



# Impaired off-line memory consolidation in depression

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## KEYWORDS

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## Abstract

Sleep is critically involved in the consolidation of procedural memory. In major depression (MD) and during antidepressant pharmacotherapy, changes in sleep EEG are well documented. Here, we test if off-line motor memory consolidation is impaired in MD. 50 medicated patients with an acute episode of MD, 50 normal controls and 12 patients with a remitted episode of MD were assessed using a sequential finger tapping task before and after a night of sleep. Although depressed patients and control subjects did not differ in practice-dependent learning, healthy subjects showed markedly overnight improvements in tapping performance of 18% while patients failed to show any improvement. This pattern became even more striking when the subjects were divided by an age threshold of 30 years: In the 30+ yrs group the healthy subjects showed 16% overnight increase in motor performance, whereas the patients showed –10% overnight decrease. In contrast, patients and controls in the  $\leq 30$  yrs group showed virtually the same motor performance, as well as remitted patients and controls in the 30+ yrs group. In addition, the younger controls showed stronger overnight improvements than the older controls. This pattern might be interpreted as a synergistic interaction between age and depression: Off-line motor memory consolidation is not affected in young patients, but severely impaired in older patients with an acute episode of MD. This impairment seems to recover after remission from depression.

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## 1. Introduction

A rapidly growing body of evidence shows that sleep is critically involved in memory consolidation, particularly for the procedural learning of motor skills. For example, subjects learning a sequential finger tapping task show a marked enhancement in tapping performance of about 10–30% after

a night of sleep but not after the same time awake (Fischer et al., 2002; Walker et al., 2002). It has been hypothesized that a stabilization phase of motor memory consolidation may occur during wakefulness or sleep, while an independent consolidation phase of post-training off-line enhancement of newly acquired motor skills is exclusively bound to sleep (Walker and Stickgold, 2006). Especially rapid eye movement (REM) sleep (Plihal and Born, 1997; Smith, 1996), and sleep stage 2 (Walker et al., 2002) seem to be related to procedural memory consolidation. In patients with depression, most studies demonstrate deficits in declarative and working memory, but intact procedural learning (Austin et al.,

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2001), although several studies report psychomotor retardation to be associated with depression (Sobin and Sackeim, 1997). Off-line components of procedural memory have not been investigated so far in affective disorders. Considering the well documented changes of sleep-electroencephalogram (EEG) in depression (Armitage, 2007; Kupfer, 1995) and during antidepressant pharmacotherapy (Wilson and Argyropoulos, 2005), it seems obvious that sleep-related memory consolidation might be altered in depression. Actually, potential effects of REM-suppressing antidepressants on procedural memory consolidation have been proposed to be a crucial topic in the sleep-memory consolidation debate (Vertes, 2004). We therefore tested the hypothesis that patients with an acute episode of major depression (MD) would show normal practice-dependent motor learning within a training session, but, unlike healthy subjects, fail to show overnight improvement. In addition, considering the age-related decline in sleep quality (Bixler et al., 1984) and a recently shown age-related decline in sleep-related memory consolidation (Spencer et al., 2007), sleep-related memory impairments should be aggravated by age. We therefore hypothesized that the impairments in off-line motor memory consolidation is pronounced in older patients, but much less so in younger patients. Because depression-related changes in sleep-EEG variables increase in the fourth decade of life (Lauer et al., 1991), we compared two patient groups divided by an age threshold of 30 years. While changes in sleep architecture associated with antidepressant pharmacotherapy gradually diminish during treatment (Wilson and Argyropoulos, 2005), characteristic disturbances of EEG sleep remain unchanged even after remission (Kupfer, 1995; Steiger et al., 1989). We therefore tested if patients with a remitted episode of MD show less strong impairments in off-line motor memory consolidation than patients with an acute episode.

