

# Effects of CPAP therapy on cognitive and psychomotor performances in patients with severe obstructive sleep apnea: a prospective 1-year study

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## Abstract

**Study objectives** We prospectively investigated the effects of continuous positive airway pressure (CPAP) on long-term cognitive and psychomotor performances, and excessive daytime sleepiness in severe obstructive sleep apnea (OSA) patients.

**Methods** A total of 40 patients were recruited and 23 patients with severe OSA fully completed the study protocol to investigate the effects of CPAP therapy on psychomotor performance at 1, 3, and 6 months and 1 year following initiation of the therapy. Psychomotor CRD-series tests measuring reaction times of light stimulus perception, solving simple arithmetic operations, and complex psychomotor limb coordination, were used in this study. The data collected following CPAP therapy were compared to baseline values prior to the CPAP treatment for each patient.

**Results** All of the measured variables improved following CPAP treatment. However, the most pronounced effect was observed in improvement of reaction times to complex psychomotor limb coordination test ( $p < 0.05$ ). Self-reported evaluation of excessive daytime sleepiness measured by Epworth Sleepiness Scale (ESS) showed significant decrease from  $10.0 \pm 1.1$  before to  $3.5 \pm 0.5$  ( $p < 0.001$ ), after 1 year on CPAP therapy.

**Conclusions** The CPAP therapy improved cognitive and psychomotor performance on CRD-series tests with the most significant improvement observed in complex psychomotor limb coordination of severe OSA patients.

**Keywords** Obstructive sleep apnea · Continuous positive airway pressure · Cognitive · Psychomotor · Sleepiness

## Introduction

Obstructive sleep apnea (OSA) is one of the most common sleep-related breathing disorders characterized by repetitive apneas and hypopneas resulting with hypoxemia and disrupted sleep [1]. OSA has been associated with various

cognitive dysfunctions in the area of non-verbal, verbal and working memory, executive and motor functioning, psychomotor speed, visuospatial functions, attention, and vigilance [2–7]. The underlying mechanism could be related to the repetitive obstructions of the upper airway and arousals resulting with sleep fragmentation, hypoxemia, and excessive daytime sleepiness (EDS) [7]. However, relative role of these compounding factors on neuropsychological changes remains to be clarified [8]. Severity of the cognitive deficits is likely to depend on severity of OSA, degree of hypoxia, and duration of OSA [9, 10].

Despite the variety of treatment options for OSA, continuous positive airway pressure (CPAP) therapy remains the first-choice treatment option in a case of severe OSA. Generally held view is that CPAP therapy improves cognition in patients with OSA [11]. Evidence was provided on effectiveness of CPAP therapy in alleviating impairments in the overnight consolidation of motor skill learning in

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patients with moderate to severe OSA [12]. However, reports on the level of cognitive improvement following CPAP therapy differ between studies [11] due to the employment of different neuropsychological tests [2]. Computerized Complex Reactionmeter Drenovac (CRD) series of cognitive tests along with basic information on the speed of mental processing provides information on the peculiarities of mental functioning in the process of psychomotor tests. Unlike conventional tests, CRD series of tests can be repeated several times on the same subjects with the same outcome of the test results. Furthermore, standard tests of the CRD series are applicable to the respondents of all ages; they do not rely on acquisition of certain language or other specific knowledge. CRD tests have been used to evaluate psychomotor performances in different study designs [13–15], and also in a 1-year prospective study for evaluation of the effects of mandibular advancement device (MAD) therapy on cognitive and psychomotor performance in mild and moderate OSA patients [16]. The current study employs a design similar to that of our previous study [16] but investigates potential benefits of CPAP therapy on long-term cognitive and psychomotor performances in patients with severe OSA.

Psychomotor tests performed in this study measured reaction times of perception to light stimulus, reaction times of solving simple arithmetic operations, and of complex psychomotor limb coordination. One could speculate that impaired perceptual motor and cognitive processes may have implications on some complex daily tasks such as driving, which could be diminished in OSA patients suffering from EDS. We hypothesized that psychomotor reaction times on the tests will be significantly improved following CPAP therapy in severe OSA patients.

## Materials and methods

The study was approved by the Ethics Committee of the University of Split School of Medicine (USSM). All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its latter amendments. Informed consent was obtained from all individual participants included in this study.

## Subjects

A total of 25 subjects (22 males, 3 females) with newly diagnosed OSA at the Split Sleep Medicine Center (SMC) were recruited. A diagnosis of OSA was defined in accordance with the guidelines of American Academy of Sleep Medicine (AASM) and European Sleep Research Society (ESRS) [17]. Exclusion criteria were (1) age younger than 18, (2)

history of any OSA treatment prior to the study enrollment, and (3) irregular use of the CPAP following the study enrollment (<4 h of use/night). Subjects included underwent initial medical history interview, physical examination, and anthropometric measurements. The proportions of comorbidities were 14/23 of patients had arterial hypertension, 6/23 diabetes, 3/23 depression, 1/23 asthma, and 4/23 had gastroesophageal reflux disease (GERD). Excessive daytime sleepiness was assessed using self-administered Epworth Sleepiness Scale (ESS), which was previously validated in Croatian language [18].

