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Sleep, Sleepiness, and Memory

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Abstract

Objective To evaluate the relationship between sleep and sleepiness with memory complaints.

Materials and Methods Patients who were submitted to polysomnography between May and September of 2022 and answered the prospective and retrospective memory questionnaire and the Epworth sleepiness scale were included, respectively. Data were entered into an Excel spreadsheet and converted to a file compatible with the SPSS software.

Results The sample consisted of 98 subjects, 62.2% male, mean age of 45.9 years, 73.4% overweight, 54.1% with comorbidities, and 51% with excessive sleepiness. There was a significant difference in sleep efficiency, respiratory disturbance index (RDI), slow wave sleep (SWS), and rapid eye movement (REM) sleep for the group with comorbidities; in latency to sleep and SWS between genders; and in RDI for the body mass index group. No correlation between RDI and memory could be identified, but there were statistically significant correlations between REM and sleep efficiency; RDI and REM sleep; RDI and SWS; SWS and sleep efficiency; and sleep efficiency and latency to sleep onset. Older adults performed better on memory tests when total sleep time (TST) is longer than 5 hours and excessive daytime sleepiness is related to complaints of prospective, retrospective, and total memory.

Keywords

- memory
- ► polysomnography
- sleepiness

Conclusion Elderly people with TST longer than 5 hours have a better memory. Although a correlation between RDI and memory was not observed, a correlation between excessive daytime sleepiness—one of the main symptoms of patients with sleep disorders—and memory was.

Introduction

For a long-lasting memory to be formed, it is necessary that the acquired memory, which is labile and susceptible to interference, become stable. This process, called consolidation, involves protein synthesis and requires several neurotransmitters and signaling pathways, but not only that: stabilization of memories happens through integration among brain structures, so the recent literature introduces

the concept of systems-level consolidation. The reactivation of memory traces, adaptive forgetting of superfluous or redundant details, and retrieval of generalities to integrate existing information and guide future behavior are part of this theory, and necessarily depend on periods in which our body is resting.²

There is no single, constant state of sleep, and it is certainly not a period of inactivity. In a typical night's sleep, the first half is mostly non-REM sleep, and the second half is

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mostly REM (rapid eye movement). Furthermore, non-REM sleep is subdivided into stages, of which stages 3 and 4 are grouped into what is called slow wave sleep (SWS), or N3.³

Sleep is known to be characterized by a brain state that optimizes memory consolidation: during SWS, newly encoded information in the hippocampus is repeatedly reactivated and redistributed to cortical structures that store long-term memory, while during REM sleep these memories are stabilized.⁴ Newly acquired memory is not instantaneously stable: from 3 to 8 hours after acquisition the memory is labile, that is, it is sensitive to internal and external interferences.¹

Prospective memory involves remembering to do something at a certain time in the future and is often necessary in everyday life. In both prospective and retrospective memories—evoking or remembering past events—sleep has active and passive functions. By preventing interference, a characteristic of the waking period, it plays a passive role in consolidation. However, it is also during sleep that physiological processes that reinforce the mnemonic trace are initiated, characterizing its active role in the consolidation of memories, especially those of a prospective nature.

Obstructive sleep apnea (OSA) is the most common sleep disorder and a chronic systemic condition, ⁷ characterized by total or partial airway obstruction during sleep that courses with excessive daytime sleepiness (EDS) and affects executive functions in the individual. ⁸ Patients with this disorder show significant impairment in episodic, procedural, and working memory when compared with a control group. ⁹

For the diagnosis of OSA and other sleep disorders, the test of choice is polysomnography, which allows the assessment of the number of obstructive events during sleep and provides indices such as total sleep time (TST), sleep efficiency, sleep onset latency, and the percentages that an individual remains in each sleep stage. Studies show that extremes of TST—below 5 hours or above 9 to 10 hours—increase the risk of mortality from cardiovascular causes. ¹⁰ Furthermore, in both young and old people it is associated with worse performance on tests of attention. ¹¹

As for EDS, it is defined as an increased propensity to sleep during periods of wakefulness, ¹² and can be assessed subjectively using the Epworth sleepiness scale (ESS), developed in 1991. ¹³ One of the main causes of EDS is insufficient sleep, but it can also be secondary to the use of medications, psychiatric illnesses, and sleep disorders; in the latter case, OSA, narcolepsy, and insomnia stand out. ¹⁴ Patients with OSA and EDS, for example, are more likely to have other symptoms, such as memory loss. ⁷

Considering the importance of sleep for the formation of memories, the presence of EDS in patients with sleep disorders, and the possible association of this symptom with memory complaints, this study aimed to describe the profile of patients who undergo polysomnography examination; to evaluate the different parameters of this exam according to the characteristics of the patients; to verify the correlation between these parameters and between memory complaints and respiratory disturbance index (RDI); to investigate whether TST in the elderly and nonelderly is related to

memory, and to analyze the relationship between EDS and memory.

