Research Article

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Sleep spindle-related electroencephalograph activity of young adults and its relation to cognitive functions

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Abstract

Objective: Sleep spindles are phasic bursts of thalamocortical activity, typically defined as 11-16 Hz (in sigma frequency band) with a duration of 0.5 and 2 seconds. Spindles are most prominent during N2 sleep and are a defining feature of this stage. The aim of the present study was to investigate the association between spindle characteristics and cognitive functions of young adults.

Methods: The study sample consisted of 17 healthy male subjects aged between 19 and 28 years. The participants had no medical or psychological conditions and were not taking any medications that might affect their sleep pattern and neuropsychological measurements. Polysomnography recordings were conducted from 22:30 to 07:00 hour for two subsequent nights. The first night was for adaptation to the laboratory conditions and to rule out sleep apnea syndrome and periodic leg movements. The second night was used to analyze macro and micro parameters of sleep. A neuropsychological test battery comprising the Serial Digit Learning Test, Raven Standard Progressive Matrices, Verbal Fluency Test, Trail Making A-B, and the Auditory Verbal Learning Test were administered before the second-night sleep session. Sleep spindles in all non-rapid eye movement stage 2 sleep were scored visually from C3-A2 electroencephalogram derivation after polysomnographic analysis was completed. Each 30-sec epoch was analyzed with a high-pass band filtered at 0.3 Hz, and a low-pass band filtered at 35 Hz. Spindle characteristics such as duration, amplitude, mean and peak frequencies were analyzed using the fast Fourier transform algorithm. The association between the characteristics of sleep spindles and the neuropsychological test scores were analyzed using Spearman correlations.

Results: Significant positive correlations were found between spindle density and both verbal auditory learning performance and verbal fluency, cognitive flexibility, and semantic organization performances. The serial digit learning test was correlated positively with mean duration, mean frequency, and peak frequency of sleep spindles. Finally, the mean duration, and mean frequency of spindles were positively correlated with verbal fluency, cognitive flexibility, and semantic organization.

Conclusion: The associations between spindle features and memory, verbal fluency, and verbal learning abilities were consistent with previous research findings suggesting that sleep spindles might be related to cognitive abilities and the potential to learn. In other words, it might be an indicator of the current level of aptitude for learning.

Keywords: Learning, memory, sleep, spindle

INTRODUCTION

Sleep spindles are phasic bursts of thalamocortical activity, typically defined as 11-16 Hz (in sigma frequency band) with a duration range from 0.5 to 2 seconds. Spindles are most prominent during N2 sleep and are a defining feature of this stage (1). A sleep spindle is an oscillatory brain pattern that has been associated with the thalamus via a network of synaptic interactions involving inhibitory gamma aminobutyric acid neurons in the reticular thalamic nuclei, thalamocortical cells, and cortical pyramidal neurons (2). Sleep spindles are influenced by genetic effects and related to brain anatomy. Thus, each individual has a different pattern of sleep spindles (3).

Functionally, sleep spindles are believed to be involved in the processes of plasticity, offline memory consolidation, and the stabilization of sleep by inhibiting external stimuli (4-6). Spindles have been correlated with more

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complex abilities and processes, such as learning ability, planning, and problem solving (7, 8). It has been proposed that spindle density, frequency, and activation could be used as a neurobiological indicator for the level of cognitive development, intelligence, and learning abilities (9, 10). Researchers have suggested that baseline sleep spindles are related to an individual's capacity for memory processing and perhaps an inherent learning aptitude or intelligence. Moreover, sleep spindles are known to reflect the efficiency of the thalamocortical system, which is the source of sleep spindles and is important for successful encoding and processing during wakefulness (11).

The consolidation of declarative memory results from a dialogue between reactivated hippocampal memory traces and neocortical networks that retain long-term memory representations (12). Sleep spindles are the key components for memory consolidation (stabilization of memory traces) at night with the synchronized activity of hippocampal ripple waves and slow waves (13). Researchers found that sleep spindles appear to actively enhance information processing via their role in memory consolidation. It has been shown that there is an association between the retention rates of information and the density of sleep spindles following a night's sleep (14, 10). Moreover, an increase in recall performance of human subjects was reported as a result of pharmacologically induced spindle activity (15). In the light of previous research, the aim of the current study was to investigate the association between spindle characteristics and cognitive functions, and to identify whether spindle activity was a marker for cognitive ability in young adults.

