ORIGINAL ARTICLE

Executive Functions in Persons with Sleep Apnea

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ABSTRACT: *Seventeen patients with sleep apnea syndrome [SAS, Respiratory Disturbance Index (RDI) = 12–85] were compared with 16 normal controls (RDI <7) on neuropsychological tests of executive functions, a domain in which SAS patients have been suggested to have deficits. SAS patients demonstrated greater deficits in the retrieval of information from semantic memory (Controlled Oral Word Association task) and in shifting responses in the face of error (Wisconsin Card Sort Test), but differences in working memory were not observed. Eliciting deficits in cognitive executive functions in SAS may require more sensitive measures than are typically used in neuropsychiatric research.*

KEYWORDS: sleep, sleep apnea, neuropsychological testing, executive functions

A broad range of neuropsychological (NP) deficits have been described in patients with Sleep Apnea Syndrome (SAS).[1–3] Among the deficits evidenced are poorer performance on tasks involving executive functions such as Trails B,[2] Wisconsin Card Sort Task (WCST), and Tower of Toronto tasks.[3] Executive functions refer to processes involved in the planning, initiation, and self-regulation of goal-oriented behavior.[4] It has been suggested that executive functioning deficits might reflect hypoxemia-induced frontal-lobe dysfunction and not be fully attributable to vigilance impairments.[3]

An important component of executive functions is working memory. Working memory is involved when motor responses are regulated by transiently stored, internal representations of information in memory, rather than by external stimuli present in the environment (see ref. 5). One variety of working memory is that for locations in space. Spatial working memory has been studied in monkey and man using delayed-response tasks. These tasks have been useful in revealing specific deficits in neuropsychiatric disorders such as schizophrenia.[6] Animal studies suggest that these memory processes are represented in the principal sulcus of the prefrontal cortex.[5,6]

In a delayed-response visual task, a target is briefly presented at a location in the visual field and after a delay in which the target location is not illuminated, the subject must identify the location that the target had occupied. The target location varies from trial to trial, so a subject must update their memory representation of the environment after each response. That is, delayed-response tasks require a person to note pertinent spatial information, keep a representation active during an interval when the stimulus is no longer present, and access this representation on cue while ignoring information from previous trials and responses.[5] Unlike many clinical neuropsychological measures, the delayed-response visual task specifically assesses only one function: spatial working memory. Spatial working memory is important to study because we must regularly keep spatial information "on line" doing everyday tasks such as driving.

In this study, we compared persons with untreated sleep apnea to normal controls on a series of executive function measures, including a visual-response task, as well as on tasks not specifically sensitive to executive function deficits. This study is unique in that it included the delayed-response visual task in an effort to specifically assess spatial working memory deficits with SAS, independently of other aspects of memory (see ref. 3).

METHODS

Seventeen subjects (Ss) with untreated SAS [Respiratory Disturbance Index, (RDI) = 12–85, $M \pm SD$ = 38.8 ± 21.0] were compared with 16 healthy controls (RDI < 7, $M \pm SD$ = 2.2 ± 1.6) matched for age, eth-

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nicity, gender, IQ, and years of education. Exclusion criteria were a history of a sleep disorder other than sleep disordered breathing, severe or unstable medical problems, neurological disease, alcohol/drug abuse, extremes in educational status, or regular use of medications that impair sensorium. All Ss were participants in a larger, ongoing study of NP consequences of obstructive SAS.[7] All executive function tasks other than the delayed-response task had been administered at a session prior to the latter task. On return for the delayed-response task testing, Ss completed the Stanford Sleepiness Scale[8] to describe their level of sleepiness at the time of this testing.

Spatial working memory was assessed using Park and Holzman's procedure.[6] On each of 32 trials, a target stimulus (small black circle) appeared for 200 ms in 1 of 8 randomly selected locations defining a circular array on a video touch screen. Immediately following the disappearance of the target stimulus, a 30-sec delay period ensued in which subjects engaged in a task requiring detection of a category change in a series of briefly presented words. This task prevented rehearsal of the target stimulus location. After the delay period, the S was required to touch the screen at the location in which the target stimulus had been presented. The accuracy and reaction time (RT) of the initial response on each trial were recorded.

A 16-trial sensory-motor control task was also administered that was identical to the spatial working memory task except that the target stimulus remained on the computer screen during the entire trial. To respond, Ss merely had to touch the location of the target stimulus on the video touch screen, following the distractor task; there was no demand on memory. Ss were instructed to respond as quickly and as accurately as possible and were given a brief rest period after every eight trials. The order of tasks was counterbalanced.