Materials and Methods

Participants

We conducted a crossectional study with patients who underwent polysomnography exams between May and September 2022 in a private clinic in the city of Passo Fundo – RS, Brazil, after approval of the Research Ethics Committee of the Federal University of Fronteira Sul (report number 5.381.543). The subjects scheduled the exam by medical recommendation, and, on the night of the test, the research team approached the patients in the clinic's waiting room, explained the procedure and the objective of the study. In case of acceptance, they were invited to read and sign the informed consent form.

The only inclusion criterion is that patients should be 18 years of age or older. Incorrectly filled-out forms or those with missing information were excluded. Furthermore, the diagnosis of diseases related to cognitive decline also led to exclusion.

Data Collection Sheet

After they agreed to participate in the research, the first step consisted of answering a short questionnaire. Information regarding patients' age, sex, weight, and height were collected for later BMI calculation, chronic diseases, and medications in use.

Epworth Sleepiness Scale (ESS)

Afterwards, the patients were asked to fill out the daytime sleepiness scale. The ESS comprises 8 situations with 4 possible answers, regarding patients' chance of dozing: 0–none; 1–small; 2–moderate; and 3–high. The summed score was categorized into normal (0–6 points), borderline (7–9 points), or excessive daytime sleepiness (10–24 points).

Prospective and Retrospective Memory Questionnaire (PRMO)

After the ESS, patients answered the questionnaire regarding memory complaints. The PRMQ was created by Smith et al. ¹⁵ and the Portuguese version was applied in this study. ¹⁶ This instrument consists of 16 questions about everyday memory problems, divided into prospective (questions 1, 3, 5, 7, 10, 12, 14, and 16) and retrospective memory (questions 2, 4, 6, 8, 9, 11, 13, and 15). Patients were instructed to respond according to a graduated scale of 1 to 5, with 1 being never; 2–rarely; 3–sometimes; 4–frequently; and 5–very frequently. The scores were summed separately according to memory type and were converted into *t*-scores by means of the freely distributed program prmqscor.exe.

Polysomnography

Once the questionnaire and tools were filled out, the patients were left in care of a polysomnography technician, who proceeded with preparation for the test. This examination is performed during the night, monitoring sleep and

providing quantitative parameters that allow doctors to evaluate the quality of sleep and diagnose related disorders. For this study, we focused on the sleep efficiency parameter, obtained by dividing the time an individual slept by the total time they stayed in bed, in percentage; sleep onset latency, the time (min) it took for the individual to start sleeping; the percentage of REM sleep, the percentage of SWS or N3 sleep, the TST in minutes, and the RDI, an index that corresponds to the sum of respiratory events: apneas + hypopnea + respiratory effort-related sleep arousal (RERA).

Statistical Analysis

The data were entered into an Excel (Microsoft Corp. Redmond, WA, USA) spreadsheet program and were converted into a file compatible with the Statistical Package Social Sciences (SPSS Inc. Chicago, IL, USA) software, version 18. Relative frequencies were calculated for nominal categorical variables and, in the case of numerical variables, mean and standard deviation (SD) were calculated. The variables were subjected to the Shapiro-Wilk test to assess normality of the data and the Levene test for homogeneity of variance. The Student t-test was used to check the difference in polysomnographic parameters according to age (under 60 and equal to or older than 60), sex (male or female), BMI (less than 25 and greater or equal to 25), and comorbidities (yes or no), as well as to evaluate the memory of elderly and nonelderly patients on the TST. The Spearman correlation was used to analyze the correlation between RDI and memory, as well as to assess the correlation between polysomnography parameters. The Kruskal-Wallis test was used to check the relationship between SDE and memory. Data were considered statistically significant when p < 0.05.