METHODS

Participants

The study sample consisted of 27 healthy male subjects aged 19-28 years. The subjects were recruited from hospital personnel and university students who were involved in a larger ongoing study which was previously approved by Gülhane Military Medical Academy Ethics Committee (03.03.2015). The current study protocol was reapproved by the Çankaya University Local Ethics Review Committee (22.10.2018/76373453-604.01/019301). Written informed consent was obtained from all participants. Among the 27 subjects, five were excluded because of short sleep duration (total sleep time <250 m) and low sleep efficiency index (SEI <85%). Subjects with primary sleep disorders were also detected and excluded from the sample according to the first night sleep recordings (three subjects were excluded due to sleep apnea). Finally, two of the recordings were excluded due to poor quality electroencephalogram recordings and artifacts. Ultimately, the sample comprised 17 subjects who had no medical or psychological conditions and did not take any medications that might affect their sleep pattern and neuropsychological measurements. All participants reported regular sleep–wake schedules and their SEI rates were higher than 85%. Only male participants participated in the study because sleep spindle measurements are known to be influenced by the menstrual cycle (16). No alcoholic drinks or caffeinated beverages were allowed the night before the sleep recordings.

Procedures

Participants stayed for two subsequent nights from 22:30 to 07:00 at the sleep laboratory and the data were collected using Grass AS40 polysomnograph (Grass Comet Plus, AS40-Plus) Amplifier System (600 East Greenwich Avenue, West Warnic, RI, USA) at a sampling frequency 200 Hz. The first night was for adaptation to the laboratory conditions and to the attached electrodes. The second night was used to analyze the macro and micro parameters of sleep. Electrodes were placed according to the International 10-20 System. Each 30-sec epoch of sleep was scored visually according to the American Academy of Sleep Medicine version 2 rules (17).

Sleep spindle activity is best viewed over the central regions of the head. To detect spindles, we focused on the left central electrode (C3) and all N2 epochs were scanned visually. Each 30-sec epoch was analyzed with a high-pass band filtered at 0.3 Hz, and a low-pass band filtered at 35 Hz. Spindles were detected and visually counted by an expert using the following steps: (1) detecting and selecting spindles from the C3-M2 channel; (2) applying the fast Fourier transform (FFT) algorithm to each spindle detected; and (3) analyzing the spindle characteristics such as frequency (mean and peak), amplitude and duration by using the FFT algorithm automatically (Table 1, Figure 1). In total, 17 subjects' sleep records, which consisted of approximately 6800 epochs, were visually detected and the spindle density of each subject was calculated as the mean number of spindles per 30 seconds.

Neuropsychological Test Battery

A neuropsychological test battery comprising the Stroop Test TBAG, Trail Making A-B, Controlled Oral Word Association Test (COWAT), Serial Digit Learning Test (SDLT), Auditory Verbal Learning Test (AVLT), and Raven Standard Progressive Matrices (RSPM) was administered before the second-night sleeping session.

