

Attention Deficits in Patients with Narcolepsy

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Study Objectives: Although attention problems are presumably responsible for a wide variety of difficulties patients with narcolepsy experience in everyday life, empirical investigation of this issue is scarce. Therefore, we conducted a systematic investigation of different aspects of attention and verbal memory in patients with narcolepsy.

Design: Control-group design with comparison of performance in four attention tests—measuring phasic alertness, focused attention, divided attention, and flexible attention—and one verbal memory test.

Participants: 19 patients with narcolepsy (NG) and 20 healthy controls (CG)

Measurements and Results: The NG showed no deficits in phasic alertness, focused attention, and verbal memory. However, specific deficits occurred in divided and flexible attention. Furthermore, the NG had generally slower and more variable reaction times in all attention tasks.

Conclusions: Our results contradict the hypothesis that attentional impairments in narcolepsy are merely a result of a temporal disturbance of information processing, i.e., deficits can be explained by slowness and variability of performance alone. Rather, deficits in attentional capacity and attentional control also seem to play an important role. Thus, in addition to impairment in the vigilance attention network, results indicate impairment in the executive attention network in patients with narcolepsy.

Keywords: narcolepsy, attention, verbal memory, alertness, selective attention, divided attention, flexible attention, focused attention

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INTRODUCTION

NARCOLEPSY IS A SLEEP DISORDER, WHICH IS CHARACTERIZED BY EXCESSIVE DAYTIME SLEEPINESS, CATAPLEXY AND UNTIMELY OCCURRENCE OF REM-SLEEP.¹ Many patients with narcolepsy complain about attention and memory problems, and those problems are presumably responsible for a wide variety of difficulties in everyday life, e.g., impaired educational and occupational performance.^{2,3} Empirical evidence for impairment in attention and memory is scarce and sometimes contradictory. Thus, the aim of our study was to investigate attention and memory in patients with narcolepsy, with a focus on attention.

Most studies on attention find that patients with narcolepsy have slower reaction times (RTs) than controls, even in relatively simple tasks, like 4-choice RT tasks.^{4,5} It is also frequently reported, that performance in patients with narcolepsy is more variable than performance in controls.^{6,7} Whether patients make more errors than controls⁸⁻¹⁰ or not¹¹ seems to depend on the task and on the specific component of attention under investigation.

The reported deficits implicate disturbances on the temporal level of information processing (i.e., decrease of performance over time, variability of performance)^{5,6} in patients with narcolepsy. However, they also raise the question, whether there is a specific pattern of attentional deficits in patients with narcolepsy. Attention is not a unitary function but is composed of several different, sometimes highly specific, components, which are responsible for the control of the flow of information in the cognitive system.¹²⁻¹⁷ The focus in our study will be on two broad subdivisions of attention: a) arousal / alertness and sustained attention

(which is similar to temporal aspects of attention) and b) selective attention / executive control of attention.

Both aspects of attention can be further subdivided: arousal can be divided into tonic arousal and phasic arousal.¹⁷ Repetitive and monotonous tasks (e.g., tests of vigilance or monitoring) try to measure tonic arousal, and patients with narcolepsy show consistent impairment in those tasks.^{5,18-20} Phasic arousal refers to the ability to develop an optimal sensitivity to expected external stimuli over a short period of time, e.g., when persons receive a warning to prepare for a critical stimulus. To our knowledge, no systematic studies thus far have investigated this aspect of attention in patients with narcolepsy.

Selective attention encompasses the abilities to select information from a certain source or of a certain content and to set priorities in information processing to enable an individual to make optimal use of limited capacities.^{14,21} It comprises the abilities to select and integrate stimuli and / or contents as well as the ability to focus on and change between such stimuli and / or contents.¹⁷ The concept of selective attention is strongly connected with the concept of limited capacity. If attention would not be limited, selectivity would not make any sense.²² Furthermore, selective attention also shows a relation to the concept of attention control. To apply attention selectively a person must be able to control his or her attention to the task at hand. Thus, three important subspects of selective attention are focused attention (i.e., the ability to attend to relevant stimuli), divided attention (i.e., the ability to share attention between different sources of information), and flexible attention (i.e., the ability to change the focus of attention).^{17,22} Studies on patients with narcolepsy seem to indicate that they have no^{23,24} or very limited¹⁰ deficits in focused attention. There is some evidence that divided attention tasks with high requirements of attentional capacity might be very sensitive to performance decrements in narcolepsy.²³ Diminished performance in driving simulation programs^{8,9,25} might also result from deficits in divided attention. There are no studies directly investigating flexible attention in patients with narcolepsy.

