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SCIENTIFIC INVESTIGATIONS

Overnight Motor Skill Learning Outcomes in Obstructive Sleep Apnea: Effect of Continuous Positive Airway Pressure

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Study Objective: To determine the effectiveness of continuous positive airway pressure (CPAP) therapy in alleviating known impairments in the overnight consolidation of motor skill learning in patients with obstructive sleep apnea (OSA).

Methods: Twenty-five patients with untreated moderate-severe OSA, 13 first-night CPAP users, 17 compliant CPAP users, and 14 healthy control patients were trained on a motor sequence learning task (Sequential Finger Tapping Task, SFTT) and were subsequently tested prior to and after polysomnographic recorded sleep. Measures of subjective sleepiness (Karolinska Sleepiness Scale) and sustained attention (Psychomotor Vigilance Task) were also completed before and after sleep.

Results: Typical analyses of overnight improvement on the SFTT show significantly greater overnight gains in motor task speed in controls (+11.6 ± 4.7%, p = 0.007) and compliant CPAP users (+8.9 ± 4.3%, p = 0.008) compared to patients with OSA (−4.86 ± 4.5%). Additional analyses suggest that these improvements in motor performance occurred prior to the sleep episode, as all groups significantly improved (15% to 22%) over a 10-min presleep rest period. Thereafter, performance in all groups significantly deteriorated over sleep (6% to 16%) with trends toward patients with OSA showing greater losses in performance compared to control patients and compliant CPAP users. No between-group differences in subjective sleepiness and sustained attention were found presleep and postsleep.

Conclusions: The current data suggest impairments in overnight motor learning in patients with OSA may be a combination of deficient stabilization of memory over a sleep episode as well as increased vulnerability to time on task fatigue effects. Compliant CPAP usage possibly offsets both of these impediments to learning outcomes by improving both sleep quality and subsequent daytime function.

Keywords: cognitive impairment, consolidation, CPAP, learning, memory, motor skills, obstructive sleep apnea, OSA, sleep dependent

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INTRODUCTION

Numerous findings suggest that sleep promotes the consolidation of memory.[1,2] After training on explicit motor sequence learning tasks, individuals typically demonstrate further significant 'offline' enhancements in motor performance (in the absence of further practice) after an episode of sleep, whereas no such improvements are found after a similar duration of wakefulness.[3,4] These benefits in performance are attributed to enhanced memory consolidation processes occurring during sleep.[5,6] Behaviorally, these skill improvements are often termed 'offline' or 'sleep dependent' learning.[7]

Recently, a number of studies have shown that patients with obstructive sleep apnea (OSA) do not demonstrate these motor skill improvements following a sleep episode.[8–11] Furthermore, this impairment has been shown to be associated with the extent of sleep fragmentation occurring during intervening sleep.[9] To our knowledge, it is still unknown if this impairment can be alleviated by effective treatment of OSA.

Continuous positive airway pressure (CPAP) is the current gold standard treatment therapy for OSA and has been shown to successfully reduce apnea-hypopnea index (AHI), alleviate primary OSA symptoms, and improve objective sleep quality.[12–15] As the successful consolidation of motor learning appears to depend specifically on the quality and continuity of the intervening sleep, CPAP would be expected to be effective in normalizing these sleep dependent processes. Furthermore, a single night of CPAP usage, if sleep is of sufficient quality, may result in a noticeable treatment effect.

The current study therefore aimed to measure overnight motor learning outcomes in control participants, patients with untreated OSA, and those using CPAP treatment at both first night of use, and after several weeks of sustained/compliant

BRIEF SUMMARY

Current Knowledge/Study Rationale: Compared to healthy controls, patients with obstructive sleep apnea (OSA) do not demonstrate typical overnight gains in the consolidation of motor skill learning. It is not currently known if this impairment can be rectified by successful treatment.

Study Impact: The findings of this study demonstrate a consistently impaired aspect of learning and memory in patients with OSA that appears to improve with successful CPAP treatment.

usage. We hypothesized that similar to control patients, motor skill learning outcomes in CPAP patients would be superior to those in patients with untreated OSA.

METHODS

Design

A between-subjects design was used to compare motor skill learning between separate groups of: untreated patients with OSA, first-night CPAP users, compliant CPAP users (> 6 h CPAP usage per night for at least 6 w) and healthy sleeping control participants.