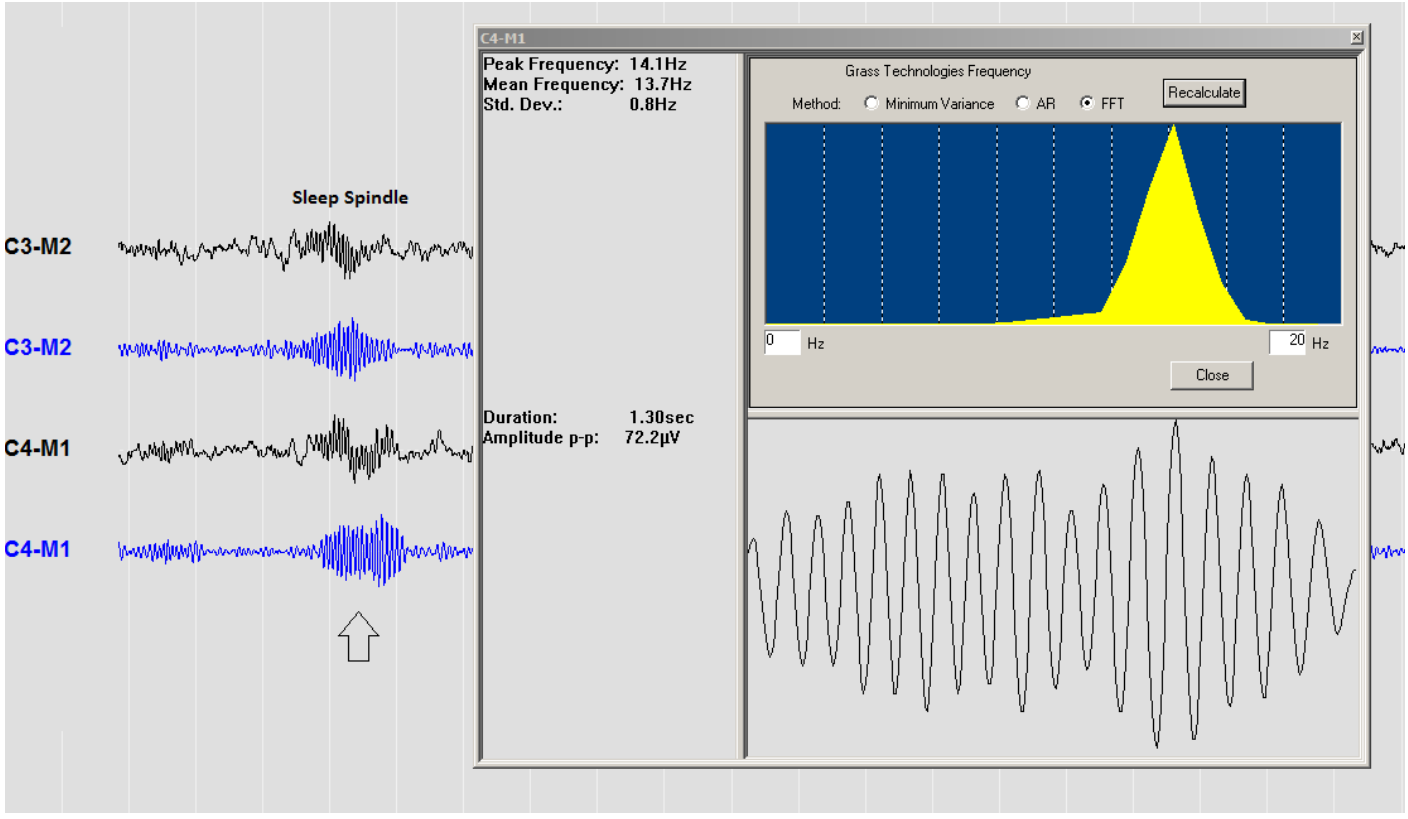
Stroop test TBAG version (SP)

The Turkish version was developed within the context of the BILNOT Battery and extensively studied for the Turkish culture.

Table 1. Definition of sleep spindle parameters

Number	The total number of spindles counted during N2 sleep
Frequency	The oscillation number of each spindle per second
Density	Mean number of spindles per 30 seconds
Duration	The starting and ending of each spindle (range between 0.5-2 sec)
Amplitude	The magnitude of each spindle

Figure 1. Illustration of the visual detection of a sleep spindle from a 30-sec epoch



It is used for measuring focused attention, selective attention, and resistance to interference. The test requires the naming of colors correctly, while suppressing the reading facility (18, 19).

Controlled oral word association test

This test measures verbal fluency, cognitive flexibility, information processing, and semantic category-organization. It uses the three letter set of K, A, and S to assess phonemic fluency. Individuals are given 1 min to name as many words as possible beginning with one of the letters. The procedure is then repeated for the remaining two letters. Finally, the tester gives the category 'animal' and asks the subject to produce as many words as possible in that category (20).

Auditory verbal learning test

The Turkish version of the test includes 2 different word lists, each comprising 15 words that are repeated over different trials and are asked to the subject to repeat. The test evaluates a wide diversity of functions: short-term auditory-verbal memory, free recall, learning, retroactive, and proactive interference, retention of information, and immediate-delayed memory (21, 22).

Serial digit learning test

The test was developed in 1943 by Zangwill. It consists of a mixed series of digits ranging from 1 to 9. The digits are read in succession, and then the subject is requested to remember and repeat the number set verbally in the correct order. This procedure is repeated a maximum of 12 times. When the subject recalls the digit series correctly the test is terminated. Standardization to the Turkish culture was made within the BILNOT battery (19, 23).

Raven standard progressive matrices

The test measures abilities such as analytical thinking, general intelligence, thinking, reasoning, and problem solving. It is regarded as a test independent from culture and language. Standardization to the Turkish culture was made within the BILNOT battery (19, 24).

Trail making test

This is a mental flexibility test that gives information about visual-motor scanning, speed of processing, set switching, working memory, and executive functions. The test consists of forms A and B, each containing 25 circles. In form A, which is administered first, participants have to follow the numbers 1 to 25 and connect them sequentially by drawing a line. In the more complex form B, circles have to be connected in the sequence number-letter (1-A, 2-B, 3-C…). Form A measures attention, sustained attention, visual scanning, motor reaction speed, and processing speed. Form B is used to measure motor control and complex attention (25, 26).