Attention and memory are closely related. In order to memorize something, one must attend to it. Therefore, if impairment in attention exists in patients with narcolepsy, an impairment of memory seems likely at first sight. However, most studies using extensive memory test batteries with verbal and visual material, testing short and long-term memory, found that patients with narcolepsy perform normally in all tests.^{26,27}

Disclosure Statement

Nothing to disclose

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This is remarkable, especially as in one study only patients who subjectively complained of many memory problems were investigated.²⁶ In contrast to those results, some other studies indicate a deficit in free recall in patients with narcolepsy,^{11,24} especially when using verbal learning tests.

To summarize, patients with narcolepsy complain about difficulties concentrating and difficulties in memory; however, empirical evidence is contradictory. In the area of attention, the only consistent and empirically validated concept is an impairment of tonic arousal, i.e., vigilance. There are no investigations on phasic arousal in patients with narcolepsy. In the area of selective attention, most studies investigate focused attention, which shows no or limited deficits. Divided attention is likely to be impaired. No systematic investigations were done on flexible attention. Many studies face the problem that the attentional tests used cover several aspects of attention. Such tasks can pinpoint to attentional deficits; however, they do not allow specifying which aspects of attention are impaired. Therefore, the main aim of this study was a systematic investigation of several aspects of attention: phasic alertness as one aspect of arousal and three aspects of selective attention (focused attention, divided attention, and flexible attention). Furthermore, if we found a memory deficit in patients with narcolepsy, we were interested in studying its relationship to attentional difficulties.

METHODS

Participants

A group of patients with narcolepsy (NG, N=19, 9 male), who were tested as inpatients of the Hepata-Klinik and a control group (CG, N=20, 10 male), recruited from the hospital staff, took part in the study. Patients with narcolepsy were either newly diagnosed or came for a change of medication to the hospital. It was not possible to test all patients medication-free; six of the 19 patients had taken stimulants on the day of testing, all other were at least 3 days free of central stimulants (see Appendix for a short summary of a subgroup analysis of medicated and unmedicated participants). According to the criteria of the *International Classification of Sleep Disorders—Revised*,¹ all patients in the NG were chronic; in 3 of them narcolepsy was mild, in 10 moderate, and in 6 severe. All patients showed daytime sleepiness, sleep attacks, and cataplexy. Seventy-five percent of the NG had a mean sleep latency of less than 5 minutes in the MSLT and 68% showed two or more sleep onset REMs. Length of illness was on the average 10.4 (SD=10.7) years, and time since diagnosis was on the average 4.9 (SD=5.6) years. Exclusion criteria were medical conditions not related to narcolepsy that could have an influence on neuropsychological test performance and German not a first language. Per institutional guidelines, all of the patients gave informed consent. None of the patients or controls were paid for participating in the study. The study conformed to the Declaration of Helsinki.

Age in the NG ranged from 23 to 57 years (M=39.9, SD=11.5); in the CG, age ranged from 18 to 60 years (M=40.1, SD=13.3). In both groups, schooling ranged from 9 to 13 years (NG: M=10.4, SD=1.7; CG: M=10.7, SD=1.6). T-tests revealed no differences between the two groups in either age ($t(37)=0.04$, $p=0.97$) or years of education ($t(37)=0.53$, $p=0.6$). The Edinburgh Inventory²⁸ was used to assess hand preference. All participants of the NG were right-handed; in the CG, 19 participants were right-handed and one participant was left-handed. Patients with narcolepsy showed significantly more daytime sleepiness in the Epworth Sleepiness Scale²⁹ (NG: M=18.8, SD=3.5; CG: M=6.5, SD=4.2, $t(37)=10.03$, $p<0.0001$).

