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Changes of Procedural Memory in the Patients with Primary Insomnia

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Abstract

Objective: To explore changes of procedural memory in the patients with primary insomnia (PI) and its characteristics.

Methods: Thirty-six PI patients and 36 controls were enrolled. The procedural memory was respectively detected by category exemplar generation and motor sequence tasks respectively, and the declarative memory was assessed by free word task.

Results: Compared to the controls, the PI patients showed few correct numbers in the category exemplar generation (7.7 ± 2.1 vs. 9.9 ± 1.0, z = 5.247, P<0.001), motion sequence task (8.1 ± 3.3 vs 12.0 ± 3.0, z = 4.676, P<0.001) and the phases of immediate recall (3.3 ± 1.1 vs 6.0 ± 1.2, z=6.634, P<0.001), delayed recall (9.0 ± 2.2 vs. 11.2 ± 1.1, z=4.718, P<0.001) and delayed recognition (14.2 ± 1.0 vs. 15.0 ±0.0, z = 4.637, P<0.001) of the free word task. For the different subtypes of PI, the early morning awakening group had significantly worse performance in the motor sequence task compared to the difficulty initiating sleep (z=–2.768, P=0.006) and difficulty maintaining sleep (z=–2.502, P=0.012) groups, and less correct numbers of the word-delayed recognition compared to the difficulty maintaining sleep group too (z=–2.707, P=0.007).

Conclusion: The procedural and declarative memories are impaired in the PI patients, especially the early morning awakening insomniacs.

Keywords: Primary insomnia; Procedural memory; Declarative memory

Introduction

Insomnia refers to the difficulty in the sleep initiating maintaining of patients with adequate hours, good sleep environment and opportunities to sleep. As a result, the patients have a subjective experience of dissatisfied sleep time and/or quality, and daytime dysfunction, such as anxiety, depression, mental activity and cognitive (e.g. learning and memory) impairment in certain degree [1-4].

The imaging studies show that the insomnia patients had cerebral hypoper fusion of blood compared to the normal controls, and this change in the basal ganglia was more obvious than those in the frontal, occipital and parietal cortexes [5]. It is found by mean of magnetic resonance imaging that patients with insomnia had significantly reduced volume in the bilateral hippocampus [6]. In accordance with sleep deprivation experiments in animals, it is suggested that sleep deprivation leaded to decline of cognitive function in humans. Studies on memory with sleep deprivation model have shown that depriving different periods of sleep in the general population would make different impacts on learning and memory. For example, total sleep deprivation impairs semantic memory; slow wave sleep (SWS) deprivation without reducing total sleep time significantly affects declarative memory (DM) and coding related hippocampal activities; rapid eye movement sleep (REMS) deprivation influences the procedural memory (PM) rather than DM [7]. Polysomnography application has revealed some sleep characteristics of insomnia patients, such as the shortened total sleep time, extended sleep onset latency, decreased sleep efficiency, reductive SWS and incremental percentage of first-phase sleep [8]. The underlying mechanism of insomnia-related cognitive changes might be due to some kinds of sleep structure disorders or a specific SWS (0.5~2.0 Hz) defect, which is harmful to the brain protein synthesis, the establishment and consolidation of new synaptic connections and the recovery of synaptic homeostasis.

However, in the early stage of chronic insomnia patients, because of the mild condition, the body tends to have sufficient time to complete any compensation. So that, cognitive function changes between insomnia of the natural course and sleep deprivation are different. So far, memory impairment in patients with primary insomnia (PI) remains to be identified. A meta-analysis showed that patients with PI existed mild to moderate damage in working memory, episodic memory and certain aspects of attention, but there was no significant difference in perceptual processing, PM, speech and executive function [9,10]. PM impairment and its characteristics of patients with PI are inconclusive, which may be owing to different evaluation methods and sample sources. In the present, we observed the changes in PM and DM with three tasks (category exemplar generation, motor sequence tasks and free word task) in the patients whose symptoms met to the PI diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [11].

Materials and Methods

Study objects

PI group: Thirty-six patients were included, who went to the Sleep and Memory Disorders Clinic of the First Affiliated Hospital, Anhui

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Medical University from September 2010 to May 2011 due to sleep difficulties. Their mean age was 37.0 ± 11.5 years, the illness duration ≥ 1 month and all of them met PI diagnostic criteria in the DSM-IV. All of them were right-handed, and were accepted high school education or above. Meanwhile, the Athens Insomnia Scale (AIS) [12] score was >6 and Montreal cognitive test scale (MoCA) [13] score was ≥ 26. Additionally, the following conditions were excluded: taking drugs (such as antidepressants, benzodiazepines, antiepileptics or other drugs/substances) possibly impacting on cognitive function past two weeks; suffering from other sleep disorders (such as sleep apnea syndrome, restless legs syndrome), medicine conditions (such as chronic obstructive pulmonary disease, chronic pain, or severe liver disease) and neuropsychiatric disorders (such as stroke, epilepsy, Parkinson's disease, dementia, depression and anxiety disorders, specifically, when 17-terms Hamilton Depression Rating Scale (HAMD-17) [14] score being ≥ 17); unable to complete the experiment; impaired visual acuity and audition. Furthermore, the patients were divided into several subgroups according to the type of insomnia: the difficultly initiating sleep group [7 males / 5 females; mean age 35.6 ± 13.2 years; education 12.5 ± 2.2 years], the early morning awakening group [6 males / 6 females; mean age 36.6 ± 10.2 years; education 12.7 ± 1.7 years] and the difficulty maintaining sleep group [5 males / 7 females; mean age 37.3 ± 11.0 years; education 13.2 ± 2.5 years]. There were no statistical differences among subgroups in gender, age and years of education (*Ps* > 0.05).

