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Most obstructive sleep apnoea patients exhibit vigilance and attention deficits on an extended battery of tests

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ABSTRACT: Excessive daytime sleepiness, fatigue and altered attention are often experienced by obstructive sleep apnoea (OSA) patients. Although attentional problems are presumably responsible for part of the daytime functioning impairment in OSA, thorough investigation is unusual. Clinicians usually attribute these symptoms to somnolence. In clinical practice, only one isolated test is generally used to assess vigilance and attentional defects. It was hypothesised that most OSA patients exhibit a broad range of attentional deficits, beyond impaired maintenance of wakefulness, and a specific battery of tests is needed to correctly assess them.

Three attentional tests were performed at 9:00, 11:00 and 13:30 h, measuring maintenance of wakefulness, sustained attention and divided attention. Twenty OSA patients (aged 51±12 yrs, apnoea/hypopnoea index 45±22 h) and 40 control subjects (aged 48.4±9.9 yrs) were tested.

OSA patients performed significantly less well on the three tests than the controls at the three sessions. This battery of tests demonstrated that 95% of patients had vigilance and/or attentional impairment. Impairment patterns varied between patients.

Vigilance is impaired in obstructive sleep apnoea patients over a wide range of attentional processes. Not only is their ability to remain awake in monotonous situations impaired but their ability to maintain attention in more stimulating conditions is also affected. A single test of vigilance is not sufficient and could underestimate impaired vigilance and attention in some patients.

KEYWORDS: Attention, daytime sleepiness, obstructive sleep apnoea, vigilance

Obstructive sleep apnoea (OSA) is characterised by repeated complete or partial collapse of the upper airway during sleep. These events cause reduction or cessation of airflow and lead to oxygen desaturation and repetitive micro-arousals. Micro-arousals and oxygen desaturation are thought to be responsible for excessive daytime sleepiness, fatigue, loss of mental flexibility, altered attention and concentration that are often experienced by OSA patients. Clinicians usually attribute all these symptoms to excessive daytime sleepiness. However, although these symptoms may be inter-related, it is conceivable that somnolence is only one of the factors implicated and that other attentional processes are also affected. In clinical practice it is unusual to systematically assess attention and vigilance deficits despite their important public health implications with regard to driving [1] and occupational safety [2, 3].

Neuropsychological studies have clearly established that attentional capacities are based on a variety of processes. These processes are controlling the flow of information to cognitive systems [4] that have been recently defined in anatomical and functional terms [5]. Thus, the maintenance of an adequate level of attention allows the application of different cognitive processes and different tests specifically dedicated to these different processes are required for an adequate assessment of daytime functioning. At the lower level of these processes, vigilance can be defined as the ability to maintain an active state of wakefulness. The Oxford Sleep Resistance (OSleR) test is a widely accepted test for the evaluation of the capacity to remain awake during a soporific task. At a higher level of the daytime processes, sustained attentional mechanisms involve continuous maintenance of alertness and receptivity over time for a particular set of stimuli or stimulus changes. Selective attentional mechanisms enhance processing to attended stimuli or features, or inhibit processing of irrelevant information. These mechanisms have

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been compared to a ''spot-light'' that illuminates appropriate information and leaves irrelevant information in the dark. This capacity can be tested by the Continuous Performance Test (CPT) based on visual signal detection. Divided attention mechanisms allow multiple activities or stimuli to be attended to concurrently. Ecologic tests have been proposed, using driving simulation to assess divided attention capacities. Finally, subjective tests allow quantification of the subject's own perception of their vigilance.

Whereas most of the studies conducted in OSA patients only assessed vigilance capacity, the few studies examining daytime function have used tests that combine several aspects of cognition: attention, intellectual abilities and motor rapidity. Moreover, none were dedicated in understanding which kind of attentional processes were altered with OSA. To the current authors' knowledge, none of the recently published reports have used a panel of attentional tests in combination, aimed at objectively and subjectively characterising the different dimensions of attention that are altered in OSA patients.

