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Sleep-dependent consolidation of motor skills in patients with narcolepsy-cataplexy

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ABSTRACT

Background and Objectives: This study investigated whether the altered organization of post-training sleep in patients with narcolepsy-cataplexy (NC) is associated with a lower off-line improvement in the consolidation of motor skills compared with normal subjects.

Study Design: Fourteen drug-naive NC patients, fulfilling the international clinical and polysomnographic diagnostic criteria, and 14 individually-matched controls underwent training at a sequential finger tapping task (FTT) and were re-tested on the next morning (after a night with polysomnographic recording) and after another six nights (spent at home).

Setting: Training and retrieval sessions were performed in a controlled laboratory setting.

Results: FTT performance was worse in NC patients than controls at training and at both retrieval sessions and showed a fairly different time course (slower than in controls) of consolidation. Several sleep indices (lower values of stage-2 NREM sleep and SWS) were compatible with a lower effectiveness of sleep for consolidation of motor skills in NC patients, although no statistically significant relationship was found between such indices and improvement rate.

Conclusion: The consolidation process of motor skills results less effective in NC patients since training and slower than in normal subjects over the week following training. The wider variations in performance scores and sleep parameters of post.-training night in NC patients relative to controls suggest that a) the lower initial consolidation may be due to a less effective encoding consequent to altered prior sleep, and b) the consolidation process over the 24 h following training is negatively influenced not only by the altered characteristics of post-training sleep, but also by the daytime sleepiness following training.

Key words

Narcolepsy-cataplexy • Altered sleep • Non-declarative memory • Consolidation process • Motor skills

Introduction

A sleep-dependent effect has been consistently observed in the consolidation process of recent (namely, acquired in the pre-sleep period) information, regardless of their declarative or non-declarative nature (i.e., "know what" and "know-how", according to Squire's taxonomy: Squire, 1993). Complementarily, the consolidation of new (in particular, non-declarative) information has shown to be negatively influenced by an acute sleep loss, as well as sleep restriction and fragmentation (for review, see Diekelmann and Born, 2010).

It seems thus plausible that the altered sleep of patients with such chronic disorders as primary insomnia (PI), obstructive sleep apnoeas (OSA), and narcolepsy-cataplexy (NC), also has a less positive effect on memory consolidation. Indeed, these disor-

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ders have often been associated with varying impairments in memory tasks on both declarative and non-declarative information (in particular, perceptual and motor skills: for review, see Fulda and Schulz, 2001; 2010). This makes it crucial to establish whether the postulated smaller gain provided by altered sleep in the consolidation of new information is at least partly responsible for the memory impairment observed in patients with chronic sleep disorders.

To date, few studies have tested this hypothesis (for review, see Cipolli et al., 2012). A lower post-night improvement in motor skills relative to normal subjects has been reported in two (Nissen et al., 2006; 2011) of the three studies (the other being that by Backhaus et al., 2006) on PI patients and in the only study on OSA patients (Kloepfer et al., 2009), whereas no study has so far investigated NC patients. Narcolepsy-cataplexy is a neurological disease associated to numerous variations in the sleep architecture. Besides an excessive daytime sleepiness, NC patients show an increased number of awakenings and stage shifts over the night, a larger proportion of stage-1 and lower proportions of stage 2 sleep and slow wave sleep (SWS) than normal subjects (AASM, 2005).

We report here the results of a study on the level and time course of motor skills consolidation in NC patients relative to matched healthy controls. Consolidation level was measured by means a sequential finger tapping task (FTT) at training, after the following night (spent in laboratory) and after a six further nights (spent at home). FTT was chosen as a) sensitive to sleep-dependent variations in motor learning in healthy subjects (Walker et al., 2002), and b) representative of skilled sequential movements (from dialling a phone number to playing the piano) at work in everyday motor behaviour (Ghilardi et al., 2009; Kvint et al., 2011).