The subjects for the reference group ( $n = 25$ ) were recruited from the pool of healthy subjects, previously tested on CRD series at Department of Neuroscience, USSM, Split, Croatia. Reference subjects were matched with the OSA patients for their gender, age, BMI, and had no medical record of sleep disturbances. They were tested once on CRD series with the same cognitive and psychomotor tests as OSA patients to compare with the OSA patients results at baseline, prior to CPAP therapy.

## Sleep assessment

Full-night in-laboratory polysomnography (PSG),  $n = 5$  (ALICE 5LE, Philips Respironics, Eindhoven, Netherlands), or full-night unattended polygraphy (PG),  $n = 18$  (PolyMesam, MAP, Martinsried, Germany; SOMNOcheck2, Weinmann, Germany; EmbletaGOLD, ON, Canada), were performed before the initiation of therapy. Data were stored on a computer, manually scored, and evaluated in accordance with the published AASM and ESRS guidelines by the certified sleep physician [19]. Sleep studies lasting less than 6 h were not accepted, and if needed, second PSG/PG was undertaken.

Apnea was defined as complete cessation of respiration airflow for a minimum duration of 10 s, whereas hypopnea was defined as a decrease in airflow of  $\geq 30$  and  $\geq 3$  % desaturation or arousal. Apnea-hypopnea index (AHI) was defined as the average number of apneas and hypopneas per hour of sleep.

## CPAP compliance

CPAP compliance was assessed using SmartCards from CPAP devices. SMC staff contacted participants during the first week in order to ensure proper use, regularity of CPAP usage, and manage any problems. Following the first week, and establishment of regularity of CPAP therapy usage ( $> 4$  h of use/night), patients were asked to regularly visit SMC at the pre-determined time points: 1, 3, 6, and 12 months after the beginning of the CPAP therapy.

## Cognitive and psychomotor performance testing

A computer-generated test, CRD series was used to measure cognitive and psychomotor performance [20]. Several studies have been conducted to evaluate its metric characteristics, particularly the prognostic validity to see how they can evaluate the success in different occupations and conditions [13, 15, 16]. It consists of the software, four electronic instruments, and provides the use of 38 standard tests. CRD series can be used for different age categories and it does not rely on language or any other specific knowledge. It is possible to use the CRD series for multiple retesting on the same subject without the possibility of memorizing the test [20]. Three representative tests were performed, from the simplest to the most complex: test of convergent thinking (CRD11) measuring speed of solving simple arithmetic operations, light signal position discrimination test (CRD311) measuring speed of perception, and test of operative thinking (CRD411) measuring complex psychomotor coordination.

Testing was performed in a quiet, translucent room, between 13:00 and 14:00, at pre-determined time points, under the supervision of an experienced research technician who was blind to the CPAP compliance. Prior to the testing, patients were tested individually using the CRD-series instruments, before reaching stable baseline results, without the tendency of improvement in order to avoid learning effect.

Six parameters were analyzed: total test solving time (TTST), minimum single task solving time (MinT), median single task solving time (MedT), start balast (SB), end balast (EB), and total balast (TB). TTST, MinT, and MedT were descriptors of speed, accuracy, and mental endurance. SB, EB, and TB were indicators of stability calculated as the sum of differences between time spent on each individual item ( $T_i$ ) and a minimum single task solving time ( $TB = \sum T_i - MinT$ ) at the first (SB) and last half (EB) of the test, and the total test (TB) [20].

## Statistical analysis

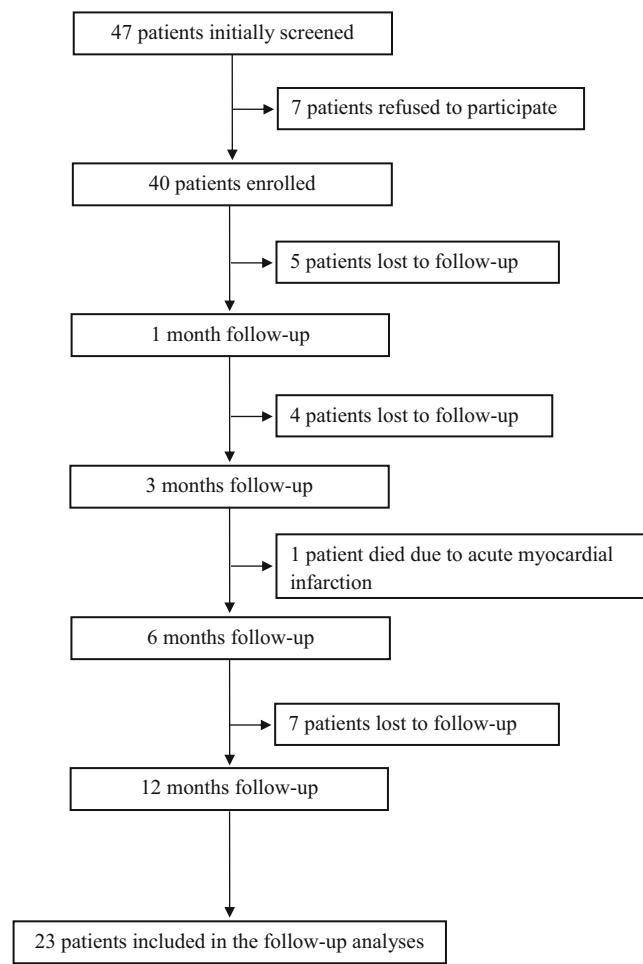
Statistical analyses were performed using statistical software MedCalc for Windows, version 11.5.1.0 (MedCalc Software, Mariakerke, Belgium). To evaluate differences between OSA subjects prior to CPAP therapy and reference group on cognitive and psychomotor test, one-way ANOVA was performed. The comparison of cognitive and psychomotor results, as well as EDS measured by ESS prior to and at pre-determined time points following CPAP treatment were tested using repeated measures ANOVA with Bonferroni post hoc correction. Correlations between improvement in cognitive and psychomotor outcomes with the change in the AHI, average nightly, and monthly CPAP use were calculated using Pearson correlation coefficients. The statistical significance was set at  $p < 0.05$ .

