Effectiveness of 6-months Continuous Positive Airway Pressure treatment in OSAS-related cognitive deficit in older adults

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1. Introduction

Obstructive Sleep Apnea Syndrome (OSAS) is a common disorder in elderly. The main symptoms reported by patients include: excessive daytime sleepiness (EDS), morning headaches, changes in mood and personality, cognitive problems and reduced quality of life.

Treatment of choice is CPAP (Continuous Positive Air Pressure), but findings on cognitive function are conflicting. Most authors have found improvement in certain cognitive functions. However some authors hold that evidences which support the potential benefit are weak due to the short treatment duration or the small sample.

2. Objectives

Few studies have followed patients older than 60 years or have administered a comprehensive neuropsychological battery. The aim of this study was to evaluate the effectiveness of CPAP in improving OSAS-related cognitive deficit in older adults.

3. Material and methods

Thirteen patients with OSAS, diagnosed by polysomnography, were assessed prior to the initiation of CPAP treatment and were compared with 29 healthy controls. 6 month after treatment with CPAP, we compared OSAS patients performance with their baseline.

Inclusion criteria were: SAOS, age > 60 years, normal MMSE, and not suffering from other chronic lung diseases, neurological or psychiatric illness. Because hypertension, dyslipidemia and diabetes are common in OSAS, these conditions were accepted along with the correct pharmacological treatment.

In the neuropsychological battery we included:

- Mini-Mental State examination (MMSE)
- Hospital Anxiety and Depression Scale (HAD)
- Short Form Medical Outcomes Survey (SF-36)
- Continuous Performance Test (CPT)
- Digits Span (Wechsler): Digits Span Forward (DSF) and Digits Span Backward (DSB)
- Spatial Span (Wechsler): Spatial Span Forward (SSF) and Backward (SSB)
- Trail Making Test, A and B (TMT)
- Symbol Digit Modality Test Oral (SDMTO)
- Stroop
- Tower of London (TOL)

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- Brown Peterson (BP)
- Paced Auditory Serial Addition Test (PASAT)
- Rey Auditory-Verbal Learning Test (RAVLT): Learning, Short Term (STM) and Long Term Memory (LTM)
- Rey-Osterreith Complex Figure Test (ROCFT)
- Grooved Pegboard Test

Nocturnal hypoxemia was assessed by analysis of the oxyhemoglobin saturation during sleep.

4. Results

OSAS patients obtained significantly lower scores ($p < 0.05$) at baseline than controls on: audioverbal span (DSF), audioverbal and visuospatial working memory (DSB, PASAT, SSB), alternating attention and cognitive flexibility (TMTB, Stroop 3), impulsivity and inhibition (Stroop 3, CPT), problem solving efficiency (TOL), processing speed (Stroop, PASAT, ROCFT time, TOL time) and dominant hand motor coordination (Grooved).

Six months after CPAP treatment, OSAS performance improved in all of them but differences are significant in a few tests: Divided attention and Working Memory (PASAT), Processing speed (PASAT and Stroop), problem solving (TOL), verbal learning and STM (RAVLT and BP).

5. Discussion

Performance of people with OSAS is significantly lower than control group except in sustained attention. Some authors obtained these results too. However most previous studies show that the OSAS group pays significantly worse in this role compared to healthy controls. We suggest that CPT may not be the test of choice, that sustained attention may be also altered in normal aging or simply we have a small sample. Our subjects improved in selective (CPT, TMTA and Stroop 3) and divided attention (PASAT).

Most authors suggest that memory deficit is due to difficulties of recovery while both storage and retrieve remain intact, showing that OSAS patients do not have the type of consolidation or storage problems seen in amnesic patients with temporal injuries and concluding that long-term memory deficits in OSAS are more related to memory disabilities associated with frontal lobe disturbances. Others suggest that memory impairment may be secondary to a deficit in storage associated to

reduced oxygen levels with the involvement of the hippocampus, a structure that has been described as vulnerable in other diseases with hypoxemia. Our OSAS patients performed worse than controls on all facets of memory assessed. They showed a normal learning curve but with lower scores than the control group. It is not a typical pattern of hippocampal memory. Their performance improved significantly after treatment in learning, verbal STM and visual LTM.

In our study we evaluated executive functions extensively and all of them have been compromised in more or less degree. After CPAP we found that only improve TOL functions, such as problem-solving ability, motor speed, planning or impulsivity. However, we must beware of these results because we did not carry out a second evaluation to the control group and we cannot be sure that this improvement is not due to the practice effect.

Visuoconstruction is one of the few functions where OSAS and controls did not show significant differences in our study. A possible explanation could be that the test used to assess this function is not adequate.

OSAS patients in this research performed less than controls on motor coordination and, after CPAP, they remained impaired. To Aloia, this may suggest an irreversible damage to the basal ganglia, sensitive to repeated episodes of nocturnal hypoxemia.

In summary, OSAS-related cognitive abilities improved significantly after treatment in selective and divided attention, working memory, verbal learning and short-term memory and visual long-term memory. We did not find significant differences pre- and post-treatment, although we also observed an improvement over the baseline, in verbal long-term memory, cognitive flexibility, perseveration, processing speed or motor coordination (see Table 1).