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) Ver. 20 (SPSS IBM Corp.;

Armonk, NY, USA) statistical package program. Spearman's Rho correlation analysis was performed to determine the correlation between the spindle characteristics and the neuropsychological tests. For the statistical analysis, a $p<0.05$ was considered statistically significant.

RESULTS

Descriptive statistics of spindle characteristics, sleep parameters, and neuropsychological test scores are given as mean, standard deviation, and minimum and maximum values (Tables 2-4). Spearman's Rho correlation analysis was performed to determine the correlation between the spindle characteristics and the neuropsychological tests (Table 5). The level of statistical significance was accepted as $p<0.05$. The mean age of the sample was 22.50 years (SD=3.43); the mean duration of education was 12.89 years (SD=1.71).

According to the results, significant positive correlations were found between spindle density (mean number of spindles per 30 seconds) and verbal auditory learning performance

Table 2. Descriptive statistics of sleep spindle parameters

Sleep spindle	Mean	±Standard deviation	Minimum	Maximum
Density	1.03	0.36	0.48	1.84
Amplitude (mV)	38.60	4.41	31.08	45.36
Duration (sec)	1.10	0.20	0.87	1.63
Mean frequency (Hz)	12.89	0.46	12.21	13.56
Peak frequency (Hz)	13.16	0.52	12.26	14.00

Table 3. Descriptive statistics of sleep parameters regarding the sleep architecture

	Mean	±Standard deviation	Minimum	Maximum
Total sleep time (min)	412.31	25.53	370.00	452.20
Sleep latency (min)	12.91	7.49	5.00	28.00
Wake duration (min)	28.04	21.20	6.50	74.00
Sleep efficiency index (%)	91.62	4.30	84.70	98.40
Stage 1 duration (min)	38.37	10.57	19.50	57.40
Stage 1 percentage (%)	9.32	2.65	4.70	13.80
Stage 2 duration (min)	213.87	22.97	185.20	270.60
Stage 2 percentage (%)	51.90	5.11	40.90	64.00
Stage 3 duration (min)	86.81	22.64	46.50	135.00
Stage 3 percentage (%)	20.97	4.99	11.00	29.90
REM duration (min)	71.90	17.68	75.00	38.00
REM percentage (%)	17.52	3.81	17.70	26.20

REM: rapid eye movement

Table 4. Descriptive statistics of neuropsychological test scores

	Mean	±Standard deviation	Minimum	Maximum
Stroop TBAG-1 (sec)	8.09	1.17	6.61	11.12
Stroop TBAG-5 (sec)	20.81	4.64	11.80	28.00
AVLT total score	50.35	6.21	39.00	60.00
AVLT delayed	10.12	2.54	5.00	14.00
AVLT retroactive	10.76	2.28	7.00	15.00
AVLT proactive	6.00	1.00	4.00	7.00
SDLT	18.29	4.87	4.00	24.00
RSPM	49.27	8.90	33.00	60.00
COWAT-semantic	20.06	4.25	9.00	27.00
COWAT-prosody	40.93	13.75	21.00	69.00
Trail making A (sec)	29.40	15.06	18.00	75.00
Trail making B (sec)	70.06	26.37	42.30	150.00

SDLT: serial digit learning test; AVLT: auditory verbal learning test; RSPM: raven standard progressive matrices; COWAT: controlled oral word association test

Table 5. The significant correlations of spindle characteristics and neuropsychological tests

	Spindle density	Spindle activity	Spindle amplitude	Spindle duration	Mean frequency	Peak frequency
SDLT	r=.248	r=.400	r= -.159	r=.727	r=.562	r=.495
	p=.337	p=.112	p=.542	p=.001	p=.019	p=.044
AVLT	r=.524	r=.274	r=.477	r=.084	r=.329	r=.234
	p=.031	p=.287	p=.053	p=.750	p=.197	p=.367
COWAT	r=.535	r=.365	r=.201	r=.548	r=.487	r=.199
semantic	p=.033	p=.164	p=.455	p=.028	p=.055	p=.460

SDLT: serial digit learning test; AVLT: auditory verbal learning test; COWAT: controlled oral word association test

(r=0.524) and verbal fluency, cognitive flexibility, and semantic organization (r=0.568). There were also positive correlations between mean duration (r=0.727), mean frequency (r=0.562), and peak frequency (r=0.495) of sleep spindles and the Serial Digit Learning Test. Finally, the mean duration (r=0.548) and mean frequency (r=0.524) of spindles were positively correlated with verbal fluency, cognitive flexibility, and semantic organization.

