Oral-appliance therapy obstructive sleep apnea-hypopnea syndrome

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Chapter 4.2

Simulated driving performance in obstructive sleep apnea-hypopnea: effects of oral appliances and continuous positive airway pressure

This chapter is based on the following publication:
* Hoekema A, Stegenga B, Bakker M, Brouwer WH, de Bont LGM, Wijkstra PJ, van der Hoeven JH. Simulated driving in obstructive sleep apnea-hypopnea; effects of oral appliances and continuous positive airway pressure. *Sleep and Breathing* (in press).

Summary

Background Impaired simulated driving performance has been demonstrated in obstructive sleep apnea-hypopnea syndrome (OSAHS) patients. Although continuous positive airway pressure (CPAP) generally improves simulated driving performance, the effects of oral-appliance therapy are unknown. The aims of this study were to determine to what extent OSAHS patients have more difficulty with a monotonous simulated driving test when compared with control subjects, and to compare the effects of oral-appliance with CPAP therapy

Methods Simulated driving performance was evaluated in 20 OSAHS patients and 16 control subjects during a 25-minute driving test. Following randomization ten patients started oral-appliance and CPAP therapy, respectively. After two to three months of treatment, patients repeated the driving test.

Results At baseline the total number of lapses of attention during driving was significantly higher in OSAHS patients as compared with control subjects (median: OSAHS patients 10 versus controls 0). As a result of treatment, the total number of lapses of attention was significantly decreased in both the oral-appliance (median: baseline 5 versus follow-up review 0) and CPAP group (median: baseline 10 versus follow-up review 0.5). When comparing driving performance between the oral-appliance and CPAP group, no significant differences were noted.

Conclusions OSAHS patients perform worse on a simulated driving test when compared with control subjects. When evaluating the effects of treatment, adequate OSAHS management with either oral-appliance or CPAP therapy usually resulted in substantial improvements of simulated driving. Conclusions beyond both treatments improving simulated driving performance are, however, not justified by the data in the present study.

Introduction

The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common sleep related breathing disorder associated with serious neurocognitive and cardiovascular sequelae.[1] In OSAHS patients respiratory related arousals during sleep cause sleep fragmentation and a depletion of rapid-eye-movement and slow-wave sleep, ultimately resulting in excessive daytime sleepiness. Daytime sleepiness may adversely affect daytime performance and consequently, among other sequelae, influence driving performance.[2,3] Studies evaluating subjective (self-reports) or objective (motor vehicle department) records sustain the opinion that OSAHS confers an increased risk for accidents when driving.[4,5] In addition, it has been shown that performance on driving simulator and vigilance tests of varying complexity is impaired in OSAHS patients.[6-10] Driving is a multifaceted and multileveled skill and it is impossible to assess all of its aspects in a simulator.[11] Depending on the nature of the disorder studied key driving tasks can be selected for clinical assessment. In OSAHS patients, the primary problem is to sustain attention in monotonous situations. Therefore, the most relevant driving task is prolonged driving on a monotonous highway. Most simulator studies in OSAHS patients use a variation of this task.[6-10]

When evaluating the effects of OSAHS treatment on motor vehicle crash risk, marked improvements are generally reported. Studies evaluating subjective and objective records indicate that continuous positive airway pressure (CPAP) therapy reduces collision and crash frequency in OSAHS patients.[4,8,12] In addition, successful treatment with CPAP therapy generally results in improvements of simulated driving performance.[13-15] Similar improvements in simulated driving performance have been demonstrated following successful OSAHS management by means of uvulopalatopharyngoplasty.[6]

Over the past decade, oral-appliance therapy has emerged as an increasingly popular alternative in the treatment of OSAHS.[16] An oral appliance aims at relieving upper airway collapse during sleep by modifying the position of the mandible, the tongue and pharyngeal structures. However, the effects of oral-appliance therapy on simulated driving performance have not been evaluated to date.[16]

The aims of this study were to determine to what extent OSAHS patients have more difficulty with a monotonous simulated driving test when compared with control subjects, and to compare the effects of oral-appliance with CPAP therapy.