Some authors have suggested that persistent cognitive impairments are related to the possibility of permanent brain damage. Periventricular white matter would be widely affected in OSAS, altering axons that connect structures. This can interfere with multiple aspects of cognitive and behavioral and, after several years without treatment, could generate a similar profile to a sub-cortical dementia.

Our study has some important limitations. First we have a relatively small number of subjects, so we have to be conservative with our findings. In addition, we have not carried out a second assessment to healthy controls, therefore, we cannot be ensure that improvements found after CPAP were due to treatment and not due to a practice effect.

Table 1
Pre and Post-treatment scores

Test and cognitive function	PRE-T	POST-T	p
<i>Digits span (wais-III)</i>			
Digits span forward (DSF) – audio-verbal attentional span	6.9± 1.41	7.2± 2	n.s.
Digits span backward (DSB) – audio-verbal working memory	4.7± 1.7	5± 1.2	n.s.
<i>Spatial span (WMS)</i>			
Spatial span forward (SSF) – visuospatial attentional span	7.2± 1.5	7.5± 1.9	n.s.
Spatial span backward (SSB) – visuospatial working memory	5.8± 0.93	5.9± 0.6	n.s.
<i>Continuos performance test (CPT)</i>			
Selective attention	17.8± 22	11.8± 13.5	0.05*
Inattention	13± 8.5	18.6± 13.4	n.s.
Sustained attention	−0.04± 0.06	−0.04± 0.04	n.s.
Impulsivity/planning	3.5± 8.6	1.8± 2.1	n.s.
Reacction time	475.6± 130.5	443± 76	n.s.
<i>Symbol digit modality test oral (SDMTO)</i>			
Correct – Processing speed	35.2± 13.5	37.5± 12.9	n.s.
Errors – Selective attention	3.7± 4.55	1.7± 2.2	n.s.
<i>Paced auditory serial addition test (PASAT)</i>			
3" correct – Working memory-IPS ^{\$}	27.7± 14.2	33.4± 15.1	n.s.
3" errors – Divided attention-IPS ^{\$}	14.4± 13.6	5.7± 3.4	n.s.
2" correct – Working memory-IPS ^{\$}	20.3± 9	25.7± 12.4	0.036*
2" errors – Divided attention-IPS ^{\$}	12.1± 12.4	6.3± 4.2	n.s.
<i>Trail making test (TMT)</i>			
Trail making test A – Selective attention	60.1± 16.9	56.8± 22.6	n.s.
Trail making test A errors	0.08± 0.3	0n.s.	
Trail making test B – Alternating attention	230± 164	181± 133	n.s.
Trail making test B errors – Cognitive flexibility	2.2± 2.4	1.3± 1.8	n.s.
<i>STROOP</i>			
Stroop 1 – Information processing speed	76.8± 18.6	79.3± 19.8	n.s.
Stroop 2 – Information processing speed	49.9± 11.9	55.2± 10.4	0.041*
Stroop 3 – Selective attention	29± 7.8	32.3± 9.2	0.035*
Stroop 3 errors – Inhibition	1.2± 1.3	0.9± 0.9	n.s.
<i>Tower of london (TOL)</i>			
Total correct – Problem solving capacity	2.9± 2.2	4.9± 2	0.007*
Total moves – Problem solving efficiency	49.1± 22.8	36.6± 21.3	0.016*
Total iniiciation time – Planning/impulsivity	94.5± 66	74.7± 32.5	n.s.
Total execution time – Executive speed	374± 196	298± 183	0.006*
Total time – Problem solving time	470± 212	372± 190	0.006*
Total time violation – Slow cognitive processing	2.8± 2.3	1.8± 2	0.009*
Total rukes violation – Capacity to maintain a complex action	1.8± 2	0.8± 1	n.s.
<i>Brown peterson task</i>			
Total – Short time memory	36.54± 8	14.3± 29	0.035*
Perseverations	5± 3.1	6.6± 4	n.s.
<i>Rey auditory-verbal learning test (TAVLR)</i>			
Learning	35.3± 11.4	40.2± 8.6	0.024*
Short term (STM)	7± 3.3	8.2± 2.6	0.032*
Long term memory (LTM)	6.8± 4.1	7.6± 2.9	n.s.
Recognition	10.5± 3.1	11.6± 2.4	n.s.
<i>Rey-osterreith complex figure test (ROCFT)</i>			
Copy time – Speed	484± 365	356± 134	n.s.
Copy – Visuoconstruction	32± 2.4	32.7± 2	n.s.
Short term (STM)	16.7± 5	19.5± 6	n.s.
Long term memory (LTM)	15.1± 5.9	18.4± 6.3	0.064 ^T
Recognition	19.2± 3.2	19.5± 1.8	n.s.
<i>Grooved pegboard test</i>			
Dominant hand – dominant hand motor coordination	83.9± 15.7	79.4± 16.1	n.s.
No dominant hand – No dominant hand motor coordination	109± 60.3	100± 46	n.s.

*Statistical significant difference pre- and post-treatment ^TTrend toward significant difference ^{\$}Information Processing Speed.

6. Conclusions

Our findings provide evidence for clinically significant benefits to some OSAS-related cognitive abilities in older adults. However we cannot associate this improvement with any particular cognitive domain.

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