## 2. Experimental procedures

### 2.1. Participants

50 inpatients with an acute episode of unipolar MD and without psychiatric or non-psychiatric comorbidity were included in this study during their first week of hospitalisation. Diagnosis was established by two independent senior psychiatrists in semi-standardized interviews according to ICD-10. Clinical status was further assessed with the 21 items version of the Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960) and in the Beck Depression Inventory (BDI, 21 items) (Beck et al., 1961), inclusion

criteria were a score of at least 18 in the HAMD and the BDI. All patients were medicated with antidepressants and several received co-medication like mood stabilizers or benzodiazepines. 12 patients were below the age of 30. This subgroup showed a small non-significant difference regarding the severity of depression, with the 30+ years patients scoring 3.4 points higher on each the HAMD and BDI ( $p > .05$  each, two-sided  $t$ -tests). 50 healthy control subjects matched for age and gender served as a control group. A semi-standardized interview revealed no history of psychiatric illness in their own and their family, no stressful life event in the last year and no non-psychiatric comorbidity. Further 12 medicated inpatients above the age of 30 years with a remitted episode of MD (BDI score lower than 8) and without psychiatric or non-psychiatric comorbidity were included during their last three days of hospitalisation. 8 of the remitted patients were already tested as a subgroup in the acute MD condition. For biographical data see Table 1. Exclusion criteria for all subjects were ambidexterity, assessed by a score between  $-50$  and  $+50$  in the Edinburgh Handedness Inventory (Oldfield, 1971), professional typing skills, musical skills on manually playable instruments like piano, shift work and transmeridian flights in the last 3 months. All subjects gave informed consent and the study was approved by the local ethics committee.

### 2.2. Procedures

Subjects were tested on two consecutive days between 09:00 and 12:00 h with a sequential finger tapping task (Walker et al., 2002). The subjects were required on the first day to repeatedly tap a sequence of 5 numbers (4-1-3-2-4) during 12 periods of 30 s, interrupted by a 20 s pause each, as often and correctly as possible with their non-dominant hand on a special 4-key computer keyboard (training session). During tapping trials, the number-sequence was displayed in white on a black background in the middle of the screen to minimize working memory load. Each key press produced a dot below the tapped number, forming a row left right to right. Once the five dots of a sequence were completed, each subsequent key press removed a dot from left to right. When the dots had all been removed, further key presses added them again. Each trial was automatically scored for the number of correctly tapped sequences, thus assessing both speed and accuracy of motor performance. In the 20 s pause between the trials, the displayed sequence was darkened and the dots were replaced with the word "Pause". Five seconds before the pause ended, an acoustic countdown signalled the upcoming start of the next trial. Changes of motor performance were measured in a three trial test session 24 h later, after a night of normal sleep (see Fig. 1). Remitted patients already tested with the original sequence had to tap an alternative sequence (1-4-2-3-1). It has been shown that this sequence is equally difficult and that practice in one sequence does not generalize to a similar sequence (Fischer et al., 2002).

**Table 1** Biographical data of all patients and controls and of subgroups above and below the age of 30 years, given as mean  $\pm$  SD. HAMD: Hamilton Depression Inventory Score. BDI: Beck Depression Inventory Score. Episodes: number of depressive episodes including the current. Duration: cumulative duration (in months) of all depressive episodes including the current.

	All patients	All controls	Patients >30	Controls >30	Patients $\leq$ 30	Controls $\leq$ 30	Remitted
<i>n</i> (females)	50 (30)	50 (30)	38 (23)	38 (23)	12 (7)	12 (7)	12 (7)
Age (yrs)	41.8 $\pm$ 12.5	41.8 $\pm$ 12.6	47.1 $\pm$ 9.1	47.0 $\pm$ 9.6	25.1 $\pm$ 3.5	25.3 $\pm$ 3.8	44.9 $\pm$ 9.7
Age range	20–65	22–63	32–65	32–63	20–30	22–29	36–65
HAMD	24.4 $\pm$ 5.7	–	25.3 $\pm$ 5.8	–	21.8 $\pm$ 4.8	–	2.1 $\pm$ 1.6
BDI	28.1 $\pm$ 7.7	–	28.9 $\pm$ 7.7	–	25.5 $\pm$ 7.6	–	4.8 $\pm$ 2.3
Episodes	3.8 $\pm$ 3.8	–	4.4 $\pm$ 4.2	–	2.0 $\pm$ 1.2	–	3.8 $\pm$ 4.0
Duration	11.0 $\pm$ 12.2	–	13.0 $\pm$ 13.2	–	4.8 $\pm$ 4.7	–	10.7 $\pm$ 12.3

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