DISCUSSION

In the present study, we aimed to investigate the association between spindle characteristics and cognitive functions by using a neuropsychological test battery. We found that those who performed better at verbal learning, learning in spite of a proactive interference, and recalling words from a semantic category also exhibited significantly higher spindle density, frequency, and duration during the subsequent night. In other words, verbal learning, verbal abilities, and declarative memory performance in young adults were associated with stage 2 sleep spindle characteristics, which might be an indicator of the current level of aptitude for learning.

Generally, previous studies were focused on macro parameters of sleep such as total sleep time, sleep latency, and percentages of sleep stages; however, micro parameters such as sleep spindles were less attended (27). A number of studies that investigated spindle activity reported that tasks regarding declarative memory improved spindle activity after a night's sleep (10, 28). It is also reported that this increment was better among subjects whose previous memory task performance (baseline level) was higher (29). In the present study, the comprehensive neuropsychological test battery, measuring verbal learning, learning despite an interference, verbal fluency, semantic recall was found to be related to the spindle features.

Sleep spindles originate from the thalamus, which has traditionally been thought as a necessary link in the flow of information from the periphery to the cortex. However, recent study findings show that lesions of the pulvinar and mediodorsal nucleus of the thalamus result with deficits in attention and memory (30). Apart from that, it is reported that the thalamic reticular nucleus (TRN) is another important structure for attention during the daytime when the subject is awake. It has also been shown that TRN activity is associated with the efficiency of the thalamocortical network and encoding process (31). A strong thalamocortical network (myelination of the thalamocortical fibers) might reflect on sleep spindle activity, which in turn might reflect on cognitive functioning (32). In parallel with those previous findings, we found that learning under an interference (AVLT-proactive) was stronger (less affected from the distractive stimuli) and verbal learning ability (SDLT) was better among subjects who had relatively high spindle density and duration.

The other neuropsychological test COWAT, which measures cognitive flexibility, response inhibition, attention, working memory, and semantic memory (33) was related to spindle density. As a result, we can conclude that the thalamocortical system might give rise to both spindles and higher cognitive functions, which enable processing, encoding, and recalling of information efficiently. Participants characterized by high performance exhibited significantly higher spindle density compared with subjects with generally low performance. The ideas that baseline sleep spindles are related to an individual's capacity for memory processing, and perhaps an inherent learning aptitude, were supported by the current results.

In the literature, the association between the sleep spindle and intelligence-general abilities has been emphasized (34, 35). In addition, it was reported that spindle density is usually quite stable from night to night (3). However, in this study, we found no correlation between general intelligence as measured using RSPM and sleep spindles. One of our limitations was focusing on just the left central electrode and not focusing on both frontal and central electrodes, which might be the reason of this result. Researchers in a recent study also found no relationship between general intelligence and sleep spindles in a large cohort study (36).

Finally, neither spindle activity nor cognitive functions were significantly correlated with the macro parameters of sleep (duration, percentage, latency). According to sleep deprivation studies, significant associations were found between total sleep time and cognitive functions (37). In our study, the mean percentage of the SEI was 91%, which indicates that they were all good sleepers and quite homogeneous.

The two limitations of the current study are the characteristics of the sample and the method used for spindle detection. Our sample consisted of young male adults, which limits us from generalizing the current findings to other age groups or females. Several methods have been reported in the literature regarding spindle detection (38). However, visual detection has been found to be the most reliable method of all the others including automatic algorithms. However, detecting spindles visually from thousands of epochs demands significant effort and time. Therefore we recommend using an automatic algorithm and conducting the study on different clinical populations in future studies.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Çankaya University (date: 22.10.2018/ no: 76373453-604.01/019301).

Informed Consent: Written informed consent was obtained from the subjects who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.T.Y., S.Y.; Design – N.T.Y., S.Y.; Supervision – S.Y.; Resources – S.Y., N.T.Y.; Materials – N.T.Y., S.Y.; Data Collection and/or Processing – N.T.Y., S.Y.; Analysis and/or Interpretation – N.T.Y., S.Y.; Literature Search – N.T.Y., S.Y.; Writing Manuscript – N.T.Y., S.Y.; Critical Review – N.T.Y., S.Y.

Conflict of Interest: The authors have no conflicts of interest to declare.

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