Results

- ► Table 1 presents the profile of patients who underwent the polysomnography examination between May and September 2022. Of the 101 patients interviewed, only 3 were excluded from the study; 1 had dementia and 2 had a diagnosis of Parkinson disease. The majority were male, overweight, with comorbidities, and excessive daytime sleepiness. Among the chronic diseases, the one most reported was hypertension (56.6%), followed by depression and anxiety (18.9%), diabetes mellitus (13.2%), and respiratory diseases (11.3%).
- ► Table 2 shows the different parameters obtained by polysomnography according to the characteristics of the patients. For age, no statistically significant differences were observed between the elderly and those under 60years-old. Considering the BMI variable, the RDI was increased in overweight patients (39.65 vs. 18.93%, p < 0.001). The RDI was also statistically different between patients with and without comorbidities (34.45 vs. 26.21%, p < 0.05). In fact, this variable showed the greatest differences between the polysomnographic parameters, with the group without comorbidities showing a higher percentage of SWS (25.09 vs. 18.32%, p < 0.05), REM sleep (12.35 vs. 9.61%, p < 0.05) and sleep efficiency (79.22 vs. 69.46%, *p* < 0.001). With respect to

Table 1 Characterization of a sample of patients submitted to polysomnography (n = 98).

	% or mean \pm SD
Sex	
Male	62.2
Female	37.8
Age	45.9 ± 14.8
ВМІ	
Low weight	2
Eutrophic	24.5
Overweight	37.8
Obesity	35.6
Comorbidities	
Yes	54.1
No	45.9
Daytime sleepiness	
Normal	29.6
Borderline	19.4
Excessive	51.0

Abbreviations: BMI, body mass index; SD, standard deviation. Notes: Age was expressed as mean \pm SD. Other variables were represented as relative frequency (%).

sex, the latency to sleep onset (36.50 vs. 18.90 min; p < 0.001) and percentage of SWS was higher in women (25.16 vs. 19.37%, p < 0.05).

The patient sleep analysis in **-Table 3** shows that sleep efficiency is correlated with REM sleep (rs 0.307; p < 0.05), sleep onset latency (rs -0.544; p < 0.001), and SWS (rs 0.232; p < 0.05). Furthermore, the RDI is correlated with REM sleep (rs -0.273; p < 0.05) and SWS (rs -0.409; p < 0.001).

As shown in **►Table 4**, there was no correlation between RDI with the different t-scores for retrospective memory, prospective memory, and the total t-score.

► Figure 1 presents the results about TST for the elderly and nonelderly and its impact on the memories of these individuals. Patients under 60 had no significant difference in total t-scores, nor for retrospective and prospective memory. However, for patients older than 60 years, sleeping more than 5 hours per night significantly impacts self-reported memory: seniors with low TST had a mean total t-score of 52.17 and seniors with TST over 5 hours had a mean of 62.00. A similar result was obtained in the t-score analysis for retrospective memory (47.00 vs. 61.13).

It can be seen in **►Table 5** that excessive daytime sleepiness is related to worse performances on the memory questionnaire for total (H = 16.99, p < 0.001), prospective (H = 15.00, p < 0.001), and retrospective (H = 16.06, p < 0.001)p < 0.001) memories in the group under 60 years of age, and for those without comorbidities [(H = 12.05, p < 0.05), (H = 11.60, p < 0.05), and (H = 11.89, p < 0.05), respectively]. These results were not confirmed for the elderly. As of the patients with comorbidities, there was a significant

 Table 2
 Polysomnographic parameters according to the profile of the patients.

	Age (years)			BMI (kg/m²)			Sex			Comorbidities	se	
	<60 (n = 83)	≥ 60 ($n = 15$)	<i>p</i> -value	< 25 (n = 26)	> 25 (n = 72)	<i>p</i> -value	M (n=61)	F (n = 37)	<i>p</i> -value	Yes (n = 53)	No (n = 45)	<i>p</i> -value
ficiency	74.83	69.03	90.0	75.76	73.12	0.20	74.76	72.27	0.20	69.46	79.22	<0.001
atency	24.95	24.68	0.48	28.37	23.54	0.20	18.90	36.50	<0.001	25.46	24.22	0.40
EM	11.20	9.20	0.37	11.96	10.41	0.19	11.07	10.50	0.37	9.61	12.35	<0.05
WS	21.30	21.88	0.87	24.17	20.25	0.09	19.37	25.16	<0.05	18.32	25.09	<0.05
DI	32.24	41.28	0.15	18.93	39.65	<0.001	37.59	26.96	0.61	34.45	26.21	<0.05

Abbreviations: RDI, respiratory disturbance index; REM, rapid eye movement; SWS, slow wave sleep; F, feminine; M, masculine.

difference only in the assessment of total memory (H = 6.20, p < 0.05).