Methods

Patient selection

Control subjects and a subset of OSAHS patients, recruited for a randomized trial comparing the effectiveness of oral-appliance and CPAP therapy, comprised the study population. All subjects were required to be aged between 21 and 70, in the possession of a driver's license, not involved in shift-work or nighttime work, and otherwise fit to drive.

Thirty consecutive OSAHS patients with an apnea-hypopnea index (AHI) >5 were considered for inclusion in the present study. Patients were recruited through the Department of Home Mechanical Ventilation of the University Medical Center Groningen (Groningen, The Netherlands) in the period of March to June 2004. Patients were excluded in case of previous treatment of OSAHS, clearly reversible morphological airway abnormalities, endocrine dysfunction (one patient with hypothyroidism, two patients with pituitary adenoma), a reported or documented history of severe cardiac or pulmonary disease (one patient with daytime respiratory insufficiency), moderate or severe periodic limb movement disorder (*i.e.*, periodic limb movement index >25) or a psychological condition precluding informed consent. Patients with a dental status that could complicate oral-appliance therapy were also excluded (three patients had an insufficient number of teeth, one patient had extensive periodontal disease).[16] Because two of the remaining 22 patients refused participation, 20 OSAHS patients could eventually be enrolled. Sixteen healthy subjects matched for age and without signs of a neurological or psychiatric disorder were recruited as control group. The control group comprised a diverse compilation of hospital employees. They had had no knowledge of having a sleeping disorder neither was there a clinical suspicion by questionnaire analyses. The randomized trial was approved by the Groningen University Medical Center's ethics committee (METc 2002/032). Written informed consent was obtained from each patient before enrolment.

Study design

Of the 20 OSAHS patients, ten were allocated to oral-appliance therapy and ten to CPAP therapy by means of block randomization.[17] It was not possible to blind the patients or clinicians to treatment assignment. At baseline, all OSAHS patients and control subjects completed the Epworth sleepiness scale[18] and an in-house questionnaire evaluating medication prescription, caffeine consumption, tobacco use, and driving experience. Thereupon simulated driving performance was evaluated in both groups during a 25-minute driving test.

The oral appliance used in this study (Thornton Adjustable Positioner, Airway Management Inc., Dallas, TX, USA) positioned the patient's mandible in a forward

and downward position. By turning a propulsion screw incorporated anteriorly in the appliance, patients could adjust the mandibular advancement with 0.2-mm increments. When commencing oral-appliance therapy the mandible was set at approximately 50% of the patient's maximum advancement. After having been accustomed to this protrusive position during a two-week period, patients were allowed to further adjust their appliance during a six-week period. To do so, patients advanced the mandible each night with one to two increments (*i.e.*, 0.2 to 0.4 mm) whenever OSAHS symptoms persisted (*e.g.*, snoring, apneas, hypopneas, or excessive sleepiness). This "titration" of the appliance was continued until OSAHS-symptoms had improved adequately or until further protrusion of the mandible resulted in discomfort.

CPAP-titration was performed during an afternoon nap. This technique, aimed at abolishing: all signs of apneas, hypopneas, and snoring—has been shown an appropriate procedure for the effective titration of CPAP.[19] Following titration an eight-week follow-up period was arranged that allowed for habituation and, if necessary, adjustments of CPAP therapy.

After patients had used an oral appliance or CPAP for eight weeks, the treatment effect was assessed with a second polysomnographic study. For patients whose AHI was still ≥5, treatment was adjusted, if possible, to improve effectiveness. For this purpose patients treated with an oral appliance were instructed to maximally protrude their mandible with the appliance. In CPAP treated patients, the pressure was raised with 1 or 2 cm H_2O (depending on the severity of residual OSAHS with CPAP). In these patients, the follow-up period was extended with another four weeks. The effect was then assessed with a third polysomnographic study. This adjustment sequence was continued until the AHI was <5 or until the adjustments became uncomfortable for the patient. Follow-up review ended with a patient's final polysomnographic evaluation or when a patient discontinued treatment because of poor tolerance or another reason. At their final follow-up review, patients again completed the Epworth sleepiness scale and driving test performed at baseline. In addition, treatment usage was evaluated at this stage by asking patients how many nights per week and how many hours per night they used their treatment.