## Results

There were a total of 23 patients with severe OSA who met the inclusion criteria and were enrolled in the study, as shown in Fig. 1, whose demographic and sleep baseline characteristics are presented in Table 1. The mean AHI decreased significantly from  $52.7 \pm 24.0$  events/h at baseline (Table 1) to  $3.1 \pm 3.1$  events/h after 1 year of CPAP therapy ( $p < 0.001$ ). Average use of the CPAP was  $83.1 \pm 21.6\%$  nights per month, with an average CPAP use per night of  $6.2 \pm 1.1$  h. Self-reported EDS measured by ESS showed significant improvement after 1 year of CPAP therapy (ESS score was  $10.0 \pm 1.1$  before and  $3.5 \pm 0.5$  1 year after CPAP therapy,  $p < 0.001$ ; Fig. 2).

## Cognitive and psychomotor performance

Comparative analyses of the baseline results obtained during CRD testing of OSA patients before CPAP therapy and reference subjects are summarized in Table 2.



**Fig. 1** Study flowchart. A total of 47 patients were screened for the study, 23 of whom completed the study follow-up

**Table 1** Demographic and sleep characteristics of patients with obstructive sleep apnea prior to CPAP therapy

Variables	Baseline (T0)
Age (year)	58.39 ± 11.15
Height (cm)	178.0 ± 10.0
Weight (kg)	106.05 ± 17.64
BMI (kg/m <sup>2</sup> )	33.48 ± 4.95
Neck circumference (cm)	46.34 ± 4.86
ESS score	10.0 ± 5.2
AHI (events/h)	52.69 ± 24.02
Mean SpO <sub>2</sub> (%)	90.19 ± 4.38
Lowest SpO <sub>2</sub> (%)	66.67 ± 11.62
ODI (events/h)	52.67 ± 24.81

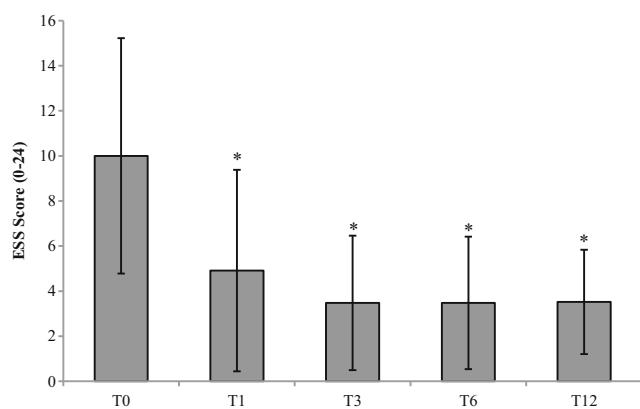
Data are presented as mean ± standard deviation

BMI body mass index, ESS score Epworth Sleepiness Scale score, AHI apnea-hypopnea index, SpO<sub>2</sub> arterial oxygen saturation, ODI oxygen desaturation index

There was improvement on all three CRD-series tests during the 1 year of CPAP therapy, considering total test solving time (TTST), median test solving time (MedT), minimal single task solving time (MinT), and ballast times (SB, EB, TB).

