DIURNAL PERFORMANCE DECLINE IN NARCOLEPSY: LIMITATION OF PROCESSING RESOURCES

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INTRODUCTION

Vigilance decline in narcolepsy has been observed repeatedly in task performance\textsuperscript{1}. However, the nature of this vigilance effect is not exactly clear. In order to investigate vigilance problems in narcolepsy, it would be informative to examine to what extent narcolepsy patients differ from healthy people in naturally occurring vigilance fluctuations throughout the day. A general tendency to perform worse has been reported\textsuperscript{2}, and this suggests that vigilance is constantly at a lower level. On the other hand, a greater post-lunch dip has been found on some measures\textsuperscript{3}. It has been argued that the most parsimonious explanation is an impairment of the circadian process in narcolepsy\textsuperscript{4}. Conversely, it is argued that an increased homeostatic sleep drive may affect the diurnal pattern. In most studies on narcolepsy, patients are allowed to nap\textsuperscript{3,4}. Naps are known to increase performance and alertness\textsuperscript{5}. The alerting effect of a nap may well influence results and might cause a relative improvement in performance in the afternoon. Therefore, vigilance may decline continuously over the day in narcoleptic patients if naps are not permitted. In this case, the homeostatic sleep drive is likely to be increased, a view that has been suggested before\textsuperscript{6}. Although a relation between vigilance and memory is plausible, the literature does not fully clarify this issue, although it is agreed that a short nap seems to improve performance in narcoleptic patients\textsuperscript{7}. In view of the experimental results mentioned above, three hypotheses are tested. First, it is predicted that an enhanced sleep drive can explain the pattern in diurnal variation for narcoleptic patients. Hence, it is expected that performance and alertness in patients will gradually decline during the day if naps are not allowed. Secondly, it is predicted that narcoleptic patients are impaired on the demanding task in particular. Thirdly, it is hypothesized that vigilance and episodic memory performance are related. There should be a simultaneous drop in memory performance if vigilance declines and variation in memory performance should correlate with changes in vigilance.

METHODS

Participants were narcoleptic patients and healthy controls. Participants in the narcolepsy group were four men and 13 women, with a mean age of 41 years (19 – 59). Five patients were not on any form of medication; nine patients used ‘Modiodal’ (modafinil) and three patients used ‘Ritalin’ (methylphenidate). Patients did not take any medication on the day of testing. Participants in the control group were nine men and ten women, with a comparable mean age of 40 years (23 – 60), who were also matched for education. All participants signed an informed consent and came to the laboratory at 9.00h. There were five testing blocks, at 9.00h, 11.00h, 13.00h, 15.00h and 17.00h. Between testing sessions, participants were
allowed to go for short walks or relax in a separate room. Each testing block consisted of parallel versions of the following tasks: two Reaction Time (RT) tasks: the SART (Sustained Attention to Response Test) and the memory-SART (a demanding working memory version of the SART), as well as a 20-words memory test. Additionally, two subjective alertness questionnaires were presented: a Visual Analogue Scale (VAS) and the Thayer subjective alertness scale. Memory performance on the 20-words test was tested for recall, both immediately after presentation (immediate recall) and 10 minutes after presentation (delayed recall). The order of the tests in each block was counterbalanced over participants, both in the control and the patient group. Participants were not allowed to nap and were awoken immediately if they did tend to fall asleep.

RESULTS AND DISCUSSION

Task performance. Despite the fact that patients were not allowed to nap, three of the seventeen narcoleptic patients were unable to stay awake all the time between 15.00h and 17.00h. Nevertheless, their data were included in the analyses. Their task performance showed a relative increase after the nap. Task data were split into two parts: the first and second part. This was done to investigate detrimental effects during the task. Misses, false alarms, and reaction times (RTs) were analyzed by repeated measures ANOVAs.

SART: false alarms. As participants were instructed not to push a button on the target, the false alarm rate is considered to be a sensitive performance parameter in this task. Tests revealed no effects in the narcolepsy group; in the control group there were more false alarms in the second part of the task, F(1,16) = 14.29; p = 0.002.

SART: misses. Misses on the SART occurred in those instances that a response to a non-target was required, but was not made. The least targets were missed at 9.00h. Patients missed increasingly more targets over the day and they missed more targets than control participants from 11.00h on (p-values < 0.01). Furthermore, their misses increased during the SART (p-values < 0.01). Hence, narcoleptic patients progressively perform worse over the day.

SART: RT. RTs were greater in the second than in the first part of the SART, F(1,28) = 19.64; p < 0.001. Patients responded slower than control participants, F(1,28) = 24.26; p < 0.001. RTs and patients responded slower in the second than in the first part of the task, F(1,12) = 23.80; p < 0.001. Hence, narcoleptic patients respond slower than healthy controls at all times and slowed down even more in the second part of the SART.

Memory-SART: misses. As participants were instructed to push a button on the target, the amount of misses was considered a sensitive performance parameter. Patients missed more targets than control participants, F(1,29) = 76.59; p < 0.001. More misses were made in the second than the first part at all times, (all p-values < 0.001), and patients missed more targets than control participants, (p-values < 0.01). At 9.00h, 11.00h and 13.00h control participants missed more targets in the second than the first part (p-values < 0.05), but in the second part patients missed many more targets (p-values < 0.01). The absolute number of misses was smaller in the memory-SART than the SART, but the relative number was greater: the SART includes 200 targets, whereas the memory-SART consists of only 25 targets. In sum, more targets were missed in the second part of the memory-SART. The amount of misses continuously increased over the day. Patients missed more targets than control participants at all testing times and were most prone to performance decline during the task. Hence, narcoleptic patients’ performance is lower and declines progressively over the day.