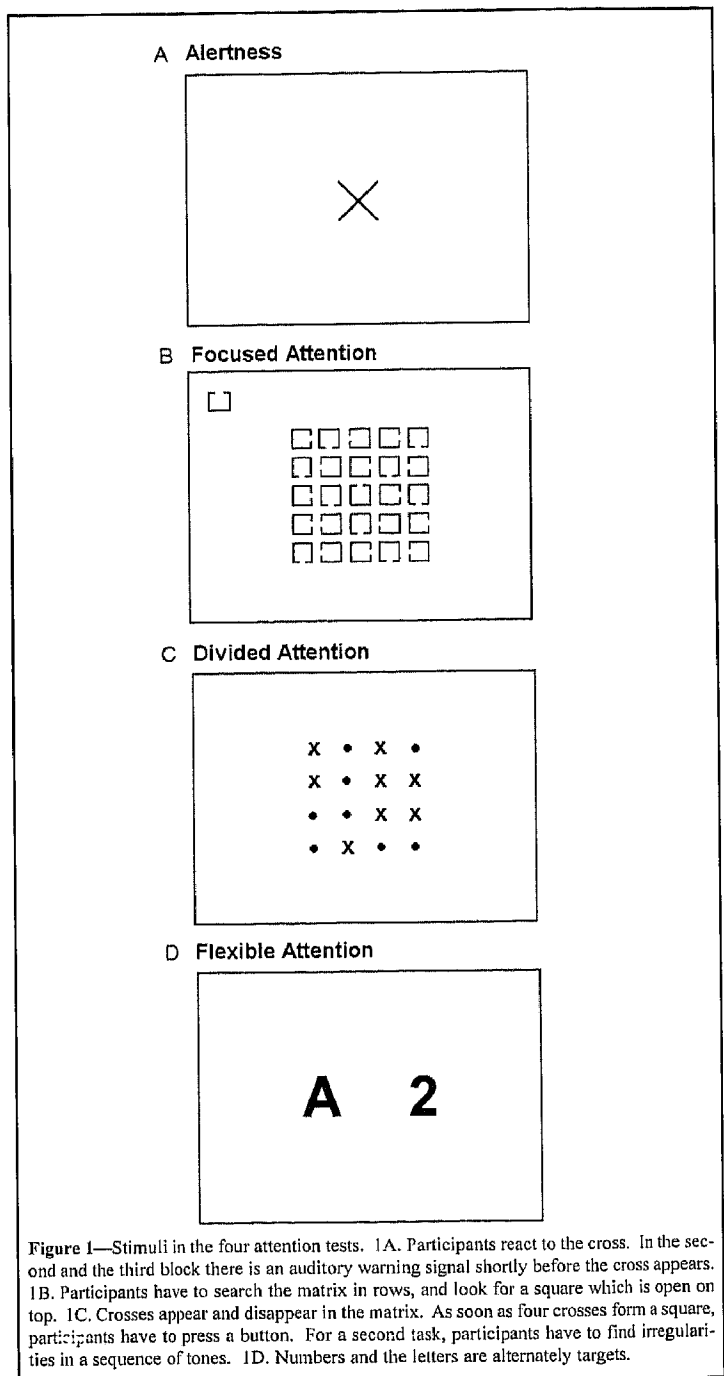
All participants were tested in the morning (start of the session between 9 am and 10 am), apart from three participants in the CG, in whom a test in the morning was impossible to arrange due to their work schedule. Patients with narcolepsy were tested 10 minutes after the first Multiple Sleep Latency Test (MSLT) at 9 am.

Neuropsychological Assessment

Attention

Four tests of the Testbatterie zur Aufmerksamkeitsprüfung (TAP)³⁰ were used to assess attention: Alertness (phasic arousal), Visual Scanning (focused attention), Dual Task (divided attention / attentional capacity), and Alternating Reactions (flexible attention / attentional control).

Alertness (AL): This test measures phasic alertness, i.e., the ability to increase the attentional level when a stimulus of high priority is likely to appear. The test consists of two conditions; in both, participants have to react to a visual stimulus (see Figure 1A). In condition A, participants are only presented the visual stimulus. In condition B, shortly prior the visual stimulus, an auditory warning signal is presented to the participants. The alertness reaction is defined as the difference between condition A and condition B; in condition B, reactions are generally faster than in condition A. The conditions were conducted in four blocks, con-



sisting of 20 trials each, in an ABBA design. Task duration is 8 to 10 minutes. Mean RTs and the SDs of the RTs of each of the four blocks were used as dependent variables.

Visual Scanning (VS, focused attention): The stimulus display consists of 5 rows and 5 columns of squares, which are always open on one side (see Figure 1B). The critical stimulus is a square, which is open on top. Participants have to decide whether it is absent or present in a certain stimulus display by pressing one of two response buttons, assigned to the left and the right hand. One hundred displays are randomly presented, 50 with and 50 without the critical stimulus. In the 50 trials with the critical stimulus, it is presented randomly 10 times in each row and each column. Participants are instructed to search the matrix "like reading." Thus, it is possible to calculate whether the participants have been searching the display in a systematic order by calculating the correlation between RT and position. The task is self-paced and takes participants approximately 10 minutes to complete. Dependent variables were the mean RTs, SDs, and errors for trials with "target present" and trials with "target absent," and the correlation of RTs with rows (row index).

Dual Task (DT, divided attention): Divided attention can be assessed in tasks in which participants have to pay attention to two different sets of stimuli concurrently. In the divided attention task of the TAP, this is done by a visual and an auditory task. In the visual task, participants see a display of 16 points (four in each row and column). Some of these points change to crosses, and participants have to press the response button as soon as four of those crosses form a small square (see Figure 1C). The auditory task consists of an alternating sequence of high and low tones; participants have to press the response button when they detect an irregularity in the sequence. One hundred visual and 200 auditory stimuli are presented in a block. The task was conducted in three blocks: a) visual stimuli only (single task), b) auditory stimuli only (single task), and c) visual and auditory stimuli together (dual task). Each block lasted 3 minutes and 40 seconds. Dependent variables were the mean RTs, SDs, and omissions under single and dual task conditions for visual and auditory stimuli.