Methods

Participants

Patients

Fourteen first-diagnosed NC patients were enrolled for the study at the Sleep Disorders Centre of the University of Bologna. NC diagnosis was based on the international clinical and polysomnographic (PSG) criteria (AASM, 2005).

Inclusion criteria were: excessive daytime sleepiness, measured by the Epworth Sleepiness Scale (ESS: Johns, 1991) and confirmed by the Multiple Sleep Latency Test (MSLT), demonstrating a mean sleep latency of eight minutes or less and at least two episodes of SOREM sleep; clear-cut cataplexy; presence of the human leukocyte antigen HLA-DQB1*0602 (Mignot et al., 1997); right-handedness. Exclusion criteria were: age under 18 and over 50 years (the wide age range depending on the rarity of the disease); less than eight years of education; a history of pharmacological treatment for sleep disorders; a history of psychiatric disorders or other neurological diseases, and brain lesions (ascertained at brain magnetic resonance imaging (MRI); moderate or severe depression (a score higher than 18 on Beck Depression Inventory: (Beck et al., 1961), visual or motor deficits, i.e. scores above the cut-off point of mild deficit in all the psychometric tests listed below (see Materials).

Control subjects

Fourteen healthy subjects individually matched with NC patients for sex, age and educational level were selected at the Psychology Department of the University of Bologna. Subjects had to sleep seven to nine hours per night without any major disruption of the sleep-wake cycle, as assessed clinically by an expert neurologist (G.P.). The exclusion criteria were the same as those adopted for NC patients, plus a score of ten or more at ESS and the need to take any medication at the time of the experiment. Subjects were paid for their participation in the study.

The study protocol was approved by the local Ethics Committee. Informed written consent according to the Declaration of Helsinki was obtained from each participant.

Apparatus

PSG recording (System 98, Micromed®; Mogliano Veneto, Italy) included EEG (four channels), vertical and horizontal EOG (two channels), EMG (three channels) for mylohyoideus and right and left anterior tibialis muscles and ECG (one channel). EEG electrodes were positioned according to the international 10-20 system on sites C3, C4, Cz, O1, with controlateral mastoid reference. Sleep stages were classified following standard criteria (Rechtschaffen and Kales, 1968).

Materials

Psychometric Testing

All participants were examined by the same psychologist, unaware of the study aims, who administered Wechsler Adult Intelligence Scale - Revised (Wechsler, 1981) for the assessment of global and specific cognitive deficits, Wechsler Memory Scale (Wechsler, 1987) for short- and long-term memory, Baddeley Logical Reasoning Test (Baddeley, 1968) for reasoning, the forms A and B of Trail Making Test for speed of processing, flexibility and executive functions (Tombaugh, 2004).

Finger Tapping

FTT requires the subject to press repeatedly a five element sequence (6-3-5-4-6) with the fingers (except thumb) of the non-dominant hand on a computer keyboard as fast and accurately as possible for 30-s trials interrupted by 30-s breaks.

FTT task was carried out without visual feedback of the tapping as the non-dominant hand was shielded from view. The numeric sequence was displayed on the screen at all times to keep working memory demands at a minimum. No accuracy feedback was provided: each key press resulted in a white dot on the screen forming a row from left to right.

At training, participants underwent twelve 30-s trials. Each 30-s trial was scored for speed (number of correctly completed sequences) and accuracy (number of correctly completed sequences out of total completed sequences). Speed and accuracy scores from the first trial were taken as "baseline" measures, while the average scores for the last three trials were taken as "fast learning" measures of motor performance. At next-day and seventh-day retrieval sessions speed and accuracy were measured on three trials.

Experimental routine

Patients

Patients underwent clinical examination (including psychometric assessment) on the first day, and nocturnal PSG recording, MSLT and MRI to exclude brain lesion in the following days. After the clinical routine, eligible patients were requested to take part in the experiment, being informed that would have to stay in the laboratory for about 26 hours from 8.00 a.m. of the set day (with PSG recording during the intervening night) and to perform a motor task (FTT) three times, always at 10.00 a.m., on the first day, the next day (after the night spent in laboratory) and after a further six nights (spent at home).