Participants

Sixty-seven patients attending hospital-based sleep laboratories for a standard diagnostic assessment of suspected OSA were recruited. Thirty-two patients who were found to have an AHI higher than 15 and were included in the OSA group. Thirteen patients attending the same laboratories for a CPAP implementation study (first night of CPAP) were recruited. An additional group of 19 'compliant' CPAP users were recruited from the general public. Compliance was defined as using CPAP for at least 6 w and to have an average nightly usage longer than 6 h per night. This usage was confirmed by data downloaded from the participant's own CPAP device. Twenty-five healthy control participants with no suspected sleep issues and classified as having low risk of OSA (as determined by the Berlin Questionnaire[16]) were also recruited from the general public. All participants (controls and compliant CPAP users) underwent full polysomnography to confirm the absence of a sleep disorder and/or appropriate control of OSA with CPAP treatment. Among the control participants, four individuals were found to have OSA (AHI > 5) and were thus excluded. Periodic leg movements (PLM) were noted during several of the overnight sleep studies, and 12 participants were excluded (4 OSA, 2 compliant CPAP, 6 controls) for having PLM indexes higher than 15. Patients in the OSA group constituted a reference group for which controls, first-night, and compliant CPAP users were matched to by age (± 5 y).

In addition to the individual group-based recruitment and screening detailed just described, all patients and participants were rigidly screened for and excluded if they had: a history of alcohol or drug dependence, a hospitalization or surgical procedure in the previous month, a history of respiratory or heart disease, any (diagnosed or suspected) learning disability, psychiatric (including depression), neurological, or other sleep condition, were currently taking any recreational, sedative, antidepressant or antipsychotic medications or drugs.

Procedure

Patients with OSA and first-night CPAP users were recruited and tested during the course of their hospital-based diagnostic or CPAP implementation sleep study. Compliant CPAP users and control participants underwent the same procedure at a university-based sleep laboratory. Participants arrived between 19:00 and 20:00. After screening and recruitment, the Epworth Sleepiness Scale (ESS)[17] and the Wechsler Abbreviated Scale of Intelligence (WASI-II)[18] were completed. The two-subtest form involving vocabulary and matrix reasoning subtests was used to generate an IQ score (Full Scale Intelligence Quotient; FSIQ-2). At 20:00, participants completed a battery of computer tasks testing subjective sleepiness (as measured by the Karolinska Sleepiness Scale [KSS][19]), sustained attention (Psychomotor Vigilance Task [PVT]), and motor skill learning as measured by the Sequential Finger Tapping Task (SFTT, described in detail in the next paragraphs). After testing, participants were prepared for polysomnographic recordings. After 21:30, participants were allowed to sleep when they desired, lights out ranged between 21:30 and 23:00 at the participant's discretion. The following morning, participants were awakened at 05:30. In order to reduce the effect of sleep inertia on task performance, a period of 20 min was allowed before participants were retested on the KSS, PVT, and SFTT. Ethics approval for thus study was obtained from the Monash Health Human Research Ethics Committee (HREC, Ref # 11265A).

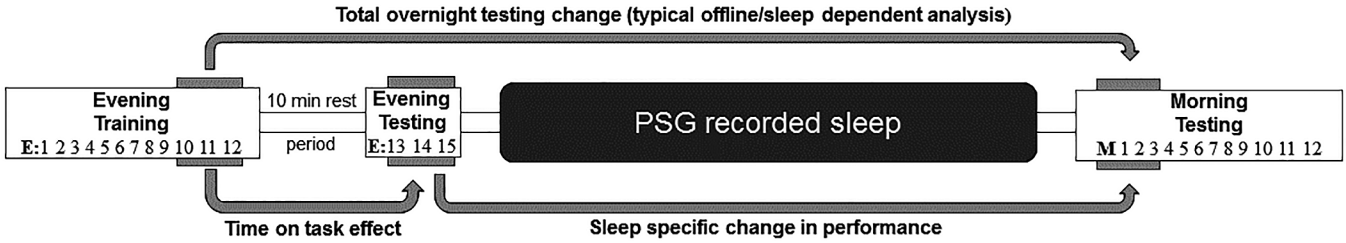
Sleep Recording

Polysomngraphic sleep recording and respiratory scoring were performed according the 2007 American Academy of Sleep Medicine scoring manual. Hypopneas were scored according to the 'alternate' criteria.[20] A six-channel electroencephalogram (EEG; including leads F3, F4, C3, C4, O1 and O2), bilateral electrooculogram (EOG), mentalis/submentalis as well as anterior tibialis electromyogram (EMG) and electrocardiogram (EEG) were used. Respiratory airflow was measured via both a nasal/oral airflow thermistor and a nasal cannula. Thoracic and abdominal respiratory inductance plethysmography (RIP) belts measured respiratory effort. Pulse and blood oxygen saturation were measured via fingertip oximeter.