Some researchers have demonstrated that only OSA patients complaining of sleepiness seem to benefit from nasal continuous positive airway pressure (CPAP) therapy [6]. An adequate test setting should be able to identify these various attentional dimensions affecting daytime functioning. Therefore, the current authors applied such a series of attentional tests, which require different levels of attention, ranging from vigilance, selective, divided and sustained attention, in 20 OSA patients and 40 control subjects. The OSleR test, CPT and the Driving Simulator Test were performed in all subjects at three different time of day. It was hypothesised that most OSA patients would exhibit impaired attention when such an extended battery of tests are used, and especially that the observed impairment would exceed the impairment related to simple somnolence.

MATERIAL AND METHODS

Population studied

Twenty patients with OSA (19 males and one female) were consecutively selected to participate in this research. Forty nonobese and nonsnorer control subjects (28 males and 12 females) recruited from hospital and university employees or from patients families were included. OSA patients had been referred to the Grenoble University Hospital, France, for clinical suspicion of sleep disordered breathing. They were either recruited from the Sleep Laboratory where they had undergone full polysomnography (PSG) or from the Ward Sleep Unit where the diagnosis of OSA had been confirmed by simplified polysomnography without EEG recordings.

Controls did not undergo polysomnography. Among these subjects, OSA was excluded using a home questionnaire demonstrating the absence of snoring, sleepiness, nocturnal urination, apnoeas described by the spouses and choking arousals. None of the controls suffered from cardiovascular diseases or other disease classically associated with OSA. In this clinical situation, FLEMONS *et al.* [7] have demonstrated that the likelihood ratio of having sleep apnoea is low, with a post-PSG probability to have OSA of $\leqslant$17%.

Subjects with a history of neurological or psychiatric disease, chronic lung disease, uncorrected visual impairment, chronic sedative intake or alcohol abuse were excluded. Subjects with significant cognitive impairment (score $<$23/30 at the Mini Mental Scale) were also excluded.

The study was approved by the institutional ethic committee. None of the participants received compensation for their participation.

Polysomnography

Details of the polysomnography techniques used in the current study have been published elsewhere [8]. Studies were scored using standard techniques and criteria [9, 10]. Microarousals ending respiratory events were called respiratory related microarousals. Altogether, seven patients did not undergo complete polysomnography, only recording of cardiovascular and respiratory parameters.

Vigilance and attention assessment

Participants were instructed to follow their usual sleeping habits the night prior the evaluation.

All subjects performed three different vigilance tests in random order: 1) the OSleR test (Stowood Scientific Instruments, Oxford, UK), which assesses the ability to remain awake during a soporific task (maintenance of wakefulness); 2) CPT (Multi-Health Systems, Toronto, Canada), which assesses sustained and selective attention; and 3) the Driving Simulator Test (Stowood Scientific Instruments), which measures divided attention. The three tests were repeated in all patients three times during the day, at 9:00, 11:00 and 13:30 h. The first test session started on average 2 h after the subjects had woken up. For all the tests, the subject was instructed on how to perform the task. The tests took place in a quiet and darkened room.

For OSA patients, the tests were considered abnormal if the value (mean of the three sessions) of one variable measured in the test was $<$2 standard deviations (95% confidence interval) of the mean value obtained for the control group.

Questionnaires

The general level of subjective sleepiness was assessed with the Epworth Sleepiness Scale (ESS) [11]. Intellectual quotient (IQ) scores were determined using the standard questionnaire [12]. As the depressive mood may affect the subjective perception of vigilance the Beck Depression Inventory (BDI) scale [13] was used to assess this confounding factor.

Maintenance of wakefulness during a soporific task: the Oxford Sleep Resistance test

The OSleR test (Stowood Scientific Instruments) corresponds to 40-min sleep-resistance challenges, measuring maintenance of wakefulness during a soporific task. Test procedure has been explained in a previous article [14]. The data collected from the OSleR test are the sleep latencies (duration of the test) and the number of omissions (nonresponses to stimuli) during the test.

Sustained and selective attention: the Continuous Performance Test

The CPT assesses the ability to detect and respond to specified stimulus changes occurring infrequently and at random intervals over 20 min while simultaneously inhibiting responses to stimuli.

Prior to the task, the subject is informed in a standardised manner about the course of the test and is given a 2-min practice test. The test takes place in a quiet, darkened room. The subject monitors a continuous presentation of letters on a computer screen. The subject is instructed to react by pressing the space bar each time a letter appears (targets) except when the letter X is presented, in which case, they must not respond (nontargets). Nonresponses to target numbers are recorded as omissions and inappropriate response to nontargets as commissions.

