Journal of Psychiatric Research 45 (2011) 555–560

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

Sleep-dependent memory consolidation of a new task is inhibited in psychiatric patients

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ARTICLE INFO

Article history:
Received 7 June 2010
Received in revised form
25 August 2010
Accepted 27 August 2010

Keywords:
Memory
Sleep
Depression
Schizophrenia
Sequential finger tapping task
Africa

ABSTRACT

Schizophrenic and depressive patients show impeded sleep-dependent procedural memory consolidation. But this has been shown mainly for tasks testing the adaptation of old skills. This study tested the overnight memory consolidation of a new task and the transfer of this new skill to a similar task. Using an adapted version of the sequential finger tapping task, keyboard-naïve Ethiopian depressive ($n = 8$) and schizophrenic ($n = 15$) patients and healthy controls ($n = 11$ and $n = 17$) were tested twice, 24 h apart. In addition the subjects underwent training in a second sequence after the retest of the first sequence. Both schizophrenic and depressive patients did not show a significant overnight change in performance (1% and 4% improvement respectively) in the task and differed significantly from the healthy control groups who did show significant improvement (16% and 22%). Further in contrast to the healthy controls both patients groups showed no significant transfer of the newly acquired skill to the second sequence. This study shows that depressive and schizophrenic patients are not only deficient in the overnight memory consolidation of a new task, but also fail to show a transfer of this new skill to similar tasks.

1. Introduction

There is an increasing amount of evidence supporting the importance of sleep in memory consolidation. Further this memory consolidation seems to be inhibited in psychiatric patients. Schizophrenic and depressed patients show decreased improvement in procedural tasks after a night of sleep (Manoach et al., 2004, 2010; Dresler et al., 2009; Dresler et al., 2010) in comparison to healthy controls.

But an important factor to consider is the newness of a specific task. It has recently been proposed that although REM sleep is involved with the reprocessing of procedural tasks that require a new cognitive strategy, simple and familiar motor tasks involve primarily stage 2 sleep (Fogel and Smith, 2006). The overnight studies on patients with Schizophrenia and Depression have used the sequential finger tapping task (SFTT), which tests the adaptation of a familiar skill (typing on a computer keyboard) to a task (typing a specific sequence). But do psychiatric patients also have a decreased memory consolidation for a newly acquired skill and is the transfer of the new skill to a similar task intact? In this study we tested Ethiopian psychiatric patients, who were mostly keyboard-naïve and had never or only on a few occasions used a computer before in their life, with the SFTT.

With 36 psychiatrists for the whole population Ethiopian psychiatry is still in the developing stage with regard to mental health care. But the prevalence of the most common psychiatric conditions (depression, bipolar disorder, schizophrenia, anxiety disorders etc.) are similar to developed countries, with only some differences, e.g. male:female ratio in schizophrenia being 4:1 instead of the 1:1 in developed countries (Awas et al., 1999; Kebede and Alem, 1999a,b). It is not entirely clear whether this has anything to do with the diagnostic algorithms, which are not validated in Ethiopia.

In this study we tested patients with acute depression or chronic schizophrenia and healthy controls with an adapted version of the SFTT for overnight memory consolidation and transfer of the newly acquired skill to a second sequence. We expected both patient groups to have no overnight improvement in the task and to differ significantly from the healthy controls.

2. Methods

2.1. Subjects

Patients with an acute depressive episode and chronic schizophrenia were recruited from the inpatient and outpatient service of

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doi:10.1016/j.jpsychires.2010.08.015

the Psychiatric Unit of Jimma Specialized University Hospital in Jimma/Ethiopia. The patients were diagnosed by an experienced psychiatrist with DSM-IV criteria and their clinical status was assessed by the Amharic version of the Kessler scale, which has been validated in the Ethiopian setting (Tesfaye et al., 2010).

21 patients with schizophrenia were tested, of which one did not type a single correct sequence during the learning phase and was excluded from the study and five never returned for retest. This resulted in 15 patients with schizophrenia, who completed both learning phase and retest and were included in the analysis. Of these 15 patients 9 received chlorpromazine some with the addition of, fluoxetine or amitriptyline and 6 patients received fluphenazine decanoate, thioridazine or haloperidol two with the addition of amitriptyline.

10 patients with an acute depressive episode were tested, of which two were excluded from the analysis resulting in $n = 8$. Of these two one did not type a single correct sequence during the learning phase and one continuously pressed too long on the keyboard buttons during the learning phase, resulting in false low number of correctly typed sequences. With the exception of one patient taking sertraline all patients were receiving amitriptyline, some with the addition of diazepam, thioridazine or fluphenazine decanoate.