Alternating Reactions (AR, flexibility of attention): Two stimuli, right and left of the center of the screen, are simultaneously presented. One of the two stimuli is always a letter; the other is always a number (see Figure 1D). Letters and numbers are alternately the critical stimulus, i.e., in the first trial participants have to react to the letter; in the second, participants have to react to the number, in the third again to the letter, and so on. Participants have to press one of two response buttons, assigned to the left and to the right hand. The task is to respond with the side on which the critical stimulus appears. One hundred trials are presented to the participant; 50 trials consist of responses with the same hand as in the trial before, 50 consist of responses with the other hand. The task is self-paced and takes participants approximately 5 to 10 minutes to complete. Dependent variables were mean RTs, SDs, and errors of same hand and other hand reactions.

Verbal Memory

A German version³¹ of the Auditory Verbal Learning Test (AVLT)³² was used. It serves as the assessment of verbal memory under learning conditions. The task consists of two word lists, containing 15 words each. The administrator reads the words of the first list (A) in a one-second rhythm. The participant has to remember and repeat as many of them as possible after the list has been read. This procedure is repeated four more times with the same list. After that, the administrator reads 15 words once from the other list (B) and the participant has to remember and repeat those. After that, the participant is asked to recall as many words as possible from the first, several-times-repeated list, without hearing it again (free recall). In the last part of the test, participants are presented 50 words, consisting of the words of lists A and B and semantic and / or phonetically similar words to those lists, and they have to decide which of those words belong to list A (recognition). Six scores were calculated from this task: a) the summary score (total score) of the five learning trials with list A, which yields a global indicator for mem-

ory performance under learning conditions; b) the number of items recalled after the first presentation of the list, which indexes immediate recall; c) the number of items recalled of list B, which, compared with immediate recall of list A, indicates the ability to switch to other material; d) the number of items recalled after the fifth presentation; e) the number of list A words remembered after the disruption by list B, which, in comparison to the number of words remembered after the fifth presentation, gives a measure of susceptibility to interference in memory; and f) the number of items recalled correctly in the recognition test.

Test Order and Sleepiness

The attentional tasks were conducted in ascending levels of difficulty and complexity. Therefore, AL was the first test and VS was the second. After that the AVLT was carried out to give participants a break from looking at a computer screen. Afterward the DT followed, and the session was finished with AR. Between the tests, participants were able to take short breaks so that the session would not become too tiresome.

The Stanford Sleepiness Scale (SSS)³³ was used to assess sleepiness during the testing session. All participants filled in the scale before and after the testing session. The NG had a mean score of 3.1 (SD=1.3) before and 3.7 (SD=1.4) after the test session. The CG had a mean score of 2.1 (SD=0.8) before and 2.8 (SD=1.3) after the testing session. A two-way ANOVA with Group as a between participant factor and Time as a within participant factor was conducted. The NG was more tired than the CG (Group: $F(1,37)=8.48$, $p=0.006$), and both groups were more tired at the end of the testing session (Time: $F(1,37)=13.73$, $p=0.0007$). However, there was no indication that the NG was more affected by the testing session than the CG (Group x Time: ($F(1,37)=0$, $p=0.97$).

Statistical analysis

Within and between group differences (Group: NG, CG) were evaluated using T-tests or repeated measures analysis of variance (ANOVA) using the SAS software package.³⁴ In case variance between the groups was heterogeneous, T-tests for heterogeneous variance were used, denoted as $t(\text{het})$ in the text. Cohen's³⁵ standardized d-values were used for the estimation of effect sizes (ESs). Correlations were calculated using the Pearson product moment correlation coefficient. All analysis of central tendency of RT were conducted with mean as well as with median values. Both analyses revealed comparable results. Since mean values are used for the calculation of effect sizes, only those are reported.

RESULTS

Alertness

Mean RTs and SDs of RTs of the AL task are shown in Table 1. To assess speed of reactions and variability of reactions, two two-factorial repeated measures ANOVA with Group as a between and Block (1, 2, 3, 4) as a within participant factor were conducted on mean RTs and SDs of RTs, respectively.

The analysis of mean RTs showed that there was a significant main effect of Group ($F(1,37)=5.43$, $p=0.025$), a significant main effect of Block ($F(3,111)=7.71$, $p=0.0001$), and a significant interaction Group x Block ($F(3,111)=5.96$, $p=0.0008$). Both groups showed significantly faster RTs in second than in the first block (NG: $t(18)=2.45$, $p=0.025$, CG: $t(19)=3.05$, $p=0.007$) and thus an improvement of RTs by the alerting tone. T-tests revealed that the NG was significantly slower than the CG in block 3 ($t(\text{het},23.9)=2.35$, $p=0.03$) and 4 ($t(\text{het},19.8)=2.85$, $p=0.01$) but not in block 1 ($t(\text{het},25)=1.26$, $p=0.22$) and 2 ($t(\text{het},28.1)=1.39$, $p=0.18$), although ESs indicate that the NG is slowed from the beginning of the task. In the third block significant differences between the NG and the CG begin to emerge. From the second to the third block (both with warning signal), the NG loses 16 ms in RT; however, it is not statistically significant ($t(18)=1.05$, $p=0.31$) and the CG

Table 1—Alertness: mean RTs, and SDs of RTs of the narcolepsy (NG) and the control group (CG).