The data obtained from this test are the number of omissions, commissions, the mean reaction time (response latencies) and the attentiveness (D′), which is a measure of how well the individual discriminates between targets and nontargets. Variation in reaction time during the 20 min testing was assessed by the mean reaction time variation between the first and the last block of stimulation.

Divided attention: driving simulator

During this divided attention test (Stowood Scientific Instruments), the subject is sitting in front of a computer screen and is required to steer a car moving on a winding road with boundaries. While steering, the subject has to scan the four corners of the screen and identify a target digit each time it appears. An image of the bonnet of the car is displayed at the bottom of the screen. The subject, using a computer steering wheel, is instructed to steer the centre of the vehicle as accurately as possible. Single digits, 1 to 9, appear randomly at each corner of the screen and change every 10 s. During the divided attention part of the test, the subject, while steering the car, has to scan the four corners of the screen and identify the target digit (number 2) each time it appears and react by pressing a button on either side of the steering wheel. If the subject does not respond within 10 s to the target number, the number changes and an omission has occurred. The test ends after 20 min or before if the car leaves the road for >15 continuous seconds. Prior to the task, the subject is given a 5-min practice test.

Data obtained are the duration of the test, the mean reaction time (perception of target numbers) and the number of ''off road'' events (when the centre of the bonnet crosses the road's edges) quoted per hour of driving to allow for different length drives.

Statistical analysis

Values were expressed as mean±SD. Normality of distribution was tested using Kurtosis and Skewness test. An unpaired t-test or Mann-Whitney U-test was used to compare control and patient groups regarding quantitative variables. The Chi-squared test was used for qualitative variables. Correlation analysis were done using Spearman test. A p-value of <0.05 indicated significance in all studies.

RESULTS

Table 1 shows characteristics of the OSA and control groups. Both groups had high-normal IQ and were not in the depressive mood range according to the Beck evaluation scale. None of the subjects in the OSA group exceed 20 (score >20 demonstrating a moderate-to-severe depressive mood). Table 2 shows polysomnographic data for the 13 OSA patients who had a full PSG. Respiratory disturbance index (RDI) for the OSA group was 46.5±26.1 per hour of sleep. There was no significant difference in the severity of sleep apnoea between the patients who had full diagnostic PSG and the ones who had simplified PSG.

TABLE 1 Characteristics of the obstructive sleep apnoea and control groups

	OSA patients	Control subjects	p-value
Subjects n	20	40	
Age yrs	51.0±11.8	48.4±9.9	NS
BMI kg·m^{-2}	29.7±6.0	23.6±2.9	0.0002
ESS	11.1±5.5	5.2±3.5	0.0002
Beck scale	6.9±5.1	5.9±6.5	NS

Data are expressed as mean±SD. OSA: obstructive sleep apnoea; BMI: body mass index; ESS: Epworth Sleepiness Scale; NS: nonsignificant.

Maintenance of wakefulness: the Oxford Sleep Resistance test

Sleep latencies obtained at the OSleR tests performed at 9:00, 11:00 and 13:30 h and the mean sleep latency of these three sessions are shown in figure 1. Sleep latencies were significantly shorter in the OSA group compared to the control group at all sessions ($p<0.01$). The mean sleep latency was 2388±41 s in the control group, and 1899±475 s in OSA patients ($p<0.01$). Only 25% (5/20) of OSA patients completed the three OSleR sessions without falling asleep, compared to 87.5% (35/40) of control subjects. In the five subjects completing the three sessions without falling asleep, the errors never exceeded two consecutive omissions. OSA patients also had more omissions than controls ($p<0.01$), even though the duration of their test was shorter on average (fig. 2). Performance was not influenced by the time at which the test was done (time effect; $p>0.05$).

TABLE 2 Polysomnographic data for the obstructive sleep apnoea group with complete polysomnography

	Mean±SD
RDI	46.5±26.1
TST min	356.2±51.4
Stage 2 %TST	45.8±10.5
SWS %TST	6.8±5.7
REM sleep %TST	20.7±7.6
MA index	28.9±18.4
Mean nocturnal O_2 sat %	93.2±4.1
Time spent with O_2 sat <90% min	9.4±26.3

RDI: respiratory disturbance index (apnoeas and hypopnoeas per hour of sleep or recording); TST: total sleep time; SWS: slow wave sleep; REM: rapid eye movement; MA index: microarousals per hour; O_2 sat: oxygen saturation. n=13.