### Light signal position discrimination test (CRD311)

Light signal position discrimination test (CRD311) measured speed of perception. In general, TTST, MedT, and MinT were reduced 1, 3, 6, and 12 months following CPAP therapy, in comparison to baseline ( $F = 3.624, p = 0.019$ ;  $F = 3.544, p = 0.022$ ;  $F = 4.468, p = 0.011$ ; respectively; Table 3 and Fig. 3a). Regarding ballast times, there were no significant differences



**Fig. 2** Epworth Sleepiness Scale (ESS) scores of OSA patients prior to CPAP therapy (T0), 1 (T1), 3 (T3), 6 (T6), and 12 months following the CPAP therapy (T12). Asterisk means significantly different from baseline ( $p < 0.002$ )

**Table 2** Performance on CRD tests for patients with severe obstructive sleep apnea before CPAP therapy and reference subjects

	OSA group (n = 23)	Reference group (n = 23)	p *
Light signal position discrimination			
MinT (s)	0.52 ± 0.11	0.48 ± 0.09	0.147
MedT (s)	0.69 ± 0.1	0.65 ± 0.1	0.568
TTST (s)	43.64 ± 6.56	40.48 ± 5.95	0.752
SB (s)	7.01 ± 3.16	6.84 ± 1.96	0.266
EB (s)	5.31 ± 1.85	4.87 ± 1.39	0.791
TB (s)	12.32 ± 4.7	11.71 ± 3.03	0.555
Solving simple arithmetic operations			
MinT (s)	3.32 ± 0.83	3.02 ± 0.54	0.157
MedT (s)	5.07 ± 1.18	4.87 ± 1.10	0.195
TTST (s)	195.58 ± 49.55	193.91 ± 50.36	0.095
SB (s)	39.3 ± 17.73	46.53 ± 25.12	0.821
EB (s)	42.99 ± 16.87	41.76 ± 14.21	0.366
TB (s)	82.28 ± 32.25	88.29 ± 36.20	0.600
Complex psychomotor coordination			
MinT (s)	0.78 ± 0.19	0.63 ± 0.16	0.005
MedT (s)	1.29 ± 0.42	1.11 ± 0.23	0.075
TTST (s)	72.29 ± 35.5	59.35 ± 16.9	0.124
SB (s)	14.66 ± 10.73	13.18 ± 6.01	0.568
EB (s)	30.22 ± 21.95	24.1 ± 10.33	0.235
TB (s)	44.88 ± 31.4	37.28 ± 14.58	0.300

Data are presented as mean ± standard deviation

CRD Complex Reactionmeter Drenovac, CPAP continuous positive airway pressure, MinT minimum single task solving time, MedT median single task solving time, TTST total test solving time, SB start ballast, EB end ballast, TB total ballast

\*p values were calculated with the use of t test for independent samples

at the pre-determined time points compared to baseline (Table 3).

There were no significant correlations between CRD311 test results and average CPAP use per night (Table 4).

### Test of convergent thinking (CRD11)

Test of convergent thinking (CRD11) measured speed of solving simple arithmetic operations. In general, TTST and MedT were significantly reduced 1, 3, 6, and 12 months following CPAP therapy, compared to baseline ( $F = 11.619, p < 0.001$ ;  $F = 22.419, p < 0.001$ ; respectively; Table 3 and Fig. 3b). MinT was significantly reduced 3, 6, and 12 months following the CPAP therapy, compared to baseline ( $F = 10.626, p < 0.001$ ; Table 3 and Fig. 3b). Regarding ballast times, the results obtained from CRD11 test showed a trend of reduction in all ballast times throughout the study period (Table 3).

There were no significant correlations between changes in CRD11 test results and average CPAP use per night (Table 4).

**Table 3** Performance on CRD tests at baseline, 1, 3, 6, and 12 months after CPAP therapy

	Baseline	1 month	3 months	6 months	12 months
Light signal position discrimination					
MinT (s)	0.52 ± 0.11	0.5 ± 0.11	0.48 ± 0.11	0.48 ± 0.09	0.47 ± 0.09*
MedT (s)	0.69 ± 0.1	0.66 ± 0.11	0.65 ± 0.12	0.65 ± 0.1	0.64 ± 0.11
TTST (s)	43.64 ± 6.56	41.53 ± 6.84	40.6 ± 7.23	41.11 ± 6.46	40.6 ± 6.88
SB (s)	7.01 ± 3.16	6.2 ± 1.63	6.31 ± 1.92	6.77 ± 2.07	6.86 ± 3.05
EB (s)	5.31 ± 1.85	5.11 ± 1.59	5.21 ± 1.54	5.33 ± 1.4	5.27 ± 1.82
TB (s)	12.32 ± 4.7	11.31 ± 2.95	11.52 ± 3.21	12.1 ± 2.95	12.14 ± 4.35
Solving simple arithmetic operations					
MinT (s)	3.32 ± 0.83	3.1 ± 0.71	3.03 ± 0.64*	2.85 ± 0.67*	2.78 ± 0.67*
MedT (s)	5.07 ± 1.18	4.6 ± 1.09*	4.56 ± 1*	4.32 ± 1.03*	4.21 ± 0.91*
TTST (s)	195.58 ± 49.55	181.46 ± 51.01*	178.96 ± 44.42*	168.61 ± 42.68*	164.55 ± 42.28*
SB (s)	39.3 ± 17.73	34.85 ± 17.99	33.58 ± 14.14	34.1 ± 13.69	33.01 ± 16.93
EB (s)	42.99 ± 16.87	38.15 ± 18.13	39.32 ± 18.85	34.75 ± 14.43	34.07 ± 17.57
TB (s)	82.28 ± 32.25	73 ± 32.23	72.9 ± 31.17	68.85 ± 26.55	67.08 ± 30.78
Complex psychomotor coordination					
MinT (s)	0.78 ± 0.19	0.66 ± 0.15*	0.66 ± 0.14*	0.66 ± 0.13*	0.63 ± 0.14*
MedT (s)	1.29 ± 0.42	1.09 ± 0.25*	1.03 ± 0.25*	1 ± 0.24*	0.97 ± 0.18*
TTST (s)	72.29 ± 35.5	57.61 ± 22.05*	54.1 ± 18.68*	47.58 ± 14.35*	50.4 ± 16.72*
SB (s)	14.66 ± 10.73	12.29 ± 8.51*	11.78 ± 8.62*	8.42 ± 4.36*	9.81 ± 5.3*
EB (s)	30.22 ± 21.95	22.15 ± 12.23	19.24 ± 8.91	16.07 ± 7.6*	18.65 ± 10.74
TB (s)	44.88 ± 31.4	34.44 ± 18.8	31.02 ± 15.4*	24.48 ± 11.32*	28.46 ± 13.32