Other NP measures of executive functions, obtained on a previous testing day, were the Wisconsin Card Sort, Trail Making B (adjusted for Form A), Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digits Backwards, a computerized version of Tower Puzzle (consisting of nine unique, partially solved puzzles), a serial subtraction task, and the Controlled Oral Word Association from the Multilingual Aphasia Examination (COWA). The WAIS-R Digit Span Forward and the California Verbal Learning Test, Trial 1 (CVLT) were included as measures of memory not specifically dependent on executive functions. See Lezak[4] for descriptions of these tests. A Choice Reaction Time task (CRT, 2-min trials) was used as a measure of psychomotor efficiency. The Multiple Sleep Latency Test (MSLT),[9] was obtained on the day of neuropsychological testing. The MSLT is an objective measure that permitted comparisons of the SAS Ss and controls on the variable of sleepiness. The procedures used to collect data were approved by the Institutional Review Board of the Cleveland VA.

RESULTS

As intended, the groups did not differ in background characteristics (Table 1). They also did not differ in subjective sleepiness (Stanford Sleepiness Scale) assessed just before the working memory task or level or objective sleepiness (MSLT) assessed on the day of the other NP testing. Average levels of oxygen saturation and oxygen saturation nadir associated with respiratory disturbance differed significantly ($p < 0.001$).

As indicated in Table 1, groups did not differ in the accuracy or response speed (RT) on the spatial working memory task, although SAS Ss were slower and more accurate than controls on the sensory-motor control task. There were differences in the expected direction of SAS Ss performing more poorly on only two measures of executive functions. The SAS group made significantly more perservative errors than controls on the WCST ($p < 0.05$). The group also tended to be less verbally fluent than controls on the COWA ($p < 0.06$). While this finding is not significant at the $p < 0.05$ level, there is a six-point difference between groups on this task. A between-group difference of this magnitude (two thirds of a standard deviation) would likely be significant if we had a larger sample size, resulting in greater statistical power to detect between-group differences at the 0.05 level.

There were no other significant between-group differences on any other tasks.

DISCUSSION

Persons with SAS in this study showed significantly poorer performance on some measures of executive functions, but not specifically in working memory. The executive function deficits in retrieval of information from semantic memory (COWA) and in shifting responses in face of error (WCST perseverative errors) were not accompanied by deficits in other neuropsychological functions. The groups were comparable for Stanford Sleepiness Scale (subjective sleepiness) and MSLT (objective sleepiness) scores, so these differences are not likely due to variation between groups in sleepiness.

The differences between groups on the sensory-motor control task were unanticipated. This is a very easy task; the average accuracy of both groups (15.3, 15.9) is virtually perfect (16). Even so, the controls are significantly less accurate here then are the SAS Ss. They are also significantly faster than SAS Ss, on average. The difference between groups in RT and accuracy is not significant on the spatial working memory task. The

TABLE 1. Comparisons between SAS and Control Subjects (N = 33)

	SAS Subjects (n = *17*)	*Control Subjects* (n = *16*)	*Statistical Value*	
Demographics				
Age	48.9 ± 8.2	44.9 ± 9.3	t (31) = 1.31	ns
Years of Education	13.4 ± 2.4	14.1 ± 1.7	t (31) = 1.00	ns
Estimated WAIS-R IQ	101.3 ± 10.6	102.1 ± 8.9	t (31) = 0.23	ns
Percent European-American (%)	65%	56%	χ^2 = 0.25	ns
Percent Females (%)	41%	69%	χ^2 = 2.53	ns
Respiration				
Respiratory Disturbance Index	38.8 ± 21.0	2.2 ± 1.6	t (16.21)† = 7.16	p <0.001
Level of Sleepiness				
Stanford Sleepiness Scale*	2.4 ± 1.3	1.9 ± .7	t (30) = 1.13	ns
Multiple Sleep Latency Test (min)‡	8.9 ± 4.9	9.6 ± 4.8	t (30) = 0.40	ns
Level of Hypoxemia				
Average SaO_2	89.9 ± 3.3	93.7 ± 1.6	t (20.48)† = 4.03	p <0.001
Low SaO_2	74.3 ± 10.1	90.6 ± 4.1	t (18.56)† = 5.76	p <0.001
Executive Functions				
Spatial Working Memory Task				
# correct	28.0 ± 4.0	27.5 ± 2.9	t (31) = 0.41	ns
Reaction time (s)	1.7 ± 0.6	1.5 ± 0.4	t (31) = 1.62	ns
Sensory-Motor Control Task				
# correct	15.9 ± 0.3	15.3 ± 0.9	t (18.45)† = 2.28	p <0.05
Reaction Time (s)	1.3 ± 0.4	0.9 ± 0.4	t (31)† = 2.69	p <0.01
Wisconsin Card Sort Test				
# of categories completed	3.9 ± 1.8	4.8 ± 2.0	t (31) = 1.43	ns
# of perseverative errors	26.7 ± 11.7	18.4 ± 9.5	t (31) = 2.22	p <0.05
Controlled Oral Word Association	39.4 ± 8.6	± 45.3 ± 8.7	t (30) = 1.95	p <0.06
Tower Puzzle				
# solved	5.7 ± 2.1	5.8 ± 1.9	t (27) = 0.17	ns
# of errors	0.8 ± 0.8	1.4 ± 1.4	t (27) = 1.59	ns
Trails B Time (s)	72.8 ± 20.8	73.3 ± 29.0	t (31) = 0.05	ns
Trails A Time (s)	31.9 ± 7.0	29.1 ± 9.8	t (27.04)† = 0.94	ns
Serial Subtraction # correct	20.2 ± 11.7	18.3 ± 9.9	t (31) = 0.51	ns
WAIS-R Digit Span Backward	6.4 ± 1.3	6.3 ± 1.8	t (31) = 0.29	ns
Other Tasks				
WAIS-R Digit Span Forward	8.3 ± 1.9	7.7 ± 2.0	t (31) = 0.90	ns
California Verbal Learning Test				
Trial 1, # of words recalled	5.9 ± 1.8	6.4 ± 1.7	t (31) = 0.90	ns
Choice Reaction Time (s)	0.6 ± 0.1	0.6 ± 0.1	t (25.84) = 0.83	ns