Healthy control group: A total of 30 cases consist of healthy adults who were subjected to health examination during the same period. The mean age was 37.3 ± 11.4 years. They were right-handed, and come from the comparable cities or countries with the similar habits, education, economics and other factors, in order to roughly match with the PI patients. Besides, they were required have no previous history of neuropsychiatric disorders and hypomnesis, and no obvious physical illness, with AIS score ≤ 4, MoCA score ≥ 26 and HAMD-17 score < 7.

This research was approved by the First Affiliated Hospital of Anhui Medical University Ethics Committee, and all participants signed informed consent.

Methods

Background information assessment: Background information, including AIS, Epworth Sleepiness Scale (ESS) [15], MoCA and HAMD-17, were completed by trained clinicians.

PM

Category exemplar generation task: Firstly, every subject was shown 10 randomized pictures of vegetables and household appliances, and then was required to name them. After 15 minutes, the subject was required to enumerate the name of vegetables and household appliances shown before as many as possible within 1 min successively, and the total correct numbers were recorded [16].

Motion sequence task: Subjects put their left fingers successively on the number keys of 1234 on the keyboard from little to index finger, and then entered a set of random sequences (such as 4-2-3-1-4) displayed on the computer screen as fast and accurate as possible within a certain period of time. After resting 24s, they would enter into the next round. They were required to complete 12 rounds in total consecutively. The average numbers of correct sequences in the last 3 rounds were counted [17].

DM

Words free recall task: Fifteen high-frequency Chinese notional words were selected in the test. Subjects were asked to read the words five times and recall them after reading immediately within 2 min. The correct number of first time recalling was defined as the immediate recall score. Then subjects recalled the free words after 15 min. The correct number of words was called the delayed recall score. After given another 15 new notional words, subjects were required to tell the word from old to new, the correct numbers of judgment of old words was called the delayed recognition score [18].

Statistical analysis

All statistical analyses were conducted by the SPSS 13.0. The data were expressed as mean ± standard deviation. The normal distribution data were analyzed by independent samples t test or ANOVA, and the non-normal distribution data were analyzed by Manne-Whitney U or Kruskal-Wallis H test.

Results

Background information

U or *t* test showed that there was no statistically difference in sex, age and years of education between the PI group and the control group (Table 1). There were no significantly difference in MoCA (z=1.781, P =0.075) and ESS (t=0.879, P=0.379) scores between the two groups, but the PI group had significantly higher scores of the AIS and HAMD-17 than the control group (z=7.345, P < 0.001; z=7.161, P < 0.001), indicating that the sample quality met requirement of the study (Table 1).

Memory testing

The U test showed that compared to the controls, the PI patients had worse performances in all measures of the immediate recall, delayed recall, delayed recognition, category generation and the motion sequence (z=6.634, 4.718, 4.637, 5.247 and 4.676, respectively, *Ps* <0.001) (Table 2).

Memories in the patients with different insomnia subtypes

The ANOVA or H test showed that there were significant or marginal differences among the three subgroups of difficultly initiating sleep, early morning awakening and difficultly maintaining sleep in the delay recall (F=3.264, P=0.051), delayed recognition (H=8.871, P=0.012) and exercise sequence (H=9.766, P=0.008) scores, but there were no significant differences in the immediate recall (H=0.840, P=0.657) and class generation (H=0.399, P=0.819) scores. Furthermore,

Groups	Gender (male/female)	Age (years)	Education Levels (years)	AIS	ESS	HAMD-17	MoCA
Insomnia	18/18	37.0 ± 11.5	13.0 ± 1.9	13.9 ± 3.1*	7.4 ± 3 .5	11.7 ± 3.9*	26.8 ± 1.2
Controls	14/16	37.3 ± 11.4	12.1 ± 2.7	2.5 ± 1.2	6.7 ± 2.1	2.6 ± 1.8	27.3 ± 1.5
Statistic	χ^2=0.073	t=0.378	z=1.262	z=7.345	z=0.879	z=7.161	z=1.781
P values	0.787	0.706	0.207	< 0.001	0.379	< 0.001	0.075

*Compare to the control group P<0.001
AIS: Athens Insomnia Scale; ESS: Epworth Sleepiness Scale; HAMD-17: 17-terms Hamilton Depression Rating Scale; MoCA: Montreal Cognitive Assessment

Table 1: Background information of the subjects (mean ± standard deviation).