The experiment was planned on non-consecutive days with respect to the clinical routine to avoid making the cognitive and emotional burden too arduous.

Control subjects

The design planned for controls was the same as for NC patients to balance the cognitive and emotional demands: subjects eligible as individually-matched controls underwent psychometric assessment and a nocturnal PSG recording for adaptation to the laboratory and started the experimental routine in the following week.

None of the participants were permitted to take a nap after training, in order to measure the influence of the following night-time sleep per se on the consolidation level. They had to avoid coffee and alcohol before and after training session and after next-day and seventh-day sessions. On the other hand, to ensure that speed and accuracy were representative of the actual level of motor skills, patients and controls could have taken a short nap, if necessary, until one hour before the task. Indeed, it is well documented that a fairly long (30 min) nap can contrast the negative effect of sleepiness on the encoding and execution of cognitive tasks (Hood and Bruck, 1996; for a review, see Fulda and Schulz, 2001).

Before each session, participants were rated on the Stanford Sleepiness Scale (Hoddes et al., 1973). Participants scoring higher than two ("able to concentrate") would have been excluded from statistical analysis. This was not the case for any participant.

As no patient reported moderate or severe sleep problems in a sleep diary for two or more of the six nights spent at home, statistical analysis was carried out on all 14 patients and corresponding controls.

Data Analysis

Psychometric indicators of depression, daytime sleepiness and cognitive functioning were separately analyzed using one-way ANOVAs, taking "Group" (NC patients/ normal subjects) as factor.

The following sleep parameters (resulting from an automatic scoring of PSG files using Vitaport2™ – Temec Instruments, Kerkrade, The Netherlands, 1997 – and an independent visual check by an expert neurologist unaware of the study aims) were mea-

sured on the files of post-training night: Total Sleep Time (TST), Sleep Efficiency (SE), Sleep Latency (SL), REM Latency (RL), proportions of REM sleep and NREM sleep stages (stage 1, stage 2 and slow wave sleep [SWS], calculated as sum of the proportions of stage 3 and stage 4) over TST. Three additional indices for REM density (calculated as number of rapid eye movements per minute of REM sleep) and two for sleep fragmentation were calculated, namely a) REM density over the first (two sleep cycles) and second halves of the night (third and following cycles) and the whole night, and b) number of stage shifts per hour (Sleep Stage Shift Index, SSSI: Sforza and Haba-Rubio, 2005) and total number of stage shifts and awakenings (defined as any stage shift to wakefulness > 15 s: AASM, 2005) per hour (Sleep Fragmentation Index, SFI: Haba-Rubio et al., 2004). The values of all sleep parameters and indices were analyzed using a one-way MANOVA, taking "Group" as factor.

The fast learning of motor skills was evaluated using a two-way ANOVA, taking "Group" and "Phase of learning" at training (baseline/last three trials) as factors.

The slow learning (i.e., off-line consolidation) was evaluated by two-way ANOVAs on speed and accuracy scores, taking "Group" and "Session" (training/ next-day retrieval/ seventh-day retrieval) as factors. The significant three-level factors and interactions in ANOVAs were analyzed using Tukey's HSD test (with $\alpha = 0.05$).

To assess the relationship between sleep parameters and improvement in consolidation a Multiple Regression Analysis (using the enter method) was carried out on speed differential values between next-day retrieval and training separately on NC patients and controls.

Results

Psychometric indicators

No indicator of cognitive functioning or depression differed significantly in NC patients compared to controls (see Table I).