Motor Skill Learning

Motor skill learning was measured using SFTT.[3] This task requires the participant to type a five-digit sequence (e.g., 4 1 3 2 4) using a computer keyboard using their nondominant hand. Participants were required to reproduce the sequence as quickly and as accurately as possible during a 30-sec trial period. Performance speed on the SFTT was measured by the number of correctly typed sequences per 30-sec trial. Typically, 12 training trials (E1–12) are completed in the evening to assess the acquisition of the motor sequence, and an additional 12 testing trials are completed in the morning following sleep (M1–12). Offline learning, or changes in performance that occur in the absence of training, is typically measured by the change in correct sequences typed between the average of the final three evening trials (E10–12) and the first three morning trials (M1–3). The current study incorporated an additional methodology for the SFTT, as described by Brawn et al.,[21] used to separate time-on-task effects on typing performance. After completing 12 evening training trials (E1–12), participants completed an additional three testing trials (E13–15) after a short 10-min rest period (**Figure 1**). Time-on-task fatigue effects on performance are allowed to alleviate over this rest and can be quantified by the difference in performance between E10–12 and E13–15 (i.e., the change in performance over this interval). The change in performance specifically occurring over the sleep episode

Figure 1—Sequential Finger Tapping Task.



Testing protocol used for the Sequential Finger Tapping Task (SFTT), adapted from Brawn et al.[21] Twelve practice trials (E1–12) are completed in the evening. Three further testing trials (E13–15) are completed 10 min later. In the morning, 12 more testing trials (M1–12) are completed. Time-on-task fatigue is measured by the change in performance from the average of E13–15 minus the average of E10–12. Sleep-specific change in performance is measured by the average of M1–3 minus E13–15. The total overnight change in performance, which represents the typically analyzed overnight/consolidation related learning change, is measured by the average of M1–3 minus the average of E10–12.

(sleep specific change) is measured as the difference between the average of final trials prior to sleep (E13–15) and the first trials completed in the morning (M1–3). It should be noted that this task and design by its nature measures changes in performance between test and retest sessions. Therefore, this task is unable to specifically differentiate whether offline changes in motor performance can be specifically attributed to the memory consolidation, storage, or retrieval processes. Therefore, these outcomes are discussed under the broader term, learning.

A minimum performance criterion of 10 sequences per trial was set. If participants were unable to produce more than 10 correct sequences on at least one trial prior to sleep, they were excluded from analysis. This criteria was based on previous findings showing particularly low-performing children and adults do not show expected offline improvements in typing performance.[22]

Statistical Analysis

Between-subjects analysis of variance (ANOVA) compared sleepiness, sustained attention, and motor skill learning between groups (OSA, first-night CPAP, compliant CPAP, controls). KSS ratings, mean response time, and the number of attention lapses (response times longer than 500 msec) on the PVT were compared between groups both presleep and postsleep. To normalize PVT data, transformations for mean response time ($\frac{1}{RT/1000}$) and number of attentional lapses ($\sqrt{N}+\sqrt{N+1}$) were completed prior to statistical analysis. The change in SFTT performance speed was compared between groups across three testing intervals of interest. (1) Over the total overnight testing period (M1–3 minus E10–12, the typically used method of measuring overnight consolidation related changes in task performance, disregarding the added intervening evening post rest testing trials). (2) Over the 10-min rest period (E13–15 minus E10–12, in order to measure offline performance changes due to time on task effects). (3) Over the sleep period (M1–3 minus E13–15, to assess the offline performance changes occurring specifically over the sleep interval). See **Figure 1**.

RESULTS

Two patients with OSA did not reach the SFTT performance cutoff of 10 sequences per trial prior to sleep (see Methods), and two participants (one with OSA, one control participant) were removed for producing the wrong typing sequence in the morning. All four patients were removed from subsequent analyses. Final groups consisted of 24 patients with untreated OSA, 13 patients with first-night CPAP, 17 compliant CPAP users, and 14 control patients.

Demographics and Sleep Variables

Table 1 shows means, standard error of the mean, and group differences for the demographic and recorded sleep variables. Importantly, there were no age differences between groups. Reflecting the differing clinical characteristics of the groups, post hoc analyses (Fisher's Least Significant Difference) show body mass index (BMI) was significantly lower in control participants compared to those with OSA ($p < 0.001$) and both first-night ($p = 0.001$) and compliant ($p = 0.043$) CPAP groups. Controls had a lower ESS score compared to each group (OSA: $p < 0.001$, first-night CPAP: $p < 0.001$, compliant CPAP: $p = 0.032$). Patients with OSA also had lower average FSIQ scores compared to controls ($p = 0.005$) as well as first-night ($p = 0.031$) and compliant ($p = 0.002$) CPAP groups.