Groups	Declarative memory			Procedural memory	
	Immediate recall	Delayed recall	Delayed recognition	Category generation	Motion sequence
Primary insomnia	3.3 ± 1.1*	9.0 ± 2.2*	14.2 ± 1.0*	7.7 ± 2.1*	8.1 ± 3.3*
Controls	6.0 ± 1.2	11.2 ± 1.1	15.0 ± 0.0	9.9 ± 1.0	12.0 ± 3.0
z	6.634	4.718	4.637	5.247	4.676
P values	<0.001	<0.001	<0.001	<0.001	<0.001

*Compare to the control group, $P<0.001$

Table 2: Memory test results of the subjects (the number of correct, mean ± standard deviation).

Groups	Declarative memory			Procedural memory	
	Immediate recall	Delayed recall	Delayed recognition	Category generation	Motion sequence
Difficultly initiating sleep	3.3 ± 1.1	9.3 ± 2.6	14.4 ± 0.8	7.9 ± 2.2	9.0 ± 2.7
Early morning awakening	3.2 ± 1.2	8.8 ± 2.0	13.4 ± 1.2#	7.2 ± 1.2	6.6 ± 2.6 *#
Difficultly maintaining sleep	3.4 ± 0.9	9.0 ± 2.2	14.7 ± 0.7	8.0 ± 2.7	8.6 ± 4.1
Statistic	$H = 0.840$	$F = 0.101$	$H = 8.871$	$H = 0.399$	$H = 9.766$
P values	0.657	0.904	0.012	0.819	0.008

*Compare to the difficultly initiating sleep group, $P<0.017$, # Compare to the difficulty maintaining sleep group, $P<0.017$

Table 3: Memory in the patients with different insomnia subtypes (correct number, mean ± standard deviation).

the U test for pair wise comparison (corrected size of the test: $\alpha=0.05 / 3=0.017$) showed the early morning awakening patients got worse scores in motion sequences and delay recall task than the difficulty maintaining sleep patients ($z=-2.502$, $P=0.012$ and $z=-2.707$, $P=0.007$, respectively, both P values < 0.017). However, when compared to the difficultly initiating sleep group, the worse performance in the early morning awakening group only occurred in the motion sequences task ($z=-2.768$, $P=0.006 < 0.017$), but not in delay recall task ($z = -2.157$, $P = 0.031 > 0.017$) (Table 3).

Discussion

One of the main functions of sleep is restoring brain synaptic plasticity and forming of new memories [19]. But previous studies have shown that patients with PI had generally no or slight damage in learning and memory [20], perhaps only in complex tasks memory [21]. An overview about the daytime function in PI patients has been exhibited i.e., no memory impairment was seen in simple tasks, such as audio verbal learning, Hopkins Verbal Learning, word matching, word recognition and visual recognition, however, the PI group had significantly worse performance than the control group in free word memory, the mirror image reading and phrase memory tasks [22]. Recent researches about mirror image reading (detecting PM) and visual verbal learning tasks (detecting DM) found that patients with PI showed decreased ability to complete these tasks [23]. In our study, the motion sequence and category generation tasks were respectively used to detect motor skill learning and priming effects on PM in the PI patients, while the free word recall task was used to detect DM. The results showed that compared to the control group, the motion sequence and category exemplar generation scores in the PI patients declined to certain degree, and three measures in the free word recall task were also damaged. Therefore, whether the PI patients have damaged PM or/and DM or not depended on a moderate difficulty of the tasks used.

Sleep plays an important role in the PM and DM, which is related to new memories and integration of existing knowledge [24]. Both REMS and SWS [25] would contribute to memory encoding, consolidation and neural plasticity. Studies on sleep deprivation have shown that the REMS deprivation only affected PM and SWS deprivation influenced DM [26]. However, the visual recognition task (a kind of DM) research found that the improved memory after sleep was only correlated to the amount of SWS in the first quarter of the night, but was also correlated to the amount of REMS in the last quarter. These results indicated that the consolidation of DM is connected with both SWS and REMS [27]. Actually, the data result from the PI patients indicated that PM also involved in the Stage 2 sleeps [28]. Relative to complex skills formation which relies more on REMS, the consolidation of existing skills and simple motor skills needs sleep spindles in Stage 2 [29]. Therefore, throughout the whole process of sleep, the memory consolidation of different types needs respectively unique pattern of sleep periods [28]. After comparison among diverse insomnia subtypes, the results showed that the early waking group had significantly impaired PM and DM when compared to the patients with difficultly maintenance sleep, and impaired PM when compared to ones with difficultly initiating sleep. We presumed that the reduction or changed percentage of REMS in early waking people may contribute to this result, because the patients with early waking mainly lose the sleep in the latter half of night, in which the REMS is predominant. Our results did not seem support the previous hypothesis that the SWS reduction in the difficultly initiating sleep patients should lead to DM damage. In fact, the difficultly initiating sleep patients often had earlier bedtime, but they don't always have reductive total sleep time or SWS. Furthermore, the changes of sleep architecture are not unitary in maintenance difficulties sleep patients, and some patients may be having a normal proportion of each phase. Without doubt, it is necessary to enlarge samples to certify our conclusion.

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