24 healthy subjects were recruited from the visiting family members of the patients on the medical ward and were screened for psychiatric conditions with the Kessler scale and for a family history of psychiatric conditions. Of these 24 healthy subjects only 17 could be found for retest and were included in the analysis. All 17 subjects were included in the control group (healthy sz) of the patients with schizophrenia. Since the depressed patients were remarkably younger than the schizophrenia group (mean of 25.0 ± 8.02 years and 38.0 ± 12.9 years respectively), a sub-control group (healthy dp) was selected for the depressive subjects. The sub-group consisted of all healthy subjects $\leq$30 years of age and one 36 and one 40 year old female, healthy subjects selected to match the two depressed patients over the age of 30, a total of 11 controls.

Additional information for all subjects is presented in Table 1.

2.2. Procedures

The subjects were tested on 2 consecutive days between 9 AM and 4 PM, but always at the same time of day on both days. The two sessions, separated by 24 h, constituted a single test of overnight improvement. Before the learning phase the study was explained to the subjects and they gave their written consent. Further the subjects completed a general questionnaire and the Kessler scale.

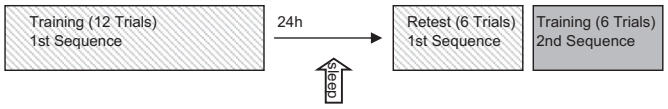

Fig. 1. Study design: The subjects first typed 12 trials of the first sequence. After 24 h and a night of sleep the subjects returned and typed the retest of the first sequence with 6 trials and afterwards the new, second sequence for 6 trials.

The Ethical Review Committee of the Jimma University Faculty of Medical Sciences, Jimma/Ethiopia, approved the research project, the experiments were carried out in accordance to the Declaration of Helsinki and all subjects gave their informed, written consent.

2.3. Learning task

To test memory consolidation we employed a sequential finger tapping task (Fischer et al., 2002; Walker et al., 2002). The task was adapted from the original guidelines to fit the Ethiopian subjects. This task required subjects to press four numeric keys on an altered computer keyboard with their dominant hand, repeating the four element sequence (4-1-3-2) as quickly and accurately as possible for a period of 30 s. To exclude any working memory component on the task, the numeric sequence was displayed on the screen. Of note, most subjects did not make a connection between the screen and the keyboard, since they had never used a computer before. For every trial the computer noted the number of complete sequences achieved, the number of errors made, and the number of correct sequences typed. The learning phase consisted of twelve trials of 30 s interrupted by 20 s rest periods, while at retest the subjects had to complete six trials. In addition, the subjects typed a second sequence (1-4-2-3) for six trials after the retest of the first sequence to see if the consolidation was sequence specific (for study design see Fig. 1). In the 20 s pause between the trials, the displayed sequence was darkened and the word “Pause” appeared. Five seconds before the pause ended, an acoustic countdown signalled the upcoming start of the next trial. The score of the correctly tapped sequences was used as outcome measure and incorporates the accuracy and speed performance. End-training performance consisted of the average score from the last three trials of the training, while retest performance was composed of the average score from all six retest trials. To measure sleep-dependent consolidation we used end-training performance as baseline and

Table 1
Characteristics of patients and controls. There was no significant difference between the patients and their control groups with the exception of the Kessler scale.

	Schizophrenia	Healthy sz	Sz vs. H	Depression	Healthy dp	Dp vs. H
Age	38.00 ± 12.9	35.06 ± 12.0	$t = -.669$ $p = 0.509$	25.00 ± 8.0	27.72 ± 6.0	$t = -.850$ $p = 0.407$
Gender	73% ♂	65% ♂	$t = -.511$ $p = 0.613$	50% ♂	64% ♂	$t = -.568$ $p = 0.578$
Years of Education	8.33 ± 5.3	6.71 ± 5.5	$t = -.845$ $p = 0.405$	8.88 ± 5.4	8.27 ± 5.4	$t = .241$ $p = 0.812$
Literate	87.7%	76.5%	$t = -.720$ $p = 0.477$	87.5%	90.9%	$t = -.226$ $p = 0.824$
Knowledge of Arabic Numerals	93.3%	88.2%	$t = -.480$ $p = 0.635$	87.5%	90.9%	$t = -.226$ $p = 0.824$
Experience with a Keyboard	13.3%	17.7%	$t = .325$ $p = 0.747$	37.5%	27.2%	$t = .451$ $p = 0.658$
Other Fine Motor Skills	6.7%	0%	$t = -1.067$ $p = 0.295$	0%	0%	
Kessler Score	11.8 ± 8.9	3.35 ± 4.4	$t = -3.470$ $p = 0.002$	20.75 ± 7.5	3.72 ± 4.7	$t = 6.078$ $p < 0.001$
Inpatient	13.3%			87.5%		
Age of Disease Onset	27.7 ± 12.1			20.5 ± 3.8		
Duration of Disease in Years	10.3			4.5		