Sleep indicators

ESS score was significantly higher in NC patients (15.64 ± 4.29) than controls (6.71 ± 2.81) ($F_{1,26}$ = 42.415; $p < 0.001$). All patients and controls had a score of 1 on the Stanford Sleepiness Scale at each session ("wide awake")

The values of PSG indicators of post-training night are reported in Table II.

A MANOVA carried out on sleep parameters showed a significant effect for "Group" ($F_{12,15} = 5.499$; $p < 0.01$). Subsequent univariate ANOVAs showed significant effects for Sleep Efficiency (lower in NC patients than in controls: $F_{1,26} = 7.675$; $p < 0.05$), proportions of Stage-1 NREM sleep (higher in NC patients: $F_{1,26} = 19.156$; $p < 0.001$), Stage-2 NREM

Table I. - Demographic and psychometric indicators (data are given as means ± SD).

	NC Patients (n = 14, 5 females)	Control Subjects (n = 14, 5 females)	p value
DEMOGRAPHIC DATA			
Age (*years*)	31.36 ± 8.41	30.86 ± 7.14	n.s.
Education Level (*years*)	13.14 ± 1.96	13.36 ± 1.74	n.s.
PSYCHOMETRIC DATA			
WAIS-R Verbal IQ	108.50 ±10.01	114.36 ± 11.87	n.s.
WAIS-R Performance IQ	104.14 ± 15.38	111.07 ±7.72	n.s.
WAIS-R Total IQ	109.43 ± 10.65	113.93 ± 9.13	n.s.
WMS total MQ	108.36 ± 10.32	112.43 ± 10.78	n.s.
Baddeley's Logical Reasoning Test	26.00 ± 10.17	34.00 ± 10.64	n.s.
Trail Making Test-A	39.36 ± 8.97	44.57 ± 9.57	n.s
Trail Making Test-B	100.27 ± 20.54	115.57 ± 23.84	n.s.
Beck Depression Inventory	7.28 ± 4.44	5.71 ± 4.16	n.s.

IQ = Intelligence Quotient; MQ = Memory Quotient.

Table II. - Indicators of sleep organization during the experimental night (data are given as means ± SD).

	NC patients (n = 14)	Matched control subjects (n = 14)
	MANOVA group effect: p < 0.001	
SLEEP PARAMETERS		
Sleep Latency, *min.*	7.84 ± 4.91	11.00 ± 6.09
REM Latency, *min.*	58.04 ± 55.95	88.86 ± 52.04
Total Sleep Time, *min.*	436.21 ± 77.45	420.31 ± 54.48
Sleep Efficiency, *%*	85.29 ± 8.88	92.24 ± 3.03
Stage 1, *%*	15.20 ± 6.17	6.87 ± 3.55
Stage 2, *%*	46.05 ± 7.34	52.01 ± 5.93
SWS, *%*	12.31 ± 5.99	18.64 ± 5.12
REM, *%*	26.44 ± 6.63	22.49 ± 4.61
REM Density (*first part of the night*)	9.13 ± 6.19	5.25 ± 3.37
REM Density (*second part of the night*)	8.67 ± 5.77	7.05 ± 3.03
REM Density (*all night*)	8.98 ± 5.89	6.30 ± 3.06
Sleep Fragmentation Index (SFI, *number per hour*)	18.77 ± 4.06	14.59 ± 3.87
Sleep Stage Shift Index (SSSI, *number per hour*)	11.70 ± 2.14	9.89 ± 2.94
SOREM (*number of subjects with*)	5	-

FTT = Finger Tapping Task; SWS = Slow Wave Sleep; SOREM = sleep onset REM; sleep parameters significantly different between groups are reported in bold text.

sleep (higher in controls: $F_{1,26} = 5.569$; $p < 0.05$), Slow Wave sleep (higher in controls: $F_{1,26} = 9.020$; $p < 0.01$), in Sleep Fragmentation Index (higher in NC patients: $F_{1,26} = 7.770$; $p < 0.01$), and in REM density in the first half of the night (higher in NC patients: $F_{1,26} = 4.224$; $p = 0.050$). Additionally, a SOREM episode occurred in 5 patients.