Treatment was considered effective when the AHI either was <5 or showed "substantial reduction",[16] defined as reduction in the index of at least 50% from the baseline value to a value of <20 in a patient who had no symptoms while using therapy. Patients not meeting these criteria at their final review were considered "nonresponsive" to treatment.

Polysomnography

Polysomnography (Embla® A10 digital recorder, Medcare, Reykjavik, Iceland) for baseline and follow-up evaluations was conducted ambulatory in the patient's

home situation. Each study started 11 AM and stopped 9 AM the next morning. Outcomes were limited to the time in bed part of the study. Standardized criteria were used to score apneas and hypopneas,[20] arousals,[21] sleep stages[22] and periodic limb movements.[23] All polysomnographic studies were evaluated and scored by one neurophysiologist (J.H. van der Hoeven) who was unaware of the patient's treatment assignment.

Driving simulator

The driving test was performed on the driving simulator of the Department of Neuropsychology.[24,25] All subjects were tested between noon and 2.00 PM. In OSAHS patients, the second driving test was conducted at the same point of time as the first evaluation. Instructions were to refrain from stimulating products (*e.g.*, caffeine) three hours before testing and not to smoke half an-hour before testing. To keep testing conditions as consistent as possible lights were dimmed, noise was shut out and room temperature was kept at 22 °C. The driving test had to be completed in absence of company, including the test leader (M. Bakker). Subjects were seated in a comfortable office chair behind a 21-inch computer screen on which the scene of a straight road was projected. Using a computer game steering wheel, the lateral position on this road could be controlled. In all conditions, the speed of driving was fixed at 50 km/h, and the only objective was to drive as straight as possible in the middle of the right lane, while compensating for the effect of a low amplitude unpredictable "side wind" signal (superposition of 1/15, 1/7.5 and 1/3.75 Hz sinusoids). Because of this unpredictable "side wind", subjects had to stay alert continuously to accomplish the task without getting out of lane. After a five-minute practice, it was ascertained that subjects had mastered the task. Subsequently, all subjects performed a 25-minute driving test in a monotonous situation. Side wind amplitude was set low so that all subjects could easily perform the task in the first five minutes, showing standard deviations of the lateral position comparable to straight road driving in "the real world".[26]

During the test, every 15 seconds the standard deviation of the lateral position (SDLP) was calculated. Driving performance was expressed in two separate parameters:

- the number of lapses of attention (LOA). For this purpose, the median of 20 consecutive SDLP's was computed, resulting in one number every five minutes. Subjects were considered to perform at a normal level during the first five test minutes, unaffected yet by the monotonous task. A lapse of attention was defined as a SDLP in a given 15 second period that was twice as high as the median SDLP of the first five test minutes.
- the time course SDLP to assess a possible individual increase in the five median SDLP's. For this purpose, an individual linear regression analysis was computed

of the five consecutive median SDLP's, resulting in a slope coefficient. The higher this number, the steeper the regression line, the larger the adverse effect of time on simulated driving performance.

Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (version 12.0, SPSS Inc, Chicago, IL, USA). Means and standard deviations, or medians and interquartile ranges in skewed distributions, are reported. The total number of LOA during the driving test was used as primary outcome measure. Other driving test outcomes included the number of LOA per five minute time stage (five epochs), and the slope coefficient of the time course SDLP. To compare outcomes between the groups, independent sample t-tests were used (Mann-Whitney U tests for variables with skewed distributions). Differences between baseline and follow-up variables in the oral-appliance and CPAP groups were compared with paired Student's t-tests (Wilcoxon's signed ranks tests for variables with skewed distributions). To measure correlations in the OSAHS group between the total number of LOA, AHI and Epworth sleepiness scale, Spearman's rank correlation coefficients were calculated. A significance level of $p<0.05$ was predefined in all cases.

Results

OSAHS patients versus control subjects

When comparing the 20 OSAHS patients and the 16 control subjects no significant differences in age, daily caffeine and nicotine consumption, or driving experience were observed at baseline (Table 1). With respect to the Epworth sleepiness scale, a significantly higher level of subjective sleepiness was observed in the OSAHS patient group.