The groups differed on a number of recorded sleep variables. Sleep efficiency was higher in compliant CPAP users compared to patients with OSA ($p = 0.011$) and patients with first-night CPAP ($p = 0.011$). Patients with OSA had significantly more N1 sleep compared to both CPAP groups (first night: $p = 0.003$, compliant: $p = 0.005$) as well as less N3 compared to all groups (control: $p < 0.001$, first-night CPAP: $p = 0.001$, compliant CPAP: $p = 0.001$). Rapid eye movement (REM) sleep duration was also significantly shorter in patients with OSA compared to compliant CPAP participants ($p = 0.006$). Expectedly, patients with OSA had higher arousal index (ArI) and AHI compared to control patients and each CPAP group (all $p < 0.001$). Periodic leg movement indexes (PLMIs) were higher in compliant CPAP patients compared to patients with OSA ($p = 0.005$) and first-night CPAP users ($p = 0.025$); as this group had a mean PLMI of 3.92 ± 89, this difference is unlikely to be clinically significant. Data from compliant CPAP users' own CPAP devices showed an average nightly usage of 401.9 ± 13.9 min and an average AHI of 1.5 ± 0.4 over the past 30 days.

Table 1—Demographic and sleep variables between groups.

	OSA (n = 24)	1st night CPAP (n = 13)	Compliant CPAP (n = 17)	Control (n = 14)	Significance
Age (y)	47.2 ± 1.7	47.7 ± 1.9	48.5 ± 2.0	47.0 ± 2.7	p = 0.930
BMI (kg/m^2)	34.8 ± 2.3	35.0 ± 2.5	30.5 ± 1.1	25.2 ± 0.8	**p = 0.001**
ESS	8.8 ± 1.2	9.7 ± 1.2	7.1 ± 0.7	3.9 ± 0.7	**p = 0.004**
FSIQ-2	100.5 ± 2.5	110.2 ± 2.6	113.5 ± 2.3	113.1 ± 5.0	**p = 0.003**
Sex	20 male	8 male	13 male	6 male	p = 0.061
TST (min)	324.7 ± 11.7	305.8 ± 20.3	350.5 ± 13.1	344.4 ± 16.3	p = 0.155
SE (%)	76.6 ± 2.4	74.8 ± 3.2	86.1 ± 2.9	82.1 ± 2.2	**p = 0.032**
SOL (min)	16.3 ± 2.7	21.2 ± 3.6	10.2 ± 3.2	15.3 ± 3.5	p = 0.158
N1 (min)	45.6 ± 6.9	18.7 ± 0.4	25.4 ± 2.7	35.5 ± 4.8	**p = 0.013**
N2 (min)	190.7 ± 13.0	153.5 ± 15.8	191.4 ± 8.8	167.6 ± 9.5	p = 0.118
N3 (min)	31.1 ± 4.8	68.9 ± 12.0	62.9 ± 6.0	74.4 ± 8.4	**p < 0.001**
REM (min)	45.1 ± 5.4	56.2 ± 10.1	69.6 ± 5.3	51.4 ± 5.5	**p = 0.030**
WASO (min)	71.6 ± 11.3	81.8 ± 15.3	44.9 ± 7.6	57.0 ± 6.5	p = 0.120
ArI (events/h)	37.8 ± 4.6	15.6 ± 2.5	6.6 ± 0.8	7.6 ± 0.8	**p < 0.001**
AHI (events/h)	58.4 ± 5.8	11.1 ± 2.8	1.1 ± 0.4	0.6 ± 0.2	**p < 0.001**
SpO_2 nadir (%)	71.8 ± 2.2	86.1 ± 1.4	90.2 ± 0.6	91.1 ± 0.7	**p < 0.001**
SpO_2 < 90% (% TST)	12.4 ± 3.0	3.2 ± 1.6	0.2 ± 0.1	0.0 ± 0.0	**p < 0.001**
PLMI (events/h)	0.6 ± 0.4	1.0 ± 1.0	3.4 ± 1.4	1.6 ± 0.9	**p = 0.034**
CPAP (cmH_2O)	–	11.3 ± 1.2	9.0 ± 0.5	–	p = 0.071
Diag AHI	–	49.6 ± 12.7	30.5 ± 4.5	–	p = 0.461