Fast learning

Both speed and accuracy at the end of training were not significantly correlated with age (Pearson's r coefficient) in NC patients (respectively, $\rho = -0.335$, $p = 0.242$, and $\rho = 0.153$, $p = 0.603$) or control subjects ($\rho = -0.192$, $p = 0.510$, and $\rho = -0.195$, $p = 0.503$). Therefore, age was not taken as covariate in the subsequent analyses.

The two-way ANOVAs carried out separately on the scores of speed and accuracy of FTT at training (see Table III) showed that speed was significantly lower in patients than controls ($F_{1,26} = 4.574$, $p < 0.05$.) and improved significantly at the end of training ($F_{1,26} = 32.323$, $p < 0.001$), without significant interaction ($F_{1,26} = 1.185$, $p = 0.286$), while accuracy did not significantly differ for "Group" ($F_{1,26} = 0.661$, $p = 0.424$), "Phase of learning" ($F_{1,26} = 1.614$, $p = 0.215$) or their interaction ($F_{1,26} = 0.057$, p. 814).

Slow learning (off-line consolidation)

Preliminary comparisons (using a two-way ANOVA) between the scores of performance speed and accuracy did not show significant differences between NC patients with (n = 5) and without occurrence of SOREM episode (n = 9) in post-training night (respectively, $F_{1,12} = 2.068$, $p = 0.176$; $F_{1,12} = 0.033$, $p = 0.858$) and the interaction "SOREM occurrence x session" (respectively, $F_{2,24} = 0.961$, $p = 0.397$; $F_{2,24} = 0.566$, $p = 0.575$.), while there was, as expected, a significant difference with respect to "session" for speed ($F_{2,24} = 4.499$; $p < 0.05$) but not for accuracy ($F_{2,24} = 0.984$; $p = 0.388$). Therefore, the subsequent analyses were conducted considering the whole sample of NC patients.

A two-way ANOVA carried out on speed scores of all patients and controls (see Table IV) showed significant differences with respect to "group" ($F_{1,26} = 8.349$, $p < 0.01$; patients had a worse performance than controls) and "session" ($F_{2,52} = 32.214$, $p < 0.001$), and a trend toward significance for their interaction ($F_{2,52} = 7.565$, $p = 0.060$). Subsequent Tukey's test on the main effect and the almost significant interaction showed that in NC patients speed value was higher at seventh-day retrieval compared with training, but not at next-day retrieval compared

Table III. - Values of Speed (number of sequences) and Accuracy (percent of correct sequences) on FTT at training session (data are given as means ± SD).

	Baseline		End of training	
	Speed	Accuracy	Speed	Accuracy
NC patients (n = 14)	6.50 ± 2.85	77.45 ± 18.09	9.67 ± 2.14	83.54 ± 8.26
Matched control subjects (n = 14)	8.43 ± 4.27	81.60 ± 20.12	13.09 ± 5.12	85.76 ± 9.19

FTT = Finger Tapping Task

with training and at seventh-day retrieval compared with next-day retrieval, whereas in controls speed was significantly higher at next-day retrieval compared with training, and at seventh-day retrieval compared with next-day retrieval and (obviously) training.

A two-way ANOVAs carried out on accuracy scores (see Table IV) showed a significant difference for "Session" ($F_{2,52} = 3.390$, $p < 0.05$) and a trend toward a difference for "Group" (patients being less accurate than controls: $F_{1,26} = 3.390$, $p = 0.077$), without an interaction effect ($F_{2,52} = 0.739$, $p = 0.483$). Tukey's test on "Session" showed that accuracy significantly improved at next-day and seventh-day retrieval compared with training, but not at seventh-day retrieval compared with next-day retrieval.