Before treatment, driving performance, as indicated by the total number of LOA, was worse in OSAHS patients than in control subjects (Table 2, Figure 1). In addition, there were significantly more LOA's in the second to the fifth epoch in OSAHS patients than in the control subjects. The slope coefficient of the time course of SDLP significantly differed in favor of the control subjects. In the OSAHS patients, no significant correlation was observed between the total number of LOA and the AHI or the Epworth sleepiness scale.

Effects of oral-appliance and CPAP therapy

Of the ten patients that were allocated to oral-appliance therapy, one patient's symptoms and driving performance deteriorated due to a severe periodic limb movement syndrome at final follow-up review (increase in periodic limb movement index from 0 to 62). This deterioration could not be explained by a residual OSAHS

TABLE 1. Baseline characteristics of OSAHS patients and control subjects.

Variable	OSAHS patients* (n = 20)	Control subjects* (n = 16)	Difference†
Male / female ratio	17 / 3	13 / 3	-
Age (years)	49 ± 11	48 ± 10	NS
Body-mass index (kg/m^2)	33 ± 6	-	-
Neck circumference (cm)	44 ± 3	-	-
Epworth sleepiness scale	14 ± 7	6 ± 4	p=0.000
Caffeine (units/day)	5.5 ± 3.3	6.7 ± 3.4	NS
Nicotine (units/day)	0.0 (0.0–9.5)	0.5 (0.0–12.5)	NS
Driving experience			
- years of driving experience	29 ± 10	29 ± 11	NS
- annual number of kilometers x 10^3	15 (10–32)	13 (6–20)	NS
AHI (no/hour)	49 ± 33	-	-
minSaO_2 (%)	76 ± 10	-	-

* Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.
† Significance for the difference in baseline characteristics between the OSAHS patients and control subjects.
Abbreviations: AHI = apnea-hypopnea index, NS = not significant, minSaO_2 = lowest oxyhemoglobin saturation during sleep, OSAHS = obstructive sleep apnea-hypopnea syndrome.

following treatment (reduction AHI from 28 to 0). This patient was, therefore, excluded from further analysis. Baseline characteristics were similar for the nine oral appliance and ten CPAP treated patients (Table 3). At final review, the mean advancement of the mandible with the oral appliance was 89 ± 23% of the maximum advancement. The mean CPAP pressure was 8.7 ± 2.2 cm H_2O at final review. The median period to final review was 81 (interquartile range 72–93) days in the oral-appliance group and 79 (interquartile range 63–102) days in the CPAP group (p>0.05).

Treatment was effective for eight patients in the oral-appliance group and for nine patients in the CPAP group. The two remaining patients were "nonresponsive" to treatment. As a result of oral-appliance and CPAP therapy, the AHI and minimum oxyhemoglobin saturation during sleep (minSaO_2) improved significantly in both groups (Table 3). No significant differences in the AHI and minSaO_2 were found between the treatment groups at final follow-up review. The Epworth sleepiness scale was significantly improved only in the CPAP-treated group. When comparing Epworth sleepiness scale values at final review, no significant differences were noted between the two groups. There were no significant differences between the treatment modalities with regard to usage (Table 3).