Values are expressed as mean ± standard error of the mean. Bold values indicate statistical significance (p < 0.05). AHI, apnea-hypopnea index; AI, arousal index; BMI, body mass index; CPAP, continuous positive airway pressure; Diag AHI, pretreatment diagnosed AHI; ESS, Epworth Sleepiness Scale; FSIQ-2, two subtest Full Scale Intelligence Quotient; PLMI, periodic leg movement index; REM, rapid eye movement; SE, sleep efficiency; SOL, sleep onset latency; SpO_2, saturation of oxygen; TST, total sleep time; WASO, wake after sleep onset.

Motor Skill Learning

Baseline SFTT performance at the beginning of practice (average number of correctly typed sequences per trial at E1–3) was higher in compliant CPAPs (15.00 ± 1.30 sequences) compared to OSA (10.40 ± 1.10, p = 008 and first-night CPAP users (9.87 ± 1.48, p = 0.011). Baseline performance for controls (12.07 ± 1.43) was not significantly different to the other groups (p < 0.05). All groups showed significant improvements in performance during the 12 evening practice trials, and at the end of training there were no longer any significant differences in total performance between groups (average number of correct sequences at E10–12, $F(3,68) = 1.745$, p = 0.167).

Total Change over the Testing Period

Total change over the testing period (typical overnight analysis[3,4]). **Figure 2** shows the change in performance from the end of practice in the evening (E10–12) to the first morning trials (M1–3), disregarding the added postpractice 10-min rest evening test trials (E13–15). This reflects the typical analysis measuring offline learning that has been used in previous studies.[8,9] Over this interval, OSA (−4.86 ± 4.5%) and first-night CPAP users (+1.6 ± 4.9%) showed nonsignificant changes in SFTT typing performance. Compliant CPAP users (+8.9 ± 4.3%) and control patients (+11.6 ± 4.7%) demonstrated significant improvements. Between-group differences are clearly evident ($F(3,68) = 3.912$, p = 0.013, partial $\mu^2 = 0.155$), with control patients (p = 0.007) and compliant CPAP users (p = 0.007) evidencing greater gains in performance compared to patients with OSA. Differences between control patients and first-night CPAP patients approached significance (p = 0.088). This statistical outcome was unchanged after covarying for group differences in FSIQ and BMI (specifically IQ lower and BMI higher in the OSA group, $F(3,67) = 3.066$, p = 0.035, partial $\mu^2 = 0.131$). To ensure that these differences were not due to or affected by unequal sample size between groups, additional independent samples *t*-tests were used to compare groups composed only of specific participant age matches (OSA-control: n = 14/14, OSA-compliant CPAP: n = 17/17). Improvements in the number of correctly typed sequences remained significantly higher for control patients ($t(26) = 3.563$, p = 0.001, $d = 1.34$) and compliant CPAP patients ($t(32) = -2.296$, p = 0.028, $d = 0.78$) compared to patients with OSA.

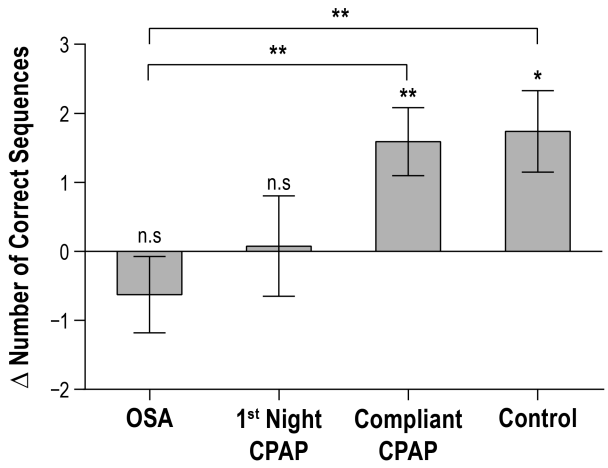
Change in Performance over 10-min Rest

Change in performance over 10-min rest (alleviation of time on task fatigue). Following the postpractice 10- min rest period, all groups demonstrated significant increases (13% to 22%) in the SFTT performance speed (all p < 0.05), see **Figure 3A**. Despite a visual trend toward greater improvement in control patients, and to a lesser extent in compliant CPAP users, the degree of performance gain did not differ between groups ($F(3, 68) = 0.884$, p = 0.454).