Multiple Regression Analysis on improvement of speed

Given the small sample size, we considered only six sleep parameters which were found in previous studies to be related to improvement in procedural skills, namely the proportions of Stage-2 NREM sleep, SWS, REM sleep, and the three indices of REM density. Separate multiple regression analysis of speed differential scores between training and next-day retrieval did not show significant results in NC patients ($R^2 = 0.302$; $F_{6,13} = 0.506$; $p = 0.788$) and control subjects ($R^2 = 0.650$; $F_{6,13} = 2.171$; $p = 0.167$).

Discussion

This study assessed the influence of the altered architecture of sleep of NC patients on the consolidation of motor skills in the night following training, by comparing speed and accuracy of performance of patients with those of controls at training and after 24 h. Moreover, to evaluate the time course of this process, speed and accuracy of performance of patients and controls were measured also after 144 h. All patients enrolled in the study were first-diagnosed (hence drug-naïve), to rule out any doubt in establishing whether sleep alterations were drug- or disease-dependent, and homogeneous as to the clinical and cognitive profile (see Table I). Moreover, training and retrieval sessions were planned in the morning, when daytime sleepiness is lower (Hood and Bruck, 1996), and participants were allowed also to take a nap until one hour before session to counteract the possibly perceived sleepiness.

Two main inferences can be drawn from the findings obtained.

1) Performance speed (i.e., number of correct sequences per 30 s) was lower at training in patients compared with controls and remained significantly lower despite improvement at next and seventh-day retrieval, with a near-significance trend toward a smaller increase (see Table IV). The difference between NC patients and controls in performance speed increased from baseline (1.93 correct sequences) to the end of training (3.42 correct sequences)

Table IV. - Values of Speed and Accuracy for FTT in the three sessions (Slow Learning; data are given as means ± SD).

	TRAINING SESSION		First-day RETRIEVAL SESSION		Seventh-day RETRIEVAL SESSION	
	Speed	Accuracy	Speed	Accuracy	Speed	Accuracy
NC patients (n = 14)	9.67 ± 2.14	83.54 ± 8.26	10.86 ± 3.32	86.63 ± 9.93	12.05 ± 3.55	85.68 ± 8.67
Matched control subjects (n = 14)	13.09 ± 5.12	85.76 ± 9.19	15.48 ± 5.17	91.63 ± 4.24	17.55 ± 5.62	91.55 ± 5.42