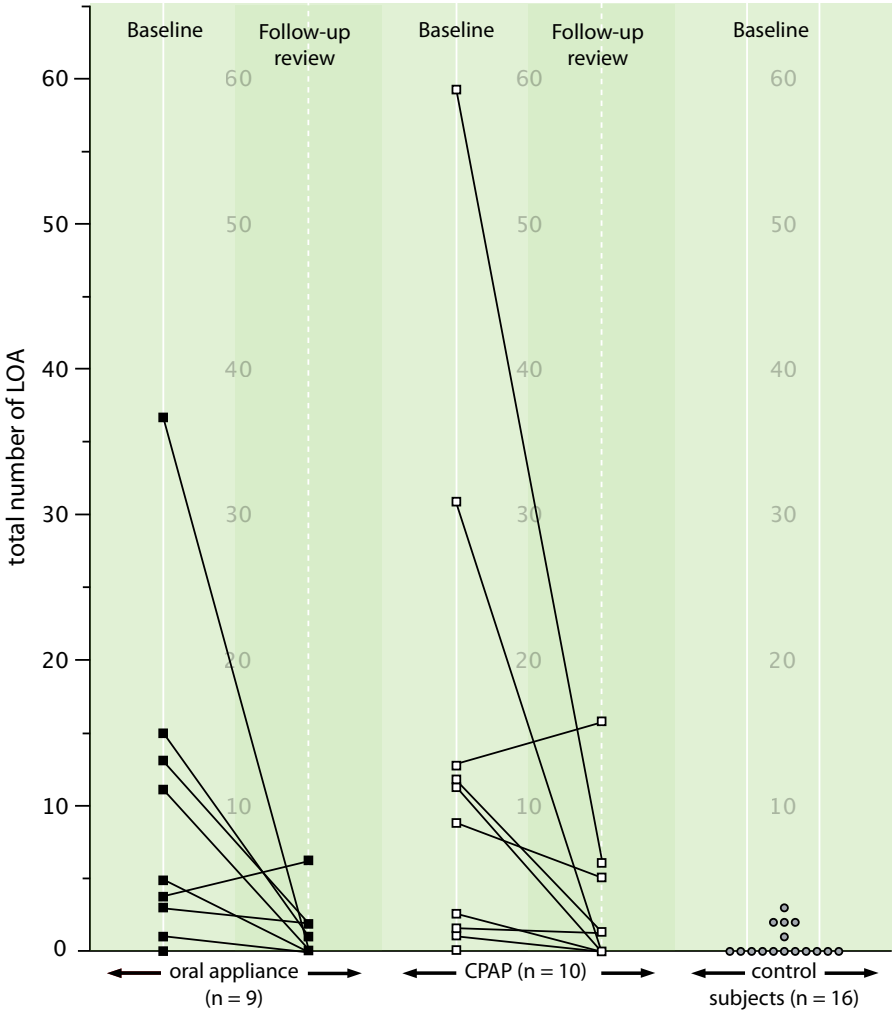

FIGURE 1. Individual values of the total number of lapses of attention in OSAHS patients and control subjects.

In OSAHS patients the total number of LOA at baseline and final follow-up review are depicted according to treatment group (*i.e.*, oral appliance or CPAP). The median treatment period from baseline until final follow-up review was 81 (interquartile range 72–93) days in the oral-appliance group and 79 (interquartile range 63–102) days in the CPAP group ($p>0.05$). The total number of LOA are not depicted for one patient allocated to oral-appliance therapy. This patient was excluded from follow-up analysis because his symptoms and driving performance deteriorated due to a severe periodic limb movement syndrome at the final follow-up review (increase in periodic limb movement index from 0 to 62). At baseline, the total number of LOA for this patient was 17.
Abbreviations: CPAP = continuous positive airway pressure, LOA = lapses of attention, OSAHS = obstructive sleep apnea-hypopnea syndrome.

TABLE 2. Baseline driving test outcomes of OSAHS patients and control subjects.

Variable	OSAHS patients* (n = 20)	Control subjects* (n = 16)	Difference†
Number of LOA			
- total (0-25 minutes)	10.0 (1.3–14.5)	0.0 (0.0–1.8)	p=0.000
- 1st epoch (0-5 minutes)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	NS
- 2nd epoch (6-10 minutes)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	p=0.02
- 3rd epoch (11-15 minutes)	1.0 (0.0–4.8)	0.0 (0.0–0.0)	p=0.005
- 4th epoch (16-20 minutes)	3.0 (0.3–5.8)	0.0 (0.0–0.0)	p=0.000
- 5th epoch (21-25 minutes)	2.5 (0.0–6.0)	0.0 (0.0–0.0)	p=0.001
Slope coefficient of time course SDLP	0.41 (0.06–0.70)	0.03 (-0.15–0.17)	p=0.006

* Values with additives in parentheses are medians with interquartile ranges.
† Significance for the difference in baseline driving test outcomes between the OSAHS patients and control subjects.
Abbreviations: LOA = lapses of attention, NS = not significant, OSAHS = obstructive sleep apnea-hypopnea syndrome, SDLP = standard deviation of the lateral position.

