI-MD. This difference between the two aMCI subtypes, is supported by the reported frequency of sleep disturbances (with more frequent sleep disturbances for the aMCI-MD), but not by the total scores for reported sleep severity and sleep distress. The novelty of this study is that financial capacity can be predicted not only by MMSE scores (as has already been supported[4–8]), but also by the frequency of sleep disturbances.

This study has several strengths as the demographic homogeneity of the sample, but a major limitation is the small sample size, the imbalance of women and men, with women being overrepresented, and the lack of a detailed sleep examination with relevant questionnaires and scales, apart from SDI. In addition to that, several factors that may influence (conjointly with sleep disorders) financial capacity, such as literacy,[14] affect,[18] perceived frailty,[19] vascular risk factors[16] and genetic factors (e.g. APOE ε4 gene)[11] could also be included in assessments in longitudinal research designs.[15] Future research could rely not only on self-reported sleep problems or problems reported by caregivers/family members, but also on neurophysiological sleep lab data.

Description of Authors' Roles

VG designed the study, collected the data, and wrote the paper. MT supervised the study.

Acknowledgments Including Sources of Support

None.

Conflict of Interest Declaration

None.

References

1 Naismith SL, Mowszowski L. Sleep disturbance in mild cognitive impairment: a systematic review of recent findings. Curr Opin Psychiatry 2018;31(02):153–159

2 Westerberg CE, Mander BA, Florczak SM, et al. Concurrent impairments in sleep and memory in amnestic mild cognitive impairment. J Int Neuropsychol Soc 2012;18(03): 490–500

3 Brzecka A, Leszek J, Ashraf GM, et al. Sleep disorders associated with Alzheimer's disease: A perspective. Front Neurosci 2018;12:330
4 Giannouli V, Tsolaki M. Vascular dementia, depression and financial capacity assessment. Alzheimer Dis Assoc Disord 2021;35 (01):84–87
5 Giannouli V, Tsolaki M. Mild Alzheimer Disease, financial capacity, and the role of depression: Eyes wide shut? Alzheimer Dis Assoc Disord 2021;35(04):360–362
6 Giannouli V, Tsolaki M. Depression and financial capacity assessment in Parkinson's disease with dementia: Overlooking an important factor? Psychiatriki 2019;30(01):66–70
7 Giannouli V, Tsolaki M. Unraveling Ariadne's thread into the labyrinth of aMCI: Depression and financial capacity. Alzheimer Dis Assoc Disord 2021;35(04):363–365
8 Giannouli V, Stamovlasis D, Tsolaki M. Exploring the role of cognitive factors in a new instrument for elders' financial capacity assessment. J Alzheimers Dis 2018;62(04):1579–1594
9 Fountoulakis KN, Tsolaki M, Iacovides A, et al. The validation of the short form of the Geriatric Depression Scale (GDS) in Greece. Aging (Milano) 1999;11(06):367–372
10 Tractenberg RE, Singer CM, Cummings JL, Thal LJ. The Sleep Disorders Inventory: an instrument for studies of sleep disturbance in persons with Alzheimer's disease. J Sleep Res 2003;12 (04):331–337
11 Giannouli V, Tsolaki M. APOE ε4 allele and financial capacity performance in Mild Alzheimer's Disease: A pilot study. J Alzheimers Dis Rep 2021;5(01):93–97
12 Giannouli V, Tsolaki M. Legal capacity of the elderly in Greece. Hell J Nucl Med 2014;17(Suppl 1):2–6
13 Giannouli V, Tsolaki M. Financial incapacity of patients with mild Alzheimer's Disease: What neurologists need to know about where the impairment lies. Neurol Int 2022;14(01): 90–98
14 Giannouli V, Tsolaki M. Financial capacity and illiteracy: Does education matter in amnestic Mild Cognitive Impairment? J Alzheimers Dis Rep 2021;5(01):715–719
15 Giannouli V, Stamovlasis D, Tsolaki M. Longitudinal study of depression on amnestic mild cognitive impairment and financial capacity. Clin Gerontol 2022;45(03):708–714
16 Giannouli V, Tsolaki M. Liberating older adults from the bonds of vascular risk factors: What is their impact on financial capacity in amnestic mild cognitive impairment? Psychiatry Clin Neurosci 2022;76(06):246–250
17 Giannouli V, Tsolaki M. A neglected drama for elders: Discrepancy between self-perception and objective performance regarding financial capacity in patients with cognitive deficits. Psychol Thought 2015;8(02):142–147
18 Giannouli V, Tsolaki M. Is negative affect associated with deficits in financial capacity in nondepressed older adults? A preliminary study. J Affect Disord Rep 2022;•••:100391
19 Giannouli V. Does higher prevalence of frailty in Greek older community-dwelling women also relate to higher prevalence of perceived financial exploitation? A new question to ponder upon. J Frailty Aging 2022;11(04):436–437