Discussion

Analysis of patients profile submitted to polysomnography showed that the mean age is 45.9 years, 73.4% are overweight, and 62.2% are male. These data are consistent with another Brazilian study, ¹⁷ in which the mean age was 44.6 years, with the majority being overweight (82.72 of men and 71.21% of women), and 59.13% male.

The group with comorbidities had a reduced percentage of sleep efficiency and REM sleep. Additionally, the SWS was below the 20% considered normal, 18 and the RDI was increased. Chronic diseases are often associated with sleep disorders; 19 therefore, the altered polysomnographic parameters in this group may be caused by a primary sleep disorder or by the adjacent clinical conditions, including situations that cause emotional distress such as anxiety and depression, drug treatments, and others. In our study, almost 20% of the patients with comorbidities were diagnosed with anxiety or depression, which may have been determinant to verify a significant reduction of REM sleep in comparison with the group without comorbidities, since the network of structures involving the amygdala, hippocampus, and medial prefrontal cortex regulates this stage of sleep and its dysfunction is related to depression.²⁰

As for gender, women have a higher percentage of SWS and longer sleep onset latency than men. Furthermore, men with OSA have shorter latency and SWS than women with OSA and men without OSA, which was associated with increased levels of leptin, a hormone associated with obesity, suggesting that this difference between sexes may have an important metabolic component.²¹ It is noteworthy here that the apnea-hypopnea index (AHI) decreases considerably in SWS; thus, a role of gender is proposed on how breathing changes through the sleep stages.²²

Analyzing the group of overweight and normal weight patients, it turns out that both have increased RDI, but the former has a significantly higher rate. It is known that obesity is a multifactorial disease associated with the pathophysiology of several other diseases, and that it predisposes OSA because subcutaneous and visceral fat decreases lung volume and obstructs the upper airways.²³ Interestingly, bariatric surgery is not only effective in controlling this syndrome in the short and medium term,²⁴ but it may also play a protective role by reducing the risk of developing this disease.²⁵

It was possible to observe the correlation between REM and sleep efficiency, although it is weak. Corroborating this finding, a study of patients referred for treatment of Obstructive Sleep Apnea-Hypopnea Syndrome (OSAHOS) found that most of those who had poor sleep efficiency also had poor or no REM sleep, and the severity of OSAHOS was greater, i.e., the AHI was higher.²⁶

Regarding the correlations observed between the polysomnographic parameters in **-Table 3**, the literature presents similar results to the ones presented in this study.

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Table 3 Correlation between the sleep parameters of patients submitted to polysomi

	REM sleep (%)	SWS (%)	Sleep onset latency (min)
Sleep efficiency (%)	rs: 0.307	rs: 0.232	rs: -0.544
	p < 0.05	p < 0.05	p < 0.001
RDI (%)	rs: -0.273	rs: -0.409	rs: -0.145
	p < 0.05	p < 0.001	p = 0.79

Abbreviations: RDI, respiratory disturbance index; REM, rapid eye movement; SWS, slow wave sleep; F, feminine; M, masculine; rs, correlation coefficient. Notes: Data do not follow the normal distribution (Shapiro-Wilk test). The Spearman correlation showed that there is a positive and weak correlation for sleep efficiency with REM sleep and SWS; a negative and weak correlation for RDI and REM sleep, RDI and N3; a negative and moderate correlation for sleep efficiency and sleep onset latency.

Table 4 Correlation between RDI and t-scores (n = 98).

	rs	<i>p</i> -value
Total t-score	0.153	0.147
t-score prospective memory	0.126	0.233
t-score retrospective memory	0.168	0.112

Abbreviations: RDI, respiratory disturbance index; rs, correlation coefficient. Notes: Data do not follow the normal distribution (Shapiro-Wilk test). The Spearman correlation showed that there is no correlation between RDI and memory.