Data are presented as mean ± standard deviation

CRD Complex Reactionmeter Drenovac, CPAP continuous positive airway pressure, *MinT* minimum single task solving time, *MedT* median single task solving time, *TTST* total test solving time, *SB* start ballast, *EB* end ballast, *TB* total ballast

\**p* values were calculated with the use of repeated measures ANOVA with Bonferroni post hoc comparison. Values significantly different from baseline, *p* < 0.05

## Test of operative thinking (CRD411)

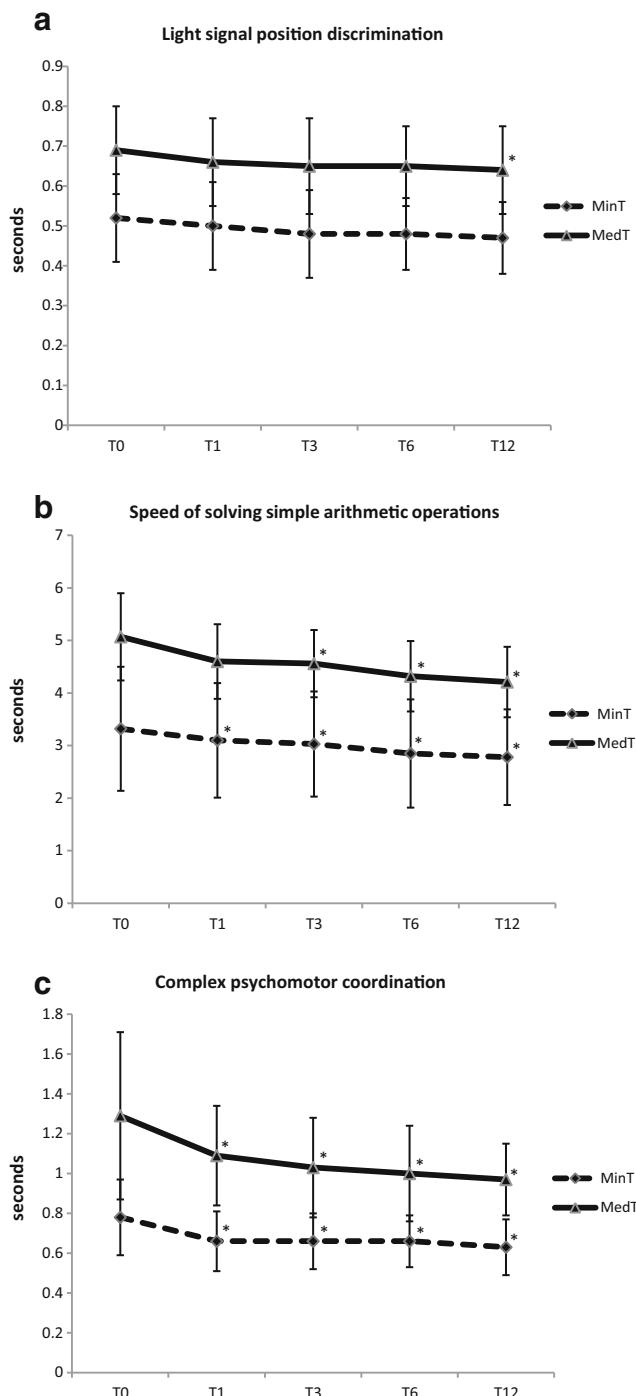
Test of operative thinking (CRD411) measured complex psychomotor coordination. In general, there were significant reductions in TTST, MedT, and MinT at all pre-determined time points during the 1 year of CPAP therapy, compared to baseline values ( $F = 13.864, p < 0.001$ ;  $F = 18.627, p < 0.001$ ;  $F = 11.686, p < 0.001$ , respectively; Table 3 and Fig. 3c). Regarding ballast times, the results obtained from CRD411 test showed a trend of reduction in all ballast times throughout the study period (Table 3).