Change in Performance over the Sleep Interval

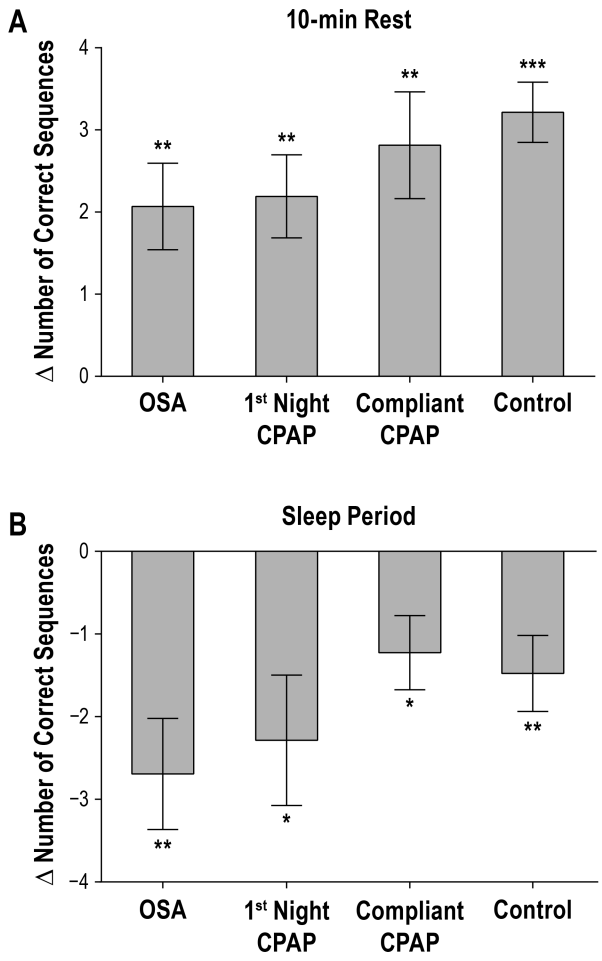
Change in performance over the sleep interval (specific change over sleep). Shown in **Figure 3B**, all groups show significant

Figure 2—Change in number of correctly typed sequences.



Change (Δ) in the number of correctly typed sequences (as measured by the Sequential Finger Tapping Task) over the total overnight testing period between groups: obstructive sleep apnea (OSA), first-night continuous positive airway pressure (CPAP), compliant CPAP, and controls. Between-subjects analysis of variance showed significant differences in performance change between groups; *post hoc* Fisher's least significant difference tests show patients with OSA displayed significantly less improvement compared to controls (p = 0.005) and compliant CPAP users (p = 0.006). Within-subjects *t*-tests were used for each separate group; to test the extent of change in performance (increase/decrease in the number of correctly typed sequences) over this interval, significance is shown above each group bar and is expressed as *p < 0.05, **p < 0.01.

Figure 3—Total overnight change in Sequential Finger Tapping Task.



Total overnight change (Δ) in Sequential Finger Tapping Task (SFTT) performance (change in number of correctly typed sequences) is categorized into two measured components. **(A)** The change over the 10-min rest period (E13–15 minus E10–12) between groups. Within-subjects *t*-tests reveal significant improvements in correctly typed sequences for each group. No between-group differences were found (p = 0.417). **(B)** The change in SFTT performance specifically over the sleep period (M1–3 minus E13–15). All groups showed significant deteriorations in performance over this interval. Once again, between-subjects analysis of variance reveals no significant differences between groups (p = 0.314). For both **(A)** and **(B)**, significance for within-subjects *t*-test are expressed as *p < 0.05, **p < 0.01, ***p < 0.001.

decreases in SFTT performance over the sleep period (all p < 0.05). Similar to the previous interval, no significant differences were found in the amount of performance deterioration between groups ($F(3,68) = 1.188$, p = 0.321). Similarly a nonsignificant visual trend appears to show less deterioration in performance for compliant CPAP users and controls.

KSS and PVT

To assess the possibility that group differences in motor learning and performance were driven by differences in sleepiness and alertness during either the evening training or morning testing sessions, analysis was performed on KSS and PVT data. As shown in **Table 2**, there were no significant differences between groups on evening or morning KSS ratings. Similarly, PVT mean response times and the number of attentional lapses were equivalent between groups at both the evening and morning time testing.