A cohort of men from the United States demonstrated that RDI was inversely associated with REM sleep and SWS, and that increased SWS was accompanied by increased sleep efficiency values.²⁷ Despite the difference in sample size, our results also indicate a positive correlation between SWS and sleep efficiency.

No correlation was observed between RDI and memory. This can be explained by the different phenotypes found in OSA, that differ according to gender, age, comorbidities, BMI, and clinical presentation.²⁸ Such characteristics associated with the pathology confer 6 possible subtypes; for this reason, a larger sample size would be needed to assess each of them and correlate them with memory complaints. Another factor that may have influenced the results is the subjective measurement of memory complaints; an individual's perception of their ability to remember is influenced by several factors and may be under- or overestimated. In this regard, only objective assessment of memory is associated with high levels of biomarkers for the Alzheimer disease (AD),²⁹ showing that subjective memory complaint does not indicate cognitive decline.

Taking that into account, in individuals over 60-yearsold, a TST of 5 hours or less is associated with increased mortality.30 This cut-off point was used to verify the relationship with memory. Since this is a crossectional study, we cannot conclude that the self-reported memory impairment in the group of elderly subjects with TST of less than 5 hours is cumulative, in other words, that sleep deprivation

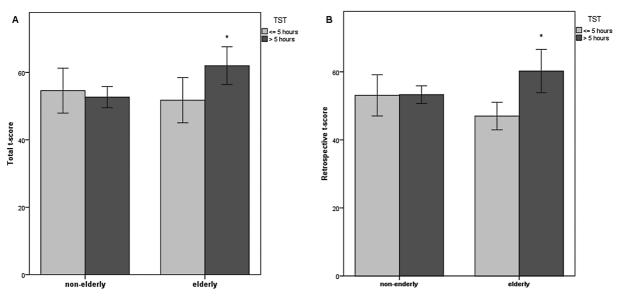


Fig. 1 Differences in memory of elderly and nonelderly according to total sleep time (TST). (A) The Student t-test showed that for the elderly there is a significant increase in the mean total t-score in TST > 5 hours group, compared with TST \leq 5 hours group (62.00 vs. 52.17; p < 0.05; n = 8/6). (B) The elderly show significant increase in mean t-score for retrospective memory in TST > 5 hours group compared with TST \leq 5 hours group (61.13 vs. 47.00; p < 0.05; n = 8/6). No difference was seen in the t-score for prospective memory (57.75 vs. 55.67; p = 0.326; n = 8/6) and in the nonelderly groups for total t-score (52.69 vs. 54.58; p = 0.610; n = 48/24), t-score for retrospective memory (53.29 vs. 53.08; p = 0.950; n = 48/24), and t-score for prospective memory (50.17 vs. 53.79; p = 0.286; n = 48/24). Data are expressed as mean \pm SEM, *p < 0.05.

Age (years)		< 60				≥ 60			
	Sleepiness	Average ranks	Н	df	р	Average ranks	Н	df	р
total t-score	Normal	55.54	16.99	2	< 0.001	6.92	2.19	2	0.33
	Borderline	49.82				12.25			
	Excessive	31.66				7.71			
t-score for	Normal	55.72	15.00	2	< 0.001	8.08	0.15	2	0.92
prospective memory	Borderline	47.41				9.00			
	Excessive	32.52				7.64			
t-score for	Normal	53.96	16.06	2	< 0.001	7.17	1.47	2	0.47
retrospective memory	Borderline	51.56				11.50			
	Excessive	31.83	1			7.71			
Comorbidities		No			Yes				
	Sleepiness	Average ranks	Н	df	р	Average ranks	Н	df	р
total t-score	Normal	32.63	12.05	2	< 0.05	31.38	6.20	2	< 0.05
	Borderline	26.75	_			32.86			
	Excessive	17.18				21.44			
t-score for prospective memory	Normal	33.17	11.60	2	< 0.05	31.68	4.87	2	0.087
	Borderline	24.63				31.00			1
	Excessive	17.60	1			22.06			
t-score for	Normal	30.50	11.89	2	< 0.05	31.44	5.65	2	0.059
retrospective memory	Borderline	30.56	1			32.23	1		
	Excessive	16.98	1	I		21.68	1	l	l

Table 5 Relationship between excessive daytime sleepiness and memory complaints by age and presence of comorbidities.