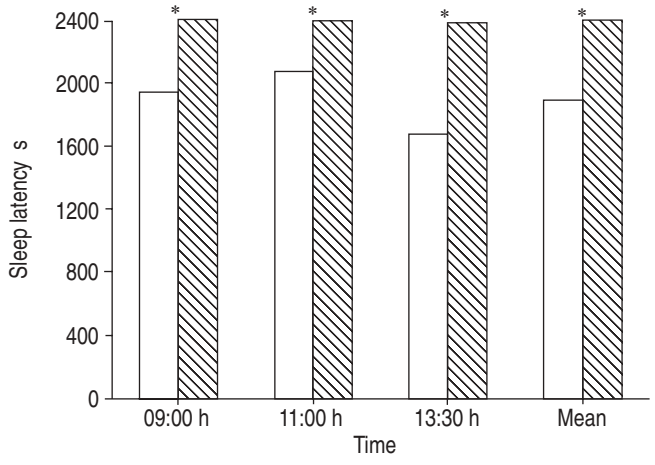

FIGURE 1. Oxford Sleep Resistance test sleep latencies (21 s) throughout the day for control (▨) and patient (□) groups. *: $p<0.05$.

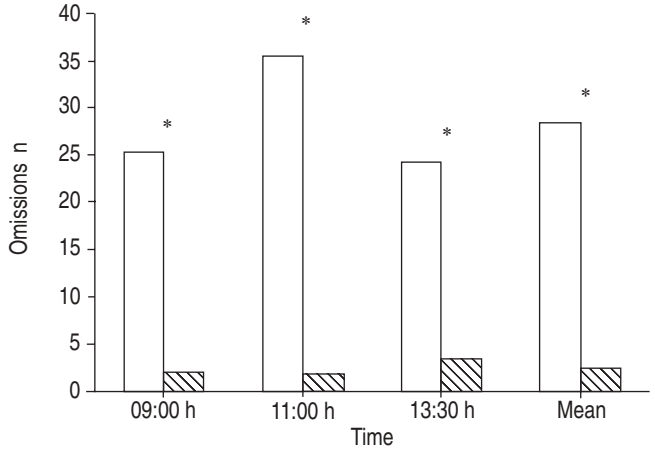

FIGURE 2. Number of omissions during the Oxford Sleep Resistance test for control (▨) and patient (□) groups, throughout the day. *: $p<0.05$.

Selective and sustained attention: the Continuous Performance Test

The OSA group and the control group had a similar mean reaction time in response to targets (mean of the three sessions: 363.4±38.3 ms *versus* 377.0±59.2 ms). For the two groups, no variation in reaction time was detected during the test (mean of the three sessions: 0.003±0.01 *versus* 0.005±0.01). For all sessions, the number of omissions (mean of the three sessions: 7.28±6.54 *versus* 1.91±2.17; $p<0.01$) and commissions (mean of the three sessions: 14.67±5.23 *versus* 10.30±5.40; $p<0.01$) were higher in the OSA group, indicating that OSA patients respond as fast as control subjects to targets, but make more mistakes. D' was therefore lower in OSA group compared with the control group (mean of the three sessions: 2.53±0.72 *versus* 3.42±0.76; $p<0.01$). There was no effect of time on the performance of the test ($p>0.05$).

Divided attention capacities: the Driving Simulator Test

OSA patients performed less well than control subjects at all sessions (table 3). OSA patients had a slower reaction time in response to target numbers (mean of the three sessions: 3.0±1.9 *versus* 1.9±1.0 s; $p<0.01$) and had more ''off road'' events (mean number of errors for the three sessions: 90.7±71.3 *versus* 40.1±36.7; $p=0.01$) than the control subjects. The duration of the test was shorter in the OSA group compared to the control group (mean of the three sessions: 989±249 *versus* 1139±115 s; $p=0.01$). Altogether, 40% (8/20) of OSA patients completed the total duration of the test (*i.e.* no off road event >15 s) compared with 67.5% (27/40) of the control subjects. A time effect was seen, as the duration of the test for both groups was better on the third session. This probably corresponds to a learning effect.