Correlational Analysis

To address the potential association between impaired learning and the extent of sleep fragmentation,[9] a correlational analysis was performed between the change in performance specifically over the sleep period and the ArI and the AHI. Due to existing between-group differences in sleep architecture, these analyses were conducted within groups. Negative correlations between sleep-specific change in SFTT performance and ArI were found for all groups (OSA: $r = -0.317$, p = 0.132; controls: $r = -0.166$, p = 0.571); however, these relationships were only statistically significant for compliant CPAP users ($r = -0.509$, p = 0.037, $r^2 = 0.259$) and first-night CPAP patients ($r = -0.559$, p = 0.047, $r^2 = 0.312$). Correlations between AHI and performance change were significant only for first-night CPAP patients ($r = -0.703$, p = 0.007, $r^2 = 0.494$).

DISCUSSION

The current study examined overnight motor skill learning outcomes as measured by the SFTT, in age-matched healthy control participants, patients with untreated OSA, and those

Table 2—Evening and morning Karolinska Sleepiness Scale ratings, mean Psychomotor Vigilance Task response times, and number of attentional lapses.

	OSA (n = 24)	1st night CPAP (n = 13)	Compliant CPAP (n = 17)	Control (n = 14)	Significance
KSS ratings					
Evening	4.0 ± 0.4	4.1 ± 0.5	4.4 ± 0.5	4.4 ± 0.5	p = 0.866
Morning	4.5 ± 0.4	5.1 ± 0.3	4.7 ± 0.4	4.7 ± 0.5	p = 0.834
PVT response time					
Evening	261.6 ± 5.5	261.2 ± 9.2	257.90 ± 6.6	275.8 ± 8.4	p = 0.334
Morning	281.6 ± 10.3	267.4 ± 9.2	257.83 ± 6.4	275.0 ± 9.6	p = 0.304
PVT # of lapses					
Evening	1.6 ± 0.5	0.9 ± 0.2	1.2 ± 0.4	0.8 ± 0.2	p = 0.766
Morning	3.3 ± 1.5	1.7 ± 0.8	0.7 ± 0.3	1.1 ± 0.5	p = 0.254

Values are expressed as mean ± standard error of the mean. CPAP, continuous positive airway pressure; KSS, Karolinska Sleepiness Scale; OSA, obstructive sleep apnea; PVT, Psychomotor Vigilance Task.

receiving CPAP treatment (at both first night and after compliant usage). Controls showed significantly greater enhancements (+11.6 ± 4.7%) in typing speed compared to patients with OSA (−5.36 ± 3.5%) over the total overnight testing period, supporting previous studies.[8–10] This period represents the typically measured overnight improvement (difference between final trials of practice E10–12 to the first trials of testing in the morning M1–3). As expected, successfully treated compliant CPAP users (+8.9 ± 4.3%) also showed significantly greater enhancements in performance compared to patients with untreated OSA. CPAP usage after the first night (+1.6 ± 4.9%), however, showed only slight nonsignificant overnight improvements. These results confirm previous findings of impaired overnight learning in patients with OSA[8–10] and extend the literature to show that this impairment is not present in patients who are receiving optimal CPAP treatment.

First-night CPAP users did not show significant improvements in overnight SFTT performance; however, this first night of CPAP usage constituted their laboratory-based implementation study and the treatment pressure was being simultaneously titrated overnight. As a result, CPAP treatment pressure is not optimal for the entire night (as shown by residual AHI of 11.1 ± 2.8 events/h). In addition, sleep quality was likely negatively affected by the novelty of the new treatment. As sleep quality remained poor in first-night CPAP users, despite greatly reduced AHI compared to patients with OSA, an improvement in overnight learning outcomes would not be expected in this group.

In agreement with previous findings,[9] a negative relationship between the arousal index and the change in motor task performance over the sleep interval was found in the CPAP-treated groups. Although not statistically significant for patients with OSA and control patients, these relationships, however, were in expected directions. These findings in general are consistent with the notion that deficient overnight learning is the result of diminished sleep quality or disrupted sleep continuity and can be improved when sleep is objectively improved with a treatment intervention.

Various cognitive impairments in patients with OSA, primarily related to attention, executive, memory, and motor function, have been described for many years.[23–26] CPAP has shown mixed success in rectifying these impairments,[23,26–29] although lingering posttreatment impairments are not uncommon.[23,30,31] In contrast, several large-scale studies in recent years have found cognitive impairment to be mild or nonsignificant in patients with OSA compared to control patients.[32–34] Furthermore, these mild decrements in functioning appear to be better related to oxygen desaturation parameters, rather than AHI or fragmented sleep characteristics.[32,33] The current study and previous studies that have investigated overnight learning outcomes using the SFTT[8–10] have established an area of cognition that appears to be consistently dysfunctional in patients with OSA of a range of different severities. Furthermore, in contrast to hypoxic associated impairments, the current deficiencies in overnight learning appear to be the result of specific insults to sleep continuity, and appear to be largely rectified with treatment-related improvements in sleep quality.

