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Neurobehavioral Manifestations in Obstructive Sleep Apnea Syndrome Before and After Treatment with Continuous Positive Airway Pressure

*J. Montplaisir, *†M. A. Bédard, †F. Richer, and †Isabelle Rouleau

**Hôpital du Sacré-Coeur and Université de Montréal, Canada; and*
†Hôpital Notre-Dame and Université du Québec à Montréal, Canada

Summary: Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent apneas during sleep, resulting in repetitive hypoxemic episodes and a constant interruption of the normal sleep pattern. Vigilance impairment and neuropsychological deficits are among the main symptoms seen in this condition. One of the major questions in this field concerns the reciprocal interactions between nocturnal hypoxemia, sleep disruption, excessive daytime sleepiness and cognitive deficits. Results of this study suggest that vigilance impairment is attributable mostly to nocturnal hypoxemia. However, in cognitive deficits, hypoxemia seems to play a major role in executive and psychomotor tasks, whereas attention and memory functions appear to be related to vigilance impairment. After treatment, hypoxemia-related deficits and some degree of sleepiness persist. These results raise the possibility of an irreversible anoxic central nervous system (CNS) damage in severe OSAS. **Key Words:** Sleep apnea—Neuropsychology—Sleepiness—Anoxia.

Clinical features of obstructive sleep apnea syndrome (OSAS) include snoring, sleep disruption, nocturnal hypoxemia and, in several cases, cardiovascular complications, which may lead to sudden death during sleep (1). However, one of the most common presenting complaints in patients with OSAS is their inability to stay awake during the day, at rest or when performing tasks (2). Impairment of cognitive functions, such as deficits in memory, attention and visuoconstructive abilities, have also been documented (3–7). Low intellectual performance in OSAS has been attributed to nocturnal hypoxemia (3–5) as well as to vigilance impairment, whereas daytime sleepiness has been related mostly to sleep disruptions (8,9). Preliminary results obtained in our laboratory (7,10) have shown that daytime somnolence and nocturnal hypoxemia may produce completely different types of impairment on cognitive tasks. Moreover, some studies have shown the reversibility of cognitive deficits after the restoration of normal breathing with continuous positive airway pressure (CPAP) (11–13), although others have not.

The aims of the present study were: to document the contribution of sleep disruption and nocturnal hypoxemia in vigilance impairment of OSAS, to assess the respective contributions of nocturnal hypoxemia and vigilance impairment on specific cognitive deficits of OSAS, to further clarify the question of the complete reversibility of daytime neurobehavioral symptoms (sleepiness cognitive deficits) in OSAS and to document the possibility of anoxic brain damage.

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Address correspondence and reprint requests to J. Montplaisir, Hôpital du Sacré-Coeur, Université de Montréal, Québec, Canada.

METHOD

Subjects

Twenty moderate to severe OSAS patients aged 35 to 65 were selected for the study. Criteria for inclusion were a sleep apnea index exceeding 10 and a minimum blood oxygen saturation value (SaO_2) of 80% or lower. Criteria for inclusion in the severe group (n = 10) were a sleep apnea index greater than 30 and a percentage of total sleep time with SaO_2 under 80% greater than 5. Ten control subjects matched for age, education and daytime blood gases were included in the study.

Experimental procedure

Subjects were recorded for two consecutive nights in the sleep laboratory with a vigilance and a neuropsychological assessment made during the intervening day. Excessive daytime somnolence was operationally defined as latency to sleep onset on the five naps of

the multiple sleep latency test (MSLT) (14). Each nap was preceded by an administration of the Four Choice Reaction Time Test (FCRTT) (15), a validated psychomotor measure of alertness. Neuropsychological tests were selected to cover a broad range of functions known to be affected in OSAS (10). The full-scale I.Q. of the WAIS-R was administered, with particular interest in some of its subtests. Memory was assessed by the stories of the Wechsler Memory Scale (WMS) and by the Rey-Osterreith Complex Figure under immediate and one-hour delayed recall conditions. Other tests were used to assess verbal fluency, manual dexterity (Purdue Pegboard) and executive functions (Trail Making Test, Mazes, Block Design and Picture Arrangement of the WAIS-R). Ten patients were also assessed 6 months after treatment with CPAP. The appropriate CPAP administration pressure was determined by the level that produced a reversal of apnea (<5 per hour of sleep) or an intolerance to further increases. Pressure levels used in the present study ranged from 7.5–10 cm H_2O.

RESULTS

Results have been published in detail elsewhere (2,7,10,16) and will be briefly summarized here.

Vigilance impairment determinants

Results showed that measures of hypoxemia, especially the minimal SaO_2 value, were the best predictors of both daytime alertness (FCRTT) and sleepiness (MSLT). Daytime alertness could be predicted, in part, by nocturnal sleep disruption, especially by the number of nocturnal awakenings.

Cognitive deficit determinants

Vigilance impairment and nocturnal hypoxemia were found to differentially contribute to the cognitive deficits of OSAS. Reductions in general intellectual measures (WAIS-R), verbal fluency and performance in executive and psychomotor tasks were found to be associated with the severity of hypoxemia. Other attention and memory deficits were found to be related to vigilance impairment.

Persistent daytime symptoms

As expected, nasal CPAP induced a significant improvement of respiratory function during sleep. There were no significant differences between respiratory measures obtained from patients after CPAP treatment and those of matched normal controls. CPAP also improved sleep organization, daytime sleepiness (MSLT) and alertness (FCRTT). Post-treatment values on the FCRTT no longer differed from normal controls. However, MLST values remained significantly lower in the treated OSAS group.

Most measures of intellectual functioning, attentional functions and verbal memory not only improved after treatment but reached levels comparable to those of the control subjects. Functions that remained statistically lower after treatment than in controls included executive functions, such as planning and regulating abilities as assessed by the mazes and the Picture Arrangement Test, and manual dexterity on the Purdue Pegboard. Moreover, two other tests known to be sensitive to executive dysfunctions were not found to improve with CPAP: the Verbal Fluency task and the Trail Making Test (Part B).

DISCUSSION

The vigilance impairment of moderate to severe OSAS patients is affected by both nocturnal hypoxemia and sleep disruption. Sleepiness, as measured by the MSLT, was more specifically related to hypoxemic variables and was found to persist to some degree after successful treatment with CPAP. Deficits in cognitive tasks requiring planning abilities, verbal fluency and manual dexterity were also found to be related to nocturnal hypoxemia and remained impaired after treatment with CPAP in spite of the normalization of sleep and respiration during sleep. These results suggest that vigilance impairment and cognitive deficits that persist after treatment may reflect an irreversible anoxic CNS damage.

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