	NG M (SD)	CG M (SD)	ES
Block 1 M	343 (112)	308 (51)	0.40
Block 2 M	316 (96)	281 (54)	0.45
Block 3 M	332 (103)	272 (43)	0.76
Block 4 M	408 (180)	287 (41)	0.93
Block 1 SD	67 (49)	41 (13)	0.73
Block 2 SD	68 (43)	42 (16)	0.80
Block 3 SD	93 (61)	43 (14)	1.13
Block 4 SD	93 (75)	43 (16)	0.92

Note. M=mean. SD=standard deviation. ES=effect size.

improves their RTs by 9 ms ($t(19)=2.04$, $p=0.056$). The groups differ even more in the fourth block, which is again conducted without a warning signal. Comparisons between the first and the fourth block, the two blocks without the warning signal showed that the NG loses 65 ms in RT ($t(18)=2.35$, $p=0.03$), but the CG actually improves performance and gains 21 ms in RT ($t(19)=2.05$, $p=0.05$) over time. Thus, speed decrements become apparent in the NG after a relatively short period of time, namely less than 10 minutes (see Figure 2A).

The analysis of SDs of RTs showed that there was a significant main effect of Group ($F(1,37)=12$, $p=0.0014$), a significant main effect of Block ($F(3,111)=3.09$, $p=0.03$), and a tendency for an interaction Group \times Block ($F(3,111)=2.41$, $p=0.07$). T-tests revealed that the NG was significantly more variable in reacting than the CG in all blocks (block 1: $t(\text{het},20.5)=2.19$, $p=0.04$, block 2: $t(\text{het},22.7)=2.52$, $p=0.02$, block 3: $t(\text{het},19.9)=3.55$, $p=0.002$, block 4: $t(\text{het},19.8)=2.85$, $p=0.01$). The Block-effect has to be interpreted with the tendency for the Group \times Block interaction together. The CG has equal values of variability over all blocks. However, the NG shows a tendency for increased variability between the second and the third block ($t(18)=1.92$, $p=0.07$, 25 ms). Thus increased variability of RTs is apparent in the NG right from the start of the task, and the results indicate that variability increases even further as time goes on, which also coincides with the decrease in RT in the third and the fourth block.

To sum the results of the AL task: patients with narcolepsy had a normal phasic alertness reaction, but they had slower and more variable RTs than controls and their performance began to deteriorate after a short time.

Focused Attention

Mean RTs, SDs of RTs, and errors of the VS task are depicted in Table 2. Three two-factorial repeated measures ANOVA with Group as a between and Target (absent, present) as a within participant factor were calculated on mean RT, SD of RT, and errors.

The analysis of mean RT revealed that there was a significant main effect of Group ($F(1,37)=3.84$, $p=0.05$), showing that the NG was slower than the CG; a significant main effect of Target ($F(1,37)=151.1$, $p=0.0001$), showing that it took participants longer to respond when the target was absent than when it was present; but no significant interaction Group \times Target ($F(1,37)=0.01$, $p=0.91$) (see Figure 2B). Participants

Table 2—Focused attention: mean RTs, row index, SDs of RTs, and errors of the narcolepsy (NG) and the control group (CG) for the target absent and target present conditions.

	NG M (SD)	CG M (SD)	ES
Absent M	5903 (1966)	5065 (1723)	0.45
Present M	3417 (1473)	2532 (495)	0.80
Row index	0.72 (0.2)	0.61 (0.3)	-0.43
Absent SD	1459 (501)	1028 (640)	0.75
Present SD	1738 (1302)	1241 (297)	0.53
Absent errors	0.63 (0.83)	0.2 (0.52)	0.62
Present errors	4.16 (5.7)	5.35 (7.26)	-0.18

Note. M=mean. SD=standard deviation. ES=effect size, row index=correlation of RTs with row number, a higher value indicates a more consistent search strategy. A negative value of the ES indicates numerically better performance of the NG.

also did not differ in their strategy to search rows ($t(37)=1.36$, $p=0.18$).

The analysis of SDs of RT revealed that there was a tendency for a Group-effect ($F(1,37)=2.84$, $p=0.1$), a significant main effect of Target ($F(1,37)=7.69$, $p=0.009$), and no significant interaction Group \times Target ($F(1,37)=0.14$, $p=0.71$). Thus, there was again a task-specific effect; participants were more variable in responding when the target was present than when it was absent. In addition, there was a tendency for the NG to be more variable in responding.