No significant differences in driving performance were observed between the two groups at baseline (Table 4). After therapy, the total number of LOA was significantly decreased in both groups. In one oral appliance and one CPAP-treated patient, the total number of LOA was increased at final follow-up review (Figure 1). Both patients were "nonresponsive" to treatment. Significant improvements in the remaining driving test outcomes were observed only in the CPAP group for the number of LOA in the fifth epoch. No significant differences were noted between the driving test data at final review for oral-appliance and CPAP therapy. For the OSAHS patient group, a significant correlation was demonstrated between changes in the total number of LOA and the Epworth sleepiness scale following treatment (r=0.570, p=0.01).

Discussion

This study shows that OSAHS patients clearly have difficulty with a simulated driving test when compared with control subjects. During the 25-minute driving test, OSAHS patients showed a considerable deterioration in simulated driving performance. When evaluating the effects of oral-appliance and CPAP therapy on driving performance, significant improvements in the total number of lapses of attention were observed in both treatment groups. These findings suggest that effective OSAHS treatment, with either oral-appliance or CPAP therapy, contributes to an improvement of simulated driving performance.

TABLE 3. Baseline and follow-up review characteristics of oral appliance and CPAP treated patients.

Variable	Oral appliance* (n = 9)	CPAP* (n = 10)	Difference†
Male / female ratio	7 / 2	9 / 1	-
Age (years)	48 ± 11	50 ± 12	NS
Body-mass index (kg/m^2)			
- baseline	33 ± 7	34 ± 5	NS
Neck circumference (cm)			
- baseline	43 ± 3	45 ± 2	NS
Epworth sleepiness scale			
- baseline	11 ± 8	15 ± 5	NS
- follow-up review‡	7 ± 6	6 ± 4	NS
- Δ	-5 ± 8	-10 ± 7§	NS
Caffeine (units/day)			
- baseline	6.2 ± 3.6	5.1 ± 3.2	NS
Nicotine (units/day)			
- baseline	0.0 (0.0–7.0)	0.0 (0.0–8.5)	NS
Driving experience			
- years of driving experience	28 ± 9	30 ± 12	NS
- annual number of kilometers x 10^3	15 (5–23)	18 (10–50)	NS
AHI (no/hour)			
- baseline	48 (12–93)	55 (23–65)	NS
- follow-up review‡	5 (0–10)	0 (0–5)	NS
- Δ	-43 (-69–-12)#	-55 (-65–-16)||	NS
minSaO$_2$ (%)			
- baseline	78 (74–81)	80 (67–83)	NS
- follow-up review‡	91 (82–93)	92 (88–94)	NS
- Δ	9 (6–15)**	13 (10–24)¶	NS
Treatment usage			
- treatment use: nights per week	6.8 ± 0.4	6.8 ± 0.6	NS
- treatment use: hours per night	7.0 ± 0.9	6.7 ± 1.4	NS

* Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.
† Significance for the difference in baseline, follow-up or Δ outcomes between treatment groups.
‡ The median treatment period from baseline until final follow-up review was 81 (interquartile range 72–93) days in the oral-appliance group and 79 (interquartile range 63–102) days in the CPAP group (p>0.05).
§ p=0.001 for difference between baseline and follow-up outcomes within treatment group.
|| p=0.005 for difference between baseline and follow-up outcomes within treatment group.
¶ p=0.007 for difference between baseline and follow-up outcomes within treatment group.
# p=0.008 for difference between baseline and follow-up outcomes within treatment group.
** p=0.01 for difference between baseline and follow-up outcomes within treatment group.
Abbreviations: AHI = apnea-hypopnea index, CPAP = continuous positive airway pressure, NS = not significant, minSaO$_2$ = lowest oxyhemoglobin saturation during sleep.

TABLE 4. Baseline and follow-up review driving test outcomes of oral appliance and CPAP treated patients.