There were no significant correlations between CRD411 results and average CPAP use per night, except for correlation between improvement in TTST and average CPAP use per night ( $r = 0.45, p = 0.03$ ; Table 4), indicating the positive impact of regular CPAP use on complex psychomotor coordination.

## Discussion

This study provided data on improvement of cognitive and psychomotor performance and reduction in EDS after 1 year of CPAP therapy in severe OSA patients. All of the measured variables such as speed of solving simple arithmetic operation, speed of perception, and complex psychomotor coordination improved following CPAP treatment. However, the largest effect was observed in improvement in speed of perception and complex psychomotor coordination, which is the most demanding task that involved coordination of both upper and lower limbs while performing tests.

The extent of cognitive dysfunction in OSA is not fully understood [21, 22], but it has been shown that OSA impairs cognitive function affecting vigilance, short- and long-term memory, attention, psychomotor performance, and executive function [4, 23]. Sleep fragmentation, EDS, hypoxemia, and



**Fig. 3** Average minimal single task solving time (MinT) and median test solving time (MedT) for all three CRD-series tests (CRD311 A, CRD11 B, and CRD411 C) at pre-determined time points; baseline (T0), 1 (T1), 3 (T3), 6 (T6), and 12 months following CPAP therapy (T12). Asterisk means significantly different from baseline ( $p < 0.04$ )

hypercarbia synergistically impair cognitive function of OSA patients, although their relative contribution to this dysfunction remains to be confirmed [2, 5, 6, 8, 10, 21].

Previous research enabled evidence that OSA patients exhibit significant impairment on several neuropsychological

tests [2, 4]. However, due to different study design the need for standardized neuropsychological battery for identification of valid, reliable and accurate pattern of cognitive dysfunction and response to treatment is still needed [4, 10, 24, 25]. As noninvasive research technique CRD tests might offer primarily indirect data on the modality and the efficacy of mental processing. CRD tests could be repeated multiple times on the same respondent with the same outcome [13, 16]. As shown in the 1-year prospective cohort study of Galic et al., it was possible to use the CRD test series without the possibility of memorizing and learning the tests [16]. CRD tests could be applied in different age groups, and the results are not related to certain language nor any other specific knowledge or skill. Aging per se increases the susceptibility to cognitive dysfunction, with particular regard to the fact that certain age group (middle aged and older) experience changes in sleep architecture such as reduction in REM and slow wave sleep, sleep fragmentation, and prolonged wake time after sleep onset [26]. It has been accepted that risk for OSA increases with age as does the risk for cognitive impairment [10]. When combined with severe OSA, due to cumulative negative effects on cognition, one could conclude that older patients are more likely to express cognitive deficits when they have severe OSA (AHI > 30). In our study, comparison of severe OSA and reference group indicated slight impairment in all CRD tests in severe OSA patients prior to the CPAP therapy. Similar was found in study of cognitive function in mild to moderate OSA patients prior to the MAD therapy [16]. However, insight in results of mild to moderate OSA patients obtained using the same CRD-series test indicated more impairment of cognitive function in severe OSA, suggesting a possible relationship between severity of OSA and cognition.

Previous studies reported positive effect of CPAP treatment adherence on improvement of cognitive functions [4, 24]. Adherence to CPAP is relevant factor in predicting cognitive improvement following CPAP treatment. Usually, adherence to CPAP is measured by average of hours of CPAP use per night and is reported as poor (< 2 h), moderate (2–5 h per night), or optimal user (> 6 h per night) [24]. In our study that utilized within-subject design, the average compliance rate was 6.2 h per night, which allowed us to qualify our patients as optimal CPAP users.

EDS is important to consider in domain of psychomotor performance, since it could result in deficit of motor coordination such as complex psychomotor coordination reported in our study. Sleepiness per se decrements driving performance that could be overcome with CPAP treatment [27]. It is difficult to distinguish effects of improvement in EDS and potential beneficial effects of CPAP treatment on sleep fragmentation and nocturnal hypoxia [10]. There have been attempts to provide explanation for possible underlying mechanisms involved in cognitive impairment of OSA patients. Aloia et al. have proposed a model of small-vessel damage of the brain that could

**Table 4** Pearson correlation coefficients between changes in CRD tests results and average nightly CPAP use

	<i>r</i>	Light signal position discrimination		Solving simple arithmetic operations		Complex psychomotor coordination	
		Δ TTST (s)	Δ MinT (s)	Δ TTST (s)	Δ MinT (s)	Δ TTST (s)	Δ MinT (s)
Average nightly CPAP use (h)	<i>r</i>	0.22	−0.06	−0.01	−0.02	0.45	0.29
	<i>p</i>	0.32	0.79	0.97	0.92	0.03*	0.18

CRD Complex Reactionmeter Drenovac, *MinT* minimum single task solving time, *TTST* total test solving time

\*Significance of the Pearson correlation coefficients

result in functional cognitive problems but excluding any particular brain domain to be responsible for deterioration of cognitive functions in older patients with severe OSA [4].