Memory-SART: false alarms. No effects were present.
Memory-SART: RT. RTs were greater in the second than the first part of the memory-SART, $F(1,24) = 9.25; p = 0.006$. Patients responded slower than control participants, $F(1,24) = 19.52; p < 0.001$. In sum, responses slowed down during the task and patients responded slower than control participants.

Memory performance. Analyses showed that less words tended to be remembered in the narcolepsy group than in the control group at 13.00h ($p = 0.054$) and 17.00h ($p = 0.091$). There was a Time effect in the Delayed recall: $F(4,25) = 6.37; p = 0.001$: more words were remembered at 9.00h than at all other times ($p$-values $< 0.05$). Although there was no Group effect, patients tended to remember fewer words than the controls.

Subjective judgment: Thayer scale and VAS. On the Thayer test patients felt more sleepy than control subjects, $F(1,29) = 46.45; p < 0.001$ and patients felt less activated than control subjects, $F(1,29) = 37.49; p < 0.001$. Additional analysis showed that the group difference was present at all testing times ($p$-values $\leq 0.001$). On the VAS patients felt less alert than control subject, $F(1,27) = 24.63; p < 0.001$. Additional analysis showed that the groups differed at all testing times ($p$-values $\leq 0.003$). The subjective scores all suggest that narcoleptic patients feel less alert than healthy controls at all times.

Correlations. Correlations were computed between memory scores on the one hand and performance scores and subjective scores on the other hand. In the control group vigilance and memory scores were not strongly related, but in the narcolepsy group vigilance and memory scores were more strongly related.

Some differences between the control and narcolepsy group were already apparent at 9.00h. Responses were slower from the start in the narcolepsy group, both on the SART and the memory-SART. Moreover, narcoleptic patients missed more targets than the control participants on the memory-SART. Furthermore, patients felt more sleepy, more physically fatigued, and less activated and alert during the whole day. These results confirm the idea that there is no time at which narcolepsy patients feel or perform at normal levels $^2$. The effect on physical fatigue was especially interesting. Apparently, sleepiness and tiredness does not merely entail mental aspects of vigilance, but also a physical component. Vigilance declined progressively over the day in the narcolepsy group, both on the SART and the memory-SART. Performance was rather stable over the day in the control group. There was no evidence for a post-lunch dip. It appears that if naps are not allowed, there is no temporary vigilance increase in the afternoon in the narcolepsy group. The diurnal performance pattern in the narcolepsy group is compatible with the view that the sleep drive is enhanced $^6$.

The two tasks differed with respect to sensitivity. Already at the start of the experiment did the memory-SART distinguish the patient group from the control group by means of all performance measures. The SART yielded a group difference for all performance measures at 11.00h. Therefore, the demanding memory-SART yielded the worst performance and was most sensitive in discriminating groups. These findings support a resource view on vigilance performance $^8$. Narcoleptic patients, having a lower level of vigilance, might run short on resources, and thus perform worse on a high-demanding task at all times. The SART, which is less demanding, requires less resources and the patient’s availability of resources needs to be declined to a greater extent before performance starts to worsen significantly. Subjective alertness and task performance were lower in the patient group than in the control group from the start of the experiment. Patients’ vigilance continuously declined further and the difference between the control and patient group grew throughout the day. No evidence was found for a greater post-lunch dip for the narcoleptic patients, who were not allowed to nap. There appears to be an enhanced sleep propensity for narcoleptic patients. The high-demanding task was more sensitive than the low-demanding task in discriminating the control group from the patient group. Memory performance tended to be worse in the narcolepsy group.
group and this effect appeared to be (at least partially) secondary to the vigilance decline. Overall, narcoleptic patients have a low level of vigilance and become even less vigilant throughout the day. Due to this vigilance lowering, they have less processing resources available, which impairs them on cognitively demanding tasks in particular. The cause of the vigilance effects is not clear. The lowering in vigilance might be a consequence of the fact that narcolepsy is associated with sleep fragmentation, which is known to lower vigilance in healthy participants as well. There might also be a direct affliction of those brain structures that are involved in the regulation of vigilance.

CONCLUSIONS

Diurnal vigilance variation was investigated in narcoleptic patients, who refrained from drug intake. Vigilance was determined with performance and subjective measures. Three hypotheses were tested. First, it was investigated whether sleep propensity is enhanced in narcolepsy, with the prediction that if patients are not allowed to nap, a continuous diurnal decline in vigilance should be present. Indeed, results showed that task performance and subjective alertness were lower for patients than for controls at all times. This indicates that performance and alertness are always at lower levels in narcoleptic patients. Patients’ vigilance continuously declined further and the difference between the control and patient group increased over the day. There thus appeared to be an enhanced sleep propensity in the narcolepsy group. Secondly, it was tested whether high-demanding tasks are sensitive measures of vigilance decline in narcolepsy. As expected it appeared that the high-demanding task was more sensitive than the low-demanding task in discriminating the control group from the patient group. Thirdly, it was investigated whether memory impairments in narcolepsy are related to vigilance decline. The patients’ memory performance tended to be worse, which appeared to be associated with the vigilance decline. In conclusion, vigilance in narcoleptic patients is lowered and declines progressively over the day. As vigilance is low, narcoleptic patients have less cognitive processing resources, which might impair them especially on high-demanding tasks.

REFERENCES