Variable	Oral appliance* (n = 9)	CPAP* (n = 10)	Difference†
Number of LOA			
total (0-25 minutes)			
- baseline	5.0 (2.0–14.0)	10.0 (1.0–16.8)	NS
- follow-up review‡	0.0 (0.0–2.0)	0.5 (0.0–5.3)	NS
- Δ	-5.0 (-12.5–0.5)§	-3.0 (-16.0–0.0)§	NS
1st epoch (0-5 minutes)			
- baseline	0.0 (0.0–1.0)	0.0 (0.0–0.0)	NS
- follow-up review‡	0.0 (0.0–0.5)	0.0 (0.0–0.0)	NS
- Δ	0.0 (-1.0–0.0)	0.0 (0.0–0.0)	NS
2nd epoch (6-10 minutes)			
- baseline	0.0 (0.0–1.0)	0.0 (0.0–1.0)	NS
- follow-up review‡	0.0 (0.0–0.0)	0.0 (0.0–0.3)	NS
- Δ	0.0 (-1.0–0.0)	0.0 (-1.0–0.3)	NS
3rd epoch (11-15 minutes)			
- baseline	0.0 (0.0–5.0)	1.0 (0.0–2.5)	NS
- follow-up review‡	0.0 (0.0–0.0)	0.0 (0.0–1.0)	NS
- Δ	0.0 (-4.5–0.0)	0.0 (-1.8–0.3)	NS
4th epoch (16-20 minutes)			
- baseline	2.0 (0.0–5.5)	3.0 (0.8–7.8)	NS
- follow-up review‡	0.0 (0.0–0.5)	0.0 (0.0–0.5)	NS
- Δ	-2.0 (-5.5–0.0)	-1.0 (-7.8–0.0)	NS
5th epoch (21-25 minutes)			
- baseline	2.0 (0.0–4.0)	4.0 (0.0–8.5)	NS
- follow-up review‡	0.0 (0.0–1.0)	0.0 (0.0–2.5)	NS
- Δ	-1.0 (-3.5–0.0)	-2.0 (-8.3–0.0)||	NS
Slope coefficient of time course SDLP			
- baseline	0.20 (0.06–0.60)	0.63 (0.04–0.90)	NS
- follow-up review‡	0.05 (-0.06–0.30)	0.14 (-0.22–0.28)	NS
- Δ	-0.01 (-0.55–0.13)	-0.15 (-1.20–0.23)	NS

* Plus-minus values are means ± standard deviations, values with additives in parentheses are medians with interquartile ranges.
† Significance for the difference in baseline, follow-up review or Δ outcomes between treatment groups.
‡ The median treatment period from baseline until final follow-up review was 81 (interquartile range 72–93) days in the oral-appliance group and 79 (interquartile range 63–102) days in the CPAP group ($p>0.05$).
§ $p=0.03$ for difference between baseline and follow-up outcomes within treatment group.
|| $p=0.04$ for difference between baseline and follow-up outcomes within treatment group.
Abbreviations: CPAP = continuous positive airway pressure, LOA= lapses of attention, NS = not significant, SDLP = standard deviation of the lateral position.

Based on the total number of LOA, OSAHS patients show worse driving performance when compared with control subjects. These findings are in keeping with other studies that also showed impaired performance in OSAHS patients during various tests of simulated driving.[7,9,10] The present study also suggests that simulated driving performance in OSAHS patients deteriorates with time-on-task, as indicated by the slope coefficient of the time course SDLP. Because already in the second epoch significantly more LOA occurred in the OSAHS group, a decline in driving performance may be expected after a relatively short period of time (*i.e.*, ten minutes). In contrast to several other simulator studies,[2] the present study only evaluated primary vehicle control. Secondary tasks, such as reaction times to specific stimuli, have been shown to actually stimulate drivers when performing a simulator test.[27] Because the driving test used in the present study proved to be sensitive to distinguish OSAHS patients from controls, it appears a valid measure of the fatiguing effects of a monotonous task.