The current study was the first to use a SFTT testing methodology designed to control for time-on-task effects[21] when examining dysfunctional overnight learning. Including three testing trials prior to sleep, completed 10 min after the end training (see **Figure 1**), allowed the measurement of overnight change in SFTT performance (the typical SFTT sleep dependent analysis), as well as to separate practice-based time-on-tasks effects from the remaining change in performance specifically occurring over the sleeping interval. A key finding of the current data was that SFTT performance speed was demonstrated to significantly improve in all groups after a 10-min rest period by approximately 13% to 22%. This finding is consistent with that of Brawn and colleagues[21] and has been attributed to the alleviation of time-on-task fatigue and reactive inhibition effects accumulated during extended periods of typing during the previous practice session. Over the specific sleep interval (change from evening postrest trials to the first three morning trials), performance was then shown to significantly deteriorate (6% to 16%) in all groups. No significant group differences were found at either of these rest or sleep intervals; however, there was a trend toward greater gains after rest, and lesser deterioration over the sleep interval in compliant CPAP users

and controls (see **Figure 3A** and **3B**). Nevertheless, the total overnight change (the typical SFTT overnight analysis) clearly showed differing outcomes for patients with OSA compared to controls or compliant CPAP users. It is possible that the current sample lacks sufficient power to differentiate these smaller component effects. Although needing further investigation, these findings suggest that these deficient enhancements in overnight learning observed in patients with OSA (and shown to be preserved in CPAP patients in the current study) may be due to a combination of smaller group differences in the ability to overcome time-on-task fatigue and a reduced ability to consolidate or stabilize learning over the sleep episode. Compliant CPAP usage would therefore be expected to offset both of these components by its effect on improving sleep quality (in relation to stabilizing learning) as well as subsequent daytime functioning (in relation to task fatigue).

Two limitations in the study design should be acknowledged. First, a within-subject or a placebo control design was not used in the current study, and therefore, a specific treatment effect of CPAP must be inferred from our independent OSA and CPAP groups. The negligible gains after the first night of CPAP (compared to OSA) and the significantly greater SFTT performance after compliance, along with the negative relationship between arousal index and task performance, suggests that improved sleep quality from compliant CPAP use likely rectifies this impairment in patients with OSA. Second, the current design did not compare changes in motor skill performance over an equivalent retention interval of daytime wakefulness (use a PM-AM, AM-PM design). Therefore, although patients with OSA demonstrate poorer overnight learning outcomes compared to controls and complaint CPAP users, the extent to which this is learning is specifically dependent on sleep is not known. Considering that this impairment in overnight learning appears to be at least partially related to a presleep fatigue effect, it is unlikely that this observed group difference is entirely a sleep dependent deficit. Additionally, the deterioration in performance measured specifically over the sleep interval may not necessarily be a sleep dependent phenomenon, as such an effect could conceivably occur over a daytime retention interval. Regardless of whether this is a sleep dependent impairment, it still entails a serious impediment to neurocognitive functioning. A particular strength of the current study was that a rigorous screening process was used to exclude patients with abnormally poor motor skill or comorbid psychiatric illness (most notably depression), both of which have been shown independently to have a negative effect of motor skill learning outcomes,[22,35] and are more common is OSA populations.

In summary, the current study is consistent with previous investigations, showing that patients with OSA display deficient overnight motor skill learning.[8–10] This study builds on this finding, showing that this impairment is not present in patients compliant with CPAP treatment. The alterations to the typical SFTT learning methodology used in the current study suggest that there are distinct intervening changes in motor performance that occur within this overnight period. These changes include rapid improvements in performance occur following a short rest, and performance deteriorating from this postrest level over the sleep interval. Small between group variations in these two effects, appear to sum into the overnight learning deficiency described above. The relative importance of this novel finding and how this relates to OSA-related impairments in motor performance and subsequent offline learning warrant more detailed investigation.

ABBREVIATIONS

ArI, arousal index
ANOVA, analysis of variance
BMI, body mass index
CPAP, continuous positive airway pressure
FSIQ, full scale intelligence quotient
KSS, Karolinska Sleepiness Scale
NREM, non-rapid eye movement
OSA, obstructive sleep apnea
PVT, psychomotor vigilance test
PLMI, periodic leg movement index
REM, rapid eye movement
SFTT, Sequential Finger Tapping Task

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