FTT = Finger Tapping Task

and seventh-day retrieval (5.50 correct sequences).
By contrast, performance accuracy (i.e., proportion of correct sequences out of the total number of sequences) was not significantly different at training in patients compared with controls and improved significantly across sessions in patients as well as in controls.
The worse (as slower) performance of NC patients at training was in line with literature reports of poor performance in new tasks involving motor (as well as perceptual) skills (for review, see Fulda and Schulz, 2001), irrespective of the time of day when tasks were performed (Schneider et al., 2004). This finding was only seemingly in contrast with those from studies on PI (Backhaus et al., 2006; Nissen et al., 2006, 2011) and OSA (Kloepfer et al., 2009) patients. These actually reached the measure-criterion at training after a higher number of trials compared with controls. Also the overall lower improvement in performance speed across sessions observed in NC patients appears coherent with the indications of almost all the four previous studies on the level of motor skills after post-training sleep in PI and OSA patients.
The above findings obtained seem reliable, given that both a process of fast (hence practice-dependent) learning resulted at work in NC patients as well as in controls, and the improvement rate of performance speed in controls (about 22% at next-day retrieval and a further 14% at seventh-day retrieval) largely replicated that observed in studies on normal subjects (Fischer et al., 2002; Walker et al., 2003).
2) The values of several PSG indicators of post-training night were significantly different in NC patients compared to controls (see Table II). The values of three sleep parameters (higher proportion of stage 1-NREM, lower proportions of stage 2-NREM and SWS) and the Sleep Fragmentation Index (higher) were both consistent with literature reports (AASM, 2005) and compatible with the possibility of a lower consolidation power of sleep in NC patients for motor skills. Indeed, the improvement of motor skills in normal subjects has shown to be related to the proportions of SWS (Huber et al., 2004) and stage-2-NREM sleep (Fogel and Smith, 2006), as well as the number of spindles (Gais et al., 2002; Peters et al., 2008) in post-training night. This possibility was not corroborated, however, by the observed (at multiple regression analysis) lack of relationships between the improvement rate at first-day retrieval and the values of sleep parameters of post-training night.
The only partial evidence obtained is a not unique outcome in the investigation on patients with chronic sleep disorders (for review, see Cipolli et al., 2012). It seems plausible that the lack of significant relationships was due to the wide inter-individual variability in both sleep parameters and performance speed of NC patients. Concerning sleep parameters, the age range in our study (about 30 years), due to the rarity of the disease and the consequent difficulty of sampling, was much higher than that of studies on normal subjects (about 5 years). This wide range, by conveying conspicuous age-related variations in the sleep parameters (in particular, Stage 2-NREM, SWS and REM sleep: Ohayon et al., 2004) with the most impact on motor skills consolidation (for review, see Diekelmann and Born, 2010), could have concealed substantial relationships between improvement rate and sleep parameters (in both patients and controls). It is apparent that pertinent evidence in favour of this interpretative hypothesis may be gathered by assessing samples of patients (possibly enrolled in collaborative studies) with a smaller age range (regardless of the difficulties of enrolment).
Concerning performance speed, the wide interindividual variability may be due to the influence of prior sleep on fast learning at training, and/or of post-training daytime sleepiness on the deterioration of this initial consolidation. The lack of subjective sleepiness at the time of training, which was contrasted by allowing to take a nap until an hour before each session (all participants always self-rated sleepiness at the lowest level on SSS), did not rule out the possibility of a negative influence of prior sleep on fast learning in NC patients. Indeed, studies on normal subjects have shown that not only acute sleep deprivation, but also altered sleep (obtained for example by provoking mild sleep disruption, which reduces overall the amount of SWS) negatively affects the encoding-related activation of hippocampus and the memory performance in the next morning (Van Der Werf et al., 2009). The higher score in the Sleep Fragmentation Index and the lower proportion of SWS in post-training night of our patients compared with controls were suggestive of similar alterations also in pre-training night.

Moreover, the trend toward a smaller improvement after post-training-night in NC patients relative to controls is also compatible with the possibility that their initial consolidation was more deteriorated because of the great daytime sleepiness experienced over the late morning and afternoon (Mullington and Broughton, 1993). Indeed, our patients were not allowed to take any post-training nap, which has a restorative function for motor (Korman et al., 2007) and visual skills (Mednick et al., 2003) in normal subjects. Post-training sleepiness could have disrupted the initial consolidation in the patients with greater daytime sleepiness, to be recovered by the following night sleep. The hypothesis of a wide variability in the detrimental effect of daytime sleepiness on the consolidation of new information fits well with the habit of NC patients of taking one or more naps (Broughton and Mullington, 1994).

Pertinent evidence in favour of the influence of either or both these factors on the fast and/or slow learning of motor skills may be expected from coordinated studies assessing the consolidation level reached after post-training night according to whether (a) prior sleep results more or less altered at PSG recording of previous night, and (b) one or naps are taken over the post-training wake interval. Were the next-day improvement more conspicuous for NC patients taking naps (and, in particular, for the patients with a prior disturbed sleep) an important effect for the consolidation of motor skills should be attributed to naps, besides that of restoring and alerting from fatigue and excessive sleepiness (Mullington and Broughton, 1993). Clarifying the possible compensatory function of daytime naps would be useful not only to refine our knowledge of the relationship between sleep and memory, but also to identify effective strategies to improve motor learning in the everyday life of NC patients.

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