Despite the fact that OSAHS patients performed worse as a group, not all patients showed impaired simulator performance when compared with the control subjects. This variability in simulated driving performance has also been observed in previous studies.[7,9,13] In the present study this phenomenon may be explained by inclusion of OSAHS patients of varying severity. However, at baseline significant correlations between the total number of LOA and the AHI or Epworth sleepiness scale could not be demonstrated. These findings are corroborated by other studies that also fail to demonstrate strong relationships between these parameters and driving simulator performance.[7,10] Therefore the question remains as to what extent other factors, beside OSAHS severity and symptoms, affect driving performance in untreated patients (*e.g.*, personality or coping strategies).

Especially in the case of more deviant performance at baseline, adequate OSAHS management by means of either oral-appliance or CPAP therapy usually resulted in substantial improvements of simulated driving. The correlation observed between changes in the total number of LOA and Epworth sleepiness scale values suggests that adequate OSAHS management ameliorates driving performance. This suggestion is supported by the fact that worse driving performance at the final review was observed in those patients who were "nonresponsive" to oral-appliance or CPAP therapy. Other studies evaluating simulator performance following CPAP therapy or uvulopalatopharyngoplasty usually also observe improvements in driving performance.[6,13-15,28] To our knowledge the present study is the first to study the effects of oral-appliance therapy on simulated driving performance. Although both groups showed significant improvements in the total number of LOA, significant improvements for the number of LOA in the fifth epoch were observed only for the subjects treated with CPAP. These findings may suggest a more pronounced effect of CPAP therapy on simulated driving performance. However, it is more likely

that methodological issues explain this phenomenon. First, our study was of an explorative character and not based on a power calculation. Secondly, despite non-significant differences, baseline values indicated more severe OSAHS and worse simulator performance in the CPAP group. In addition, with respect to baseline and follow-up values, no significant differences in simulated driving performance could be demonstrated between CPAP and oral appliance treated patients.

Despite the observed differences with control subjects and the favorable effects of treatment on simulator performance, there are a number of limitations to the present study. The first limitation refers to the control group. Control subjects were hospital employees and approximately 70% agreed after being asked to participate. Therefore, selection bias may have occurred. In addition, because polysomnographic data were not available in this group, subjects with "sub-clinical" OSAHS may have been included. However, questionnaire analyses raised no evidence of OSAHS symptoms in the control subjects. Therefore, based on the definition criteria employed in the present study,[20] the chance of having included patients with OSAHS in the control group is unlikely. A second limitation refers to a possible "learning effect" on the driving simulator when evaluating patients at the final follow-up review. Previous studies have failed to demonstrate profound learning effects in simulated driving performance in OSAHS patients.[7,28] Our driving simulator test could easily be performed by all subjects because the difficulty level was low and subjects were allowed to master the task during a practice session. If a learning effect had been present, it would therefore have had a limited effect on the performance during the second driving test. In addition, any residual learning effect was controlled for between the two treatments by a parallel study design. Thirdly, changes in simulator performance may (at least in part) result from a placebo effect. In addition, simulator performance may be influenced by volition and motivation, which may add further noise to the observed improvements in simulator performance. Trials comparing placebos with therapeutic CPAP, however, have failed to demonstrate strong placebo effects with respect to simulated driving performance.[14] A fourth limitation may be the fact that patient's reported treatment usage was not objectified in the present study. Whereas CPAP usage can be monitored covertly with a mechanism built into the device, oral-appliance usage cannot be assessed covertly in any reliable way. To eliminate bias, we ensured that treatment usage was assessed in the same manner by basing the assessments on self-reports in both groups. Questionnaire analysis indicated adequate treatment usage in both groups. However, self-reports usually overestimate the use of treatment by one hour per night.[29] When we adjusted for this factor, adherence to treatment was still adequate.[30]

From the present investigation we conclude that OSAHS patients perform worse on a monotonous simulated driving test when compared with control subjects.

When evaluating the effects of treatment, adequate OSAHS management with either oral-appliance or CPAP therapy usually resulted in substantial improvements of simulated driving. Although our findings suggest a more pronounced effect of CPAP on simulated driving performance, this phenomenon is largely explained by the relatively small study groups and large inter-group variance. Conclusions beyond both treatments improving simulated driving performance are therefore not justified. Studies with larger sample sizes that use a placebo group are warranted to elucidate the specific differences in effects of oral-appliance and CPAP therapy on simulated driving performance.

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