TABLE 3 Driving Simulator Test

		OSA patients	Control subjects	p-value
Subjects n		20	40	
Mean	Test duration s	989±249	1139±115	0.01
	Reaction time s	3.0±1.9	1.9±1.0	0.004
	''off road events'' $n \cdot h^{-1}$	90.7±71.3	40.1±36.7	0.01
09:00 h	Test duration s	956±314	1178±80	0.02
	Reaction time s	3.0±2.2	1.9±1.1	0.02
	''off road events'' $n \cdot h^{-1}$	116±93	48±44	0.002
11:00 h	Test duration s	1021±277	1141±173	0.06
	Reaction time s	2.9±1.9	1.9±1.1	0.02
	''off road events'' $n \cdot h^{-1}$	91±75	42±41	0.02
13:30 h	Test duration s	991±268	1099±252	0.03
	Reaction time s	3.1±2	1.8±0.9	0.002
	''off road events'' $n \cdot h^{-1}$	64±68	30±34	0.02

OSA: obstructive sleep apnoea.

Summary of vigilance and attention assessment in obstructive sleep apnoea patients

Results of the three vigilance tests performed in the 20 OSA patients are summarised in table 4. ESS and BDI scores are also presented for each patient. Altogether, 75% (15/20) of OSA patients failed the maintenance of wakefulness test (OSleR test), 65% (13/20) failed the CPT and 55% (11/20) failed the divided attention test (Driving Simulator Test). Among the 20 OSA patients tested, only one successfully completed the three tests and therefore showed no impairment of vigilance. Four subjects failed all tests, most of them denying excessive daytime sleepiness on the ESS. Of the five OSA patients who successfully completed the OSleR test (without falling asleep), four showed alteration of vigilance in the other tests.

Correlation analysis

A weak association was found between the performance at the OSleR test and the performance at the CPT ($R=0.50$, $p=0.026$) for test duration at the OSleR test and the number of omissions at the CPT. Otherwise, the performance at one test did not predict the performance at another test. There was no correlation between the performance at any of the vigilance test and ESS score, RDI or any sleep variables measured.

TABLE 4 Vigilance assessment in obstructive sleep apnoea patients

Patients	ESS	Beck	OSleR	CPT	DS
1	12	3	X	X	
2	12	10	X	X	X
3	4	2	X	X	X
4	19	9	X		
5	10	9	X	X	X
6	3	2		X	X
7	19	18	X		
8	11	5	X		
9	6	7	X		X
10	19	9	X		X
11	15	12	X	X	
12	9	4		X	X
13	9	15	X	X	X
14	10	6	X	X	
15	3	0		X	X
16	18	15	X	X	
17	18	5	X		X
18	12	3		X	
19	6	4	X	X	X
20	6	0			
Patients failing the test %			75	65	55

ESS: Epworth sleepiness scale; OSleR: Oxford Sleep Resistance test; CPT: continuous performance test; DS: driving simulator; X: failed test (performance <2 SD from the mean performances of the control group).

DISCUSSION

This study is the first to use a panel of tests to understand which aspect of attention is altered in OSA patients. The study investigated different attentional processes, including a measure of vigilance (ability to remain awake), selective, sustained and divided attention capacities in OSA patients and control subjects.

The results showed that OSA patients performed less well than controls in all vigilance and attention tests at any time during the day. These results support the conclusion that not only was their ability to remain awake in monotonous situations impaired (OSleR test) but also their capability to maintain attention in more stimulating conditions. These results suggest that a large spectrum of attentional processes are altered in this disorder.

Most of the studies investigating diurnal dysfunction associated with respiratory diseases have evaluated only one isolated domain of attention, namely vigilance, by the use of specific techniques, such as the maintenance of wakefulness test [15] or multiple sleep latency test [16]. Other attentional domains have rarely been evaluated, and the few neuropsychological studies done in the area of sleep apnoea generally used tests that jointly involved attention and other cognitive capabilities, making the dissociation difficult.