There are few limitations in our study. Participants were middle-aged to older persons, and as such are representative of age group with highest prevalence of OSA. Therefore, the presence of both OSA and increasing age prevent us from differentiation of whether patients' cognitive impairments are indicative of dementia per se or are consequence of OSA impact on cerebrovascular and cognitive reserve. A number of studies have implicated improvement of sleepiness following CPAP treatment [5, 17, 28]. However, similar to previous studies, in our study, EDS was not objectively evaluated, but instead, it relies on subjectively self-reported evaluation obtained at ESS [24, 29]. It is important to consider that OSA and EDS are both common, especially in middle-aged and older population, and may coexist without necessarily cause-and-effect relationship. Nevertheless, we believe that obvious reduction in EDS following 1 year of CPAP treatment in our study design could be accepted as attribute to cognitive improvement of severe OSA patients.

Impaired overnight memory consolidation has been established in OSA patients and others suffering from sleep disorders that are characterized with fragmented sleep [30]. As shown in our study, compliant CPAP usage offsets speed of perception and complex psychomotor coordination possibly by diminishing negative effects of intermittent hypoxia, improving sleep quality, and reducing EDS. There are many contributors that could be related to psychomotor impairment of OSA patients among which, a recent research targeting peripheral neuropathy received notable attention, reporting of subclinical axonal damage to the motor and sensory nerves of upper and lower limbs in a group of moderate to severe OSA patients [31]. It remains to be determined whether cognitive impairment could have any relationship with peripheral neuropathy that could be overcome with CPAP therapy.

Driving is an activity which requires high level of psychomotor-cognitive functioning, receiving discernible attention due to considerable importance for public safety. Question remains whether our results could be extrapolated and predict risk for traffic accidents in severe OSA patients.

Future studies are required to investigate correlation of driving skills in subjects suffering from OSA with the results obtained on CRD-series tests measuring speed of solving simple arithmetic operations, speed of perception, and complex psychomotor limb coordination.

In conclusion, we believe that usage of CRD-series tests could be reliable tool for assessing improvement in cognitive and psychomotor abilities in OSA patients during CPAP therapy. The results of this study indicate that compliant CPAP treatment in severe OSA patients appears to have significant effect on complex psychomotor limb coordination.

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The sponsor had no role in the design or conduct of this research.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethics Committee of the University of Split School of Medicine (USSM)) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References

1. American Academy of Sleep Medicine Aiawt, SOCIETY ESR, RESEARCH JSOS, SOCIETY LAS (2014) International Classification of Sleep Disorders – Third Edition (ICSD-3)
2. Decary A, Rouleau I, Montplaisir J (2000) Cognitive deficits associated with sleep apnea syndrome: a proposed neuropsychological test battery. *Sleep* 23(3):369–381
3. Aloia MS, Ilniczky N, Di Dio P, Perlis ML, Greenblatt DW, Giles DE (2003) Neuropsychological changes and treatment compliance in older adults with sleep apnea. *J Psychosom Res* 54(1):71–76