The analysis of performance errors revealed that there was no significant main effect of Group ($F(1,37)=0.14$, $p=0.72$) and no significant interaction Group \times Target ($F(1,37)=0.6$, $p=0.44$). However, there was a significant main effect of Target ($F(1,37)=17.23$, $p=0.0002$). Thus, here again there was a task-specific effect; participants made more errors when the target was present (i.e., overlooked the target), but no group-specific effects appeared.

To summarize the results of the VS task: the NG had longer RTs and showed a tendency to be more variable in responding, but quality of performance and search strategy were equal to the CG.

Divided Attention

Mean RTs, SDs of RTs, and omissions of the DT task can be seen in Table 3. Three three-factorial repeated measures ANOVA with Group as a between and Task (single, dual) and Stimulus (auditory, visual) as within participant factors were conducted on mean RT, SD of RT, and omissions.

The analysis of mean RT revealed a significant main effect of Group ($F(1,37)=13.25$, $p=0.0008$), showing that the NG was slower than the CG, and a significant main effect of Stimulus ($F(1,37)=255.83$, $p=0.0001$), a task-specific effect, indicating that RTs were faster to auditory than to visual stimuli but no significant Task-effect ($F(1,37)=0$, $p=0.95$). The interaction Task \times Group ($F(1,37)=1.8$, $p=0.19$) was also not significant, but the interaction Stimulus \times Group ($F(1,37)$, $p=0.06$) showed a tendency and the interaction Task \times Stimulus ($F(1,37)=12.55$, $p=0.001$) was significant. The interaction task \times Stimulus is task-specific. The three-way interaction Group \times Task \times Stimulus was not significant. Thus, the NG was consistently slower than the CG, but there was no disproportional impairment in the dual-task situation. However, there was a tendency for an interaction Stimulus \times Group, which indicates that the difference between RTs to visual and auditory stimuli is larger in the NG ($M=332$, $SD=130$) than in the CG ($M=260$, $SD=100$; $t(37)=1.94$, $p=0.06$). Or, described alternatively, the difference between the groups is larger for visual stimuli (ES: 1.05) than for auditory stimuli (ES: 0.635).

The analysis of SD of RT revealed a significant main effect of Group ($F(1,37)=7.41$, $p=0.01$), showing that the NG was more variable than the CG, and a significant main effect of Stimulus ($F(1,37)=94.63$, $p=0.0001$), indicating that there was a task-specific effect of RTs being more variable to visual than to auditory stimuli. All other effects were not significant (main effect task: $F(1,37)=0.06$, $p=0.81$, interaction task \times Group: $F(1,37)=0.91$, $p=0.35$, interaction Stimulus \times Group:

Table 3—Divided attention: mean RTs and SDs of RTs of the narcolepsy (NG) and the control group (CG).

	NG M (SD)	CG M (SD)	ES
Single, visual M	1009 (161)	856 (103)	1.13
Dual, visual M	948 (131)	841 (86)	0.97
Single, auditory M	628 (101)	566 (111)	0.58
Dual, auditory M	664 (71)	610 (84)	0.69
Single, visual SD	242 (91)	182 (76)	0.72
Dual, visual SD	217 (90)	191 (72)	0.32
Single, auditory SD	107 (36)	81 (33)	0.75
Dual, auditory SD	119 (63)	96 (33)	0.46
Single, visual omissions	1.26 (1.45)	0.75 (0.79)	0.44
Dual, visual omissions	1.42 (1.3)	0.8 (0.95)	0.39
Single, auditory omissions	0.68 (1.29)	0.25 (0.91)	0.54
Dual, auditory omissions	1.37 (2.14)	0.25 (0.44)	0.72

Note. M=mean. SD=standard deviation. ES=effect size.

$F(1,37)=0.72$, $p=0.4$, interaction task \times Stimulus: $F(1,37)=1.61$, $p=0.21$, three-way-interaction task \times STIMULUS \times Group: $F(1,37)=0.87$, $p=0.36$).

The analysis of omissions revealed a significant main effect of Group ($F(1,37)=4.5$, $p=0.04$), a significant main effect of Stimulus ($F(1,37)=6.73$, $p=0.01$) and a tendency for task ($F(1,37)=3.44$, $p=0.07$). Of the interactions, Group \times task showed tendency ($F(1,37)=2.71$, $p=0.1$); the other three interactions were not significant (Stimulus \times Group: $F(1,37)=0.42$, $p=0.5$, task \times Stimulus: $F(1,37)=0.79$, $p=0.38$, task \times STIMULUS \times Group: $F(1,37)=1.15$, $p=0.29$). The main effect of Group shows that the NG made more omissions than the OG, and the tendency for a task \times Group interaction shows that the difference of the number of omissions between dual-task and single-task conditions had a tendency to be higher in the NG than in the CG (NG: $M=0.8$, $SD=1.7$; OG: $M=0.05$, $SD=1.3$; $t(37)=1.65$, $p=0.1$). Thus, the NG showed a lower performance quality, and there is some indication that the NG is more affected by the dual-task situation in this respect (see Figure 2C).