Notes: Data do not follow the normal distribution (Shapiro-Wilk test). The Kruskal-Wallis test showed that there is an effect of the excessive sleepiness group on the total t-scores, for prospective and retrospective memories in the nonelderly and without comorbidities. Such an effect was observed for the group with comorbidities only on the total t-score.

throughout life has caused this impairment. However, it is reported that sleep deprivation alters the connectivity of the hippocampus—a brain structure necessary for the formation of long-term memories and related to learning³¹—which could reinforce the hypothesis that memory complaints in the elderly population can be caused by chronic reduction of sleep throughout life.

It is noteworthy that all groups had very reduced REM sleep, considering an ideal range between 20 and 25% in adults, and 20% in the elderly. Several reasons may trigger reduced REM sleep: the use of substances such as marijuana—which can facilitate and induce sleep, but also impairs REM—and alcohol; medications such as antidepressants, benzodiazepines, and anticholinergics (which suppresses the activity of acetylcholine, the main neurotransmitter involved in REM); sleep disorders, which include insomnia, insufficient sleep syndrome, and OSA; lifestyle and behavioral factors, such as the use of excessive artificial light during the night and alarm clock routine. 32

According to the American Academy of Sleep Medicine,³³ insufficient sleep syndrome is characterized by hypersomnia due to chronic voluntary sleep restriction or extended wakefulness. This condition that has become more prevalent in recent years, especially due to work routine and the demands

of modern society, being more frequent in night workers, women, and also in children and adolescents. ³⁴ It is imperative that individuals maintain a TST below the minimum recommended for their age. ³⁵ In this case, the body prioritizes non-REM over REM sleep. ³²

Recently, the COVID-19 pandemic has brought many uncertainties, fear, anguish, and social isolation, changing everyone's habits and lifestyles, and it could not be any different in relation to sleep. A survey conducted in Brazil showed that this population's number of hours of sleep decreased during the pandemic, increasing dissatisfaction with their sleep, and the main complaint was difficulty getting to sleep on 3 or more nights throughout the week. ³⁶ In our study, subjects were not asked about sleep before the pandemic, but it is possible that the results found about memory are part of one of the many sequelae of COVID-19.

The data present in **Table 5** suggest that excessive daytime sleepiness is related to worse performances on the PRMQ in the nonelderly group. This shows that our finding was not due to age-related cognitive changes. The relationship between sleepiness and memory was also assessed separately for people without and with comorbidities, but in this case both groups showed a significant difference when total memory was assessed. Among the

chronic diseases, the most reported one was hypertension. However, in individuals with moderate to severe OSA, higher daytime sleepiness scores were also seen in normotensive individuals,³⁷ which in our study could indicate that selfperception of memory and daytime sleepiness are independent of other pathologies.

People with sleep disturbance and persistent daytime sleepiness show a decline in cognitive function and increased memory complaints, mainly because attention is impaired early in these cases.³⁸ Individuals with EDS should be monitored for the onset of dementia, since it increases the risk of cognitive decline by 30%, regardless of sociodemographic, behavioral, and clinical factors.³⁹

Limitations of this study include sample size, which prevented us from analyzing some categorical variables. It is also important to note that most articles associating sleep disturbances with memory complaints have worked with cohorts, which themselves are more relevant. Furthermore, in those studies, the subjects' sleep was assessed objectively while memory was assessed subjectively. Finally, the absence of a cutoff point of categories for the PRMQ restricted statistical analysis.

Conclusion

Our findings reinforce the idea that sleep is not a single event. Each patient has different sleep profiles: women take longer to fall asleep while men spend less time in SWS, overweight people have higher RDI, as well as individuals with comorbidities, who also have lower percentages of sleep efficiency, REM sleep, and SWS. However, the parameters studied are correlated, which makes the analysis of sleep even more complex.

The TST results have shown that the elderly benefit from more hours of sleep and perform better on memory assessments, but this data does not refute the importance of sleeping more than 5 hours daily, since memory impairment in the elderly can be cumulative. Future studies may focus on following patients over a period of time before aging to assess whether insufficient TST over a lifetime plays a role on memory in the elderly population.

We have also found that sleep and memory are indirectly related. The EDS symptom is present in individuals with sleep disorders and negatively impacts the performance of daily activities. In this study, EDS patients had decreased scores on the PRMQ, showing that the ability to retain and recall information is compromised in this group.

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Conflict of Interests

The authors have no conflict of interests to declare.

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