The results from the current study confirm the difficulty to maintain wakefulness during a soporific task during the day in OSA patients that was previously reported in others studies [17, 14]. During the OSleR test, 75% of OSA patients exhibited vigilance alteration, characterised by shortened sleep latency and a higher number of errors during the test. However, this vigilance alteration occurring in soporific situation was not the only attentional process altered in our patients. In a more stimulating context, OSA patients also exhibited lower performances compared to controls. During the selective and sustained attentional test (CPT), OSA patients responded as fast as controls to the stimuli presented, but exhibited more errors than the controls. These results reveal that OSA patients have difficulty adapting their reaction time to the task, preferring rapidity to response's relevance, which corresponds to an alteration of their selective attentional processes. REDLINE *et al.* [18] showed a discrepancy of reaction time in the last part of the test, and concluded that a sustained attention difficulty was present in these patients [18]. This discrepancy was not observed in the current study. There was no difference in variation of reaction time during the 20 min testing between the two groups. However, this lack of difference does not mean that the patients are free of sustained attention deficits. The absence of any deterioration in reaction time through the 20 min test may be related to the superficial attentional processing, the reaction time being possibly maintained owing to the overall poor performance in selected attention.

When asked to perform two simultaneous tasks (DST), OSA patients showed impairment in divided attention characterised by lower reaction time and increased number of off road-events (twice as many as controls). This was related to the OSA patients difficulty in sharing their attention between visual tracking and driving in this particular task, illustrating the severity of their attentional deficit.

The current study also showed that the magnitude of attentional deficits varied among OSA patients. Some presented with specific difficulties to maintain wakefulness without any other attentional abnormality, whereas others exhibited attentional difficulties only when the information was presented in a more stimulating environment.

These different impairment profiles strengthen the hypothesis that attentional capacities could be selectively altered [5] and reinforce the need for multifactorial investigation in OSA patients. These results also showed that somnolence alone (measured by the OSleR test) did not account for the cognitive dysfunction seen in OSA patients insofar as some of them exhibited attentional alteration without significant excessive daytime sleepiness.

These results fit within the framework of the neuropsychological theory that assumes the existence of functionally and anatomically independent attentional processes distributed between frontal and parietal cortex [5, 19].

Numerous studies reported that a significant proportion of OSA patients do not subjectively complain of impaired vigilance. Thus, there is only a weak correlation between sleep fragmentation indices and the ESS, whether provided by patients [20] or their bed partners [21]. This study confirms the lack of congruence between the level of vigilance felt by patients and the level of vigilance objectively quantified using attentional testing. Data from the current study confirms that subjective somnolence *i.e.* ESS is not sensitive enough to

identify significant impairment in vigilance in sleep apnoea patients. Among the 10 patients without subjective complaint of alteration of vigilance (Epworth $\leqslant 10$), nine exhibited concurrent abnormalities in at least one of the three objective attentional tests (table 4).

In some OSA patients, prescribing CPAP seems difficult owing to an absence of subjective sleepiness, a critical determinant of CPAP use. Thus, applying a sensitive battery of vigilance and attentional tests could improve the identification of patients that could benefit and respond to treatment. However, whether these subjects may perceive a subjective benefit from CPAP treatment remains to be established. As a vast majority of patients exhibited alteration, at least in one of the attentional tests, this suggests treating OSA patients without perceived sleepiness, in opposition to a previous study by BARBÉ *et al.* [6]. Indeed, the reduction in attentional deficits may potentially improve quality of life and driving ability.

Discussing with the patients their vigilance and attention results may be a way to raise patients' awareness to the risks of driving and stress their responsibility. In addition, explaining that the risk is not only to fall sleep but also to present lower attentional capacity during driving or other daily life activities could prove useful.

Conclusion

When using an adequate panel of vigilance tests to assess the ability to remain awake, and to maintain selective, sustained and divided attention, a large majority of sleep apnoea patients demonstrated attention defects. To date, in clinical practice, vigilance is generally assessed only by subjective scales or one isolated attentional test. The data presented in this study suggest that this is clearly insufficient to evaluate the attention defects occurring in a majority of OSA patients.

Using one isolated test could lead to the disregard of some patients with impaired vigilance and attentional deficits. Specific tools should be used to adequately detect deficits in vigilance and attention capacity. Whether the different alterations are associated with specific risks of accidents or respond differently to treatment should be further studied.

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