To sum the results of the DT, patients of the NG were slower and more variable in reacting; in addition, they made more errors. There was a tendency for the NG to make more errors in the dual-task situation, indicating a divided attention deficit of the NG. Interestingly RT differences between the groups were larger for visual than for auditory stimuli.

Flexible Attention

Mean RTs, SDs of RTs, and errors of the AR task can be seen in Table 4. Three two-factorial repeated measures ANOVA with Group as a between and Block (same, different) as a within participant factor were calculated on mean RT, SD of RT, and errors.

The analysis of mean RT showed that there was a significant main effect of Group ($F(1,37)=11.03$, $p=0.002$), with the NG being slower than the CG. In addition, there was a significant main effect of Block ($F(1,37)=10.78$, $p=0.002$), a task-specific effect, indicating that it took participants longer to respond when they had to use the same hand as in the trial before. The interaction Group \times Block ($F(1,37)=0.01$, $p=0.91$) was not significant.

The analysis of SDs of RT revealed a significant main effect of Group ($F(1,37)=16.01$, $p=0.0003$), indicating that the NG was more variable than the CG. In addition there was a significant main effect of Block ($F(1,37)=7.22$, $p=0.01$), showing that participants were more variable when they responded with the same hand as in the trial before. The interaction Group \times Block ($F(1,37)=0.0$, $p=0.97$) was not significant.

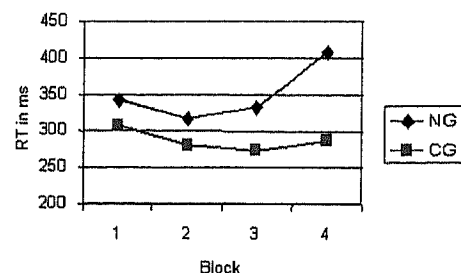
The analysis of errors revealed that there was a significant main effect of Group ($F(1,37)=6.42$, $p=0.016$), with the NG making more errors than the CG. In addition, there was a significant main effect of Block ($F(1,37)=18.62$, $p=0.0001$), showing that participants made more errors when they responded with the same hand as in the trial before. Furthermore, there was a tendency for a Group \times Block interaction ($F(1,37)=3.16$, $p=0.08$), indicating that the NG had an especially high error rate in the same-hand condition. However, ESs are nearly the same for same-hand and other-hand conditions (see Figure 2D).

In sum, the results of the AR task showed that the NG was slower, showed more variable RTs, and made more errors than the CG; the latter indicates a deficit in flexible attention.

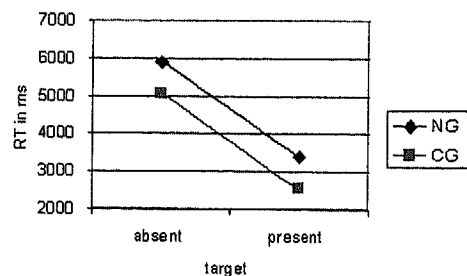
Verbal Memory

Scores of the ALVT can be seen in Table 5. The NG and the CG did not differ in total learning and memory performance (Total score: $t(37)=0.34$, $p=0.74$). To analyze immediate recall (List A, 1st) and the ability to switch to new material (List B), a two factorial repeated measures analysis of variance with Group as a between and LIST (A, B) as a within participant factor was conducted. There was no significant main effect of Group ($F(1,37)=0.0$, $p=0.99$), a significant main effect of LIST ($F(1,37)=7.94$, $p=0.008$), and no significant interaction Group \times LIST ($F(1,37)=0.10$, $p=0.76$). Thus there was only a task-specific effect; both groups learned fewer items with the new material, but they differed neither in immediate recall nor in their ability to switch to new material. To analyze free recall after a disruption by other material (List A, 6th in

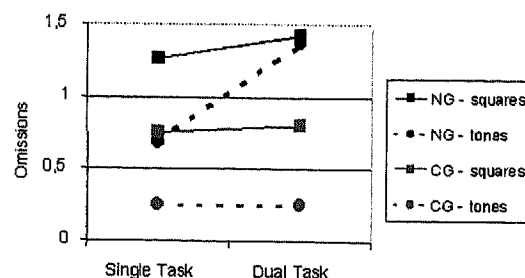
A Alertness



B Focused Attention



C Divided Attention



D Flexible Attention

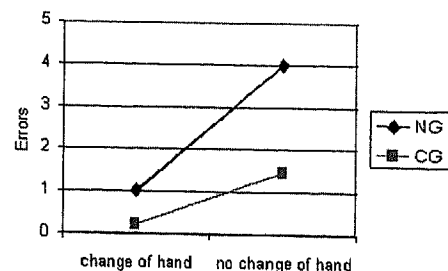


Figure 2—The most important results of the attention tasks. NG = narcolepsy group, CG = control group, squares = reaction to squares, tones = reaction to tones, RT = reaction times. 2A. The NG shows a pronounced decrement in RT in the fourth block. 2B. The NG is slower than the CG. 2C. The NG makes more errors than the CG. In addition, error rate in the NG is more affected by the dual task situation. 2D. The NG makes more errors than the CG.