4. Aloia MS, Arnedt JT, Davis JD, Riggs RL, Byrd D (2004) Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. *J Int Neuropsychol Soc* : JINS 10(5):772–785. <https://doi.org/10.1017/S1355617704105134>
5. Engleman HM, Douglas NJ (2004) Sleep. 4: sleepiness, cognitive function, and quality of life in obstructive sleep apnoea/hypopnoea syndrome. *Thorax* 59(7):618–622
6. Bucks RS, Olaite M, Eastwood P (2013) Neurocognitive function in obstructive sleep apnoea: a meta-review. *Respirology* 18(1):61–70. <https://doi.org/10.1111/j.1440-1843.2012.02255.x>
7. Stranks EK, Crowe SF (2016) The cognitive effects of obstructive sleep apnea: an updated meta-analysis. *Arch Clin Neuropsychol* 31(2):186–193. <https://doi.org/10.1093/arclin/acv087>
8. Knoepke CAM (2009) Proposed mechanism of cognitive dysfunction in obstructive sleep apnea. *Primary Psychiatry* 16(10):51–66
9. Verstraeten E, Cluydts R, Pevernagie D, Hoffmann G (2004) Executive function in sleep apnea: controlling for attentional capacity in assessing executive attention. *Sleep* 27(4):685–693
10. Grigg-Damberger M, Ralls F (2012) Cognitive dysfunction and obstructive sleep apnea: from cradle to tomb. *Curr Opin Pulm Med* 18(6):580–587. <https://doi.org/10.1097/MCP.0b013e328358be18>
11. Kylstra WA, Aaronson JA, Hofman WF, Schmand BA (2013) Neuropsychological functioning after CPAP treatment in obstructive sleep apnea: a meta-analysis. *Sleep Med Rev* 17(5):341–347. <https://doi.org/10.1016/j.smrv.2012.09.002>
12. Landry S, O'Driscoll DM, Hamilton GS, Conduit R (2016) Overnight motor skill learning outcomes in obstructive sleep apnea: effect of continuous positive airway pressure. *J Clin Sleep Med* : JCSM : Off Publ Am Acad Sleep Med 12(5):681–688. <https://doi.org/10.5664/jcsm.5794>
13. Karanovic N, Carev M, Kardum G, Pecotic R, Valic M, Karanovic S, Ujevic A, Dogas Z (2009) The impact of a single 24 h working day on cognitive and psychomotor performance in staff anaesthesiologists. *Eur J Anaesthesiol* 26(10):825–832. <https://doi.org/10.1097/EJA.0b013e32832bb6e4>
14. Petri NM, Dropulic N, Kardum G (2006) Effects of voluntary fluid intake deprivation on mental and psychomotor performance. *Croat Med J* 47(6):855–861
15. Radic J, Ljutic D, Radic M, Kovacic V, Sain M, Dodig-Curkovic K (2011) Is there differences in cognitive and motor functioning between hemodialysis and peritoneal dialysis patients? *Ren Fail* 33(6):641–649. <https://doi.org/10.3109/0886022X.2011.586480>
16. Galic T, Bozic J, Pecotic R, Ivkovic N, Valic M, Dogas Z (2016) Improvement of cognitive and psychomotor performance in patients with mild to moderate obstructive sleep apnea treated with mandibular advancement device: a prospective 1-year study. *J Clin Sleep Med* : JCSM : Off Publ Am Acad Sleep Med 12(2):177–186. <https://doi.org/10.5664/jcsm.5480>
17. Epstein LJ, Kristo D, Strollo PJ, Jr., Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 5 (3):263–276
18. Pecotic R, Dodig IP, Valic M, Ivkovic N, Dogas Z (2012) The evaluation of the Croatian version of the Epworth Sleepiness Scale and STOP questionnaire as screening tools for obstructive sleep apnea syndrome. *Sleep Breath* 16(3):793–802. <https://doi.org/10.1007/s11325-011-0578-x>
19. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J, Jr., Friedman L, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T, Loube DL, Owens J, Pancer JP, Wise M (2005) Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep* 28 (4):499–521
20. Drenovac M (2001) An analysis of some attributes of the dynamics of mental processing. *Rev Psychol* 8:61–67
21. Quan SF, Wright R, Baldwin CM, Kaemingk KL, Goodwin JL, Kuo TF, Kaszniak A, Boland LL, Caccappolo E, Bootzin RR (2006) Obstructive sleep apnea-hypopnea and neurocognitive functioning in the sleep heart health study. *Sleep Med* 7(6):498–507. <https://doi.org/10.1016/j.sleep.2006.02.005>
22. Sforza E, Roche F (2012) Sleep apnea syndrome and cognition. *Front Neurol* 3:87. <https://doi.org/10.3389/fneur.2012.00087>
23. Beebe DW, Gozal D (2002) Obstructive sleep apnea and the pre-frontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *J Sleep Res* 11(1):1–16
24. Ferini-Strambi L, Marelli S, Galbiati A, Castronovo C (2013) Effects of continuous positive airway pressure on cognition and neuroimaging data in sleep apnea. *Int J Psychophysiol* : Off J Int Org Psychophysiol 89(2):203–212. <https://doi.org/10.1016/j.ijpsycho.2013.03.022>
25. Olaite M, Bucks RS (2013) Executive dysfunction in OSA before and after treatment: a meta-analysis. *Sleep* 36(9):1297–1305. <https://doi.org/10.5665/sleep.2950>
26. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV (2004) Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep* 27(7):1255–1273
27. George CF, Boudreau AC, Smiley A (1997) Effects of nasal CPAP on simulated driving performance in patients with obstructive sleep apnoea. *Thorax* 52(7):648–653
28. Kushida CA, Nichols DA, Holmes TH, Quan SF, Walsh JK, Gottlieb DJ, Simon RD, Jr., Guilleminault C, White DP, Goodwin JL, Schweitzer PK, Leary EB, Hyde PR, Hirshkowitz M, Green S, McEvoy LK, Chan C, Gevins A, Kay GG, Bloch DA, Crabtree T, Dement WC (2012) Effects of continuous positive airway pressure on neurocognitive function in obstructive sleep apnea patients: the apnea positive pressure long-term efficacy study (APPLES). *Sleep* 35 (12):1593–1602. doi:<https://doi.org/10.5665/sleep.2226>
29. Munoz A, Mayorlas LR, Barbe F, Pericas J, Agusti AG (2000) Long-term effects of CPAP on daytime functioning in patients with sleep apnoea syndrome. *Eur Respir J* 15(4):676–681
30. Landry S, Anderson C, Andreartha P, Sasse A, Conduit R (2014) The impact of obstructive sleep apnea on motor skill acquisition and consolidation. *J Clin Sleep Med* : JCSM : Off Publ Am Acad Sleep Med 10(5):491–496. <https://doi.org/10.5664/jcsm.3692>
31. Mihalj M, Lusic L, Dogas Z (2016) Reduced evoked motor and sensory potential amplitudes in obstructive sleep apnea patients. *J Sleep Res* 25(3):287–295. <https://doi.org/10.1111/jsr.12368>