Values $M \pm SD$, unless otherwise indicated, df's are indicated ( ).
ns denotes a non-significant between-group difference
*Denotes data collected on day that spatial working memory and sensory-motor tasks were administered.
†Denotes degrees of freedom adjusted for heterogeneous variances.
‡Denotes data collected on day of NP testing.

pattern suggests that controls sacrificed accuracy for speed on the sensory-motor control task but slowed down when performing on the intrinsically more difficult visual delay-response task. Further, it should be pointed out that although the SAS group was on average 0.4 sec slower (yet more accurate) in responding on the sensory motor control task, they were not significantly slower on any other speeded task (CRT, or Trail Making). Thus, a general psychomotor slowing cannot account for the difference on this one task.

In summary, the present analyses found some of the executive function deficits reported by others (errors on WCST,[3] verbal fluency[2]), but did not find as extensive a range of executive deficits (such as Trails B[2] and Tower tasks[3]) shown by some authors. Further, a specific deficit in spatial working memory was not evidenced. This finding is similar to another study that showed decreased SAS performance on a double-encoding verbal-spatial working memory task, but investigators attributed poorer performance on this task to a more general reduction in short-term memory.[3] Perhaps working memory, per se is not impaired in SAS, but rather the more general ability to recall isolated information from short-term memory (see ref. 3). However, unlike other researchers,[2,3] our SAS Ss did not evidence deficits on immediate or short-term memory tasks that required only simple recall of presented information, independent of working memory. In sum, our study did not demonstrate vast SAS decline in either executive functions or general short-term memory evidenced in previous research.

The more limited evidence of neuropsychological deficits in these subjects may be due to several features of this sample. The level of RDI in this study was lower than in typical clinical samples and, perhaps, more im-

portantly, these subjects were identified on the basis of sleep studies conducted independently of any clinical concerns or suspicions about SAS. Neuropsychological deficits in SAS may perhaps be more readily detected in samples where subjects are initially identified clinically (because of complaints about sleepiness, sleep disruption, or problems in function). This hypothesis is supported by the recent findings from a community-based sample on working adults that suggested that deficits in neuropsychological function may be milder than originally suggested by clinic reports.[10]

Of interest also are findings from two preliminary studies of patients with severe SAS who underwent cerebral Single Photon Emission Photography (SPET) that reported abnormalities in the frontal and temporal areas of the brain, indicating localized perfusion or metabolic defects.[11,12] Perplexingly, was the failure to demonstrate any deficits in neurocognitive function in these patients, as assessed using the standard neuropsychological batteries. It is possible that the contextual triggers that influence performance during routine NP testing (which could be "alerting") mask the relatively modest deficits suffered by patients with sleepiness or intermittent hypoxemia. The discordance between anatomical/physiological and performance measures found in recent studies, as well as our failure to demonstrate working memory deficits suggests the need to reconsider the utility of routinely administered NP tests to characterize functional abnormalities in SAS. Further studies, assessing the role of measures sensitive to NP processes likely to be impaired in SAS are needed.

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