Table 4—Flexibility of attention: mean RTs, SDs of RTs, and errors of the narcolepsy (NG) and the control group (CG).

	NG M (SD)	CG M (SD)	ES
Same hand M	1278 (601)	869 (175)	0.92
Other hand M	1201 (478)	786 (134)	1.18
Same hand SD	447 (260)	224 (110)	1.12
Other hand SD	399 (224)	178 (70)	1.33
Same hand errors	4 (4.7)	1.45 (1.6)	0.73
Other hand errors	1 (1.6)	0.2 (0.4)	0.69

Note. M=mean, SD=standard deviation, ES=effect size.

comparison to List A, 5th) a two factorial repeated measures analysis of variance with Group as a between and Disruption (before, after) as a within participant factor was conducted. There was no significant main effect of Group ($F(1,37)=0.04$, $p=0.84$), a significant main effect of Disruption ($F(1,37)=45.15$, $p=0.0001$), and no significant interaction Group \times Disruption ($F(1,37)=0.02$, $p=0.89$). Thus there was again only a task-specific effect; both groups produced fewer items of list A after disruption by other material, but showed similar performance levels. Finally, the two groups also did not differ in recognition performance ($t(37)=0.43$, $p=0.67$). Overall, the NG showed no memory deficit in comparison to the CG. One of our questions was whether a memory deficit (should it appear) could be explained by attentional difficulties. Since we obtained no memory deficits for the NG, we did not analyze correlations between attention and memory.

DISCUSSION

In contrast to previous studies, we investigated several different aspects of attention in patients with narcolepsy. The present study indicates that patients with narcolepsy have a divided attention deficit, probably due to attentional capacity limitations, and a flexible attention deficit, probably due to attention control deficits. Patients with narcolepsy, however, have a normal phasic alertness reaction and no deficits in focused attention. Patients were generally slower, more variable in reacting, and made more errors than controls. No memory deficit was apparent.

The impairment of RTs in the NG and the higher variability of RTs are in accordance with previous studies.⁴⁻⁷ What specific deficits did occur, apart from those general characteristics of the patient's performance? Patients with narcolepsy did show a normal phasic alertness reaction, i.e., an improvement in RT from the first block without warning signal to the second block with warning signal. This indicates that they do not have a deficit in phasic arousal. However, the AL task showed a rapid decline in performance in the last two blocks, which can be interpreted as a decrement in tonic arousal. The rapid decline of performance in the last two blocks of the test is remarkable—it took place even though task duration was only 10 minutes. Previous studies also found that a 10-minute RT task was sensitive enough to detect performance deficits in patients with narcolepsy.⁴ Similar to our study, performance deficits were worse in the second half of the test.

In the VS task, patients showed that they were able to adopt a search strategy as well as controls. Patients had slower and more variable RTs, but performance quality was not impaired. Therefore patients with narcolepsy do not have any specific focused attention deficit; they do not seem to be easily distracted and maintain the logical order of scanning. Our results are in contrast to a previous study in which RT latencies in a serial search task were not longer, but the error rate was higher for patients with narcolepsy.¹⁰ It might be that in that study participants adopted a different strategy and did not take the time they needed to perform with high quality, which they did in our study. This difference might be due to instructions; we emphasized accuracy.

In the divided attention task, patients showed longer RTs and more performance variability than controls; however, no specific interaction between task condition (single, dual) and group occurred in those variables, which indicates that the dual-task situation does not lead to a specific decline of speed and performance stability. However, quality of

performance, i.e., the number of omissions made, differed between the groups, and the NG was more affected by the dual task situation. Thus, there is a specific deficit of the NG in the dual task situation, which shows up in the quality of performance. Dual tasks are often used to make conclusions about capacity limitations of the attention system. As expected, the rate of external information exceeded the capacity of the processing mechanism in both groups, since both groups performed worse in the dual task situation, but error rates indicate that the capacity of the attention processing mechanism was more affected in the NG than in the CG.

In the flexible attention task, the NG showed longer RTs and more variability in RTs and made more errors than controls. Unfortunately, for this task there are no baseline data like in the divided attention task. However, in contrast to the divided attention task, it is a self-paced task, which means that participants could theoretically easily compensate for high information processing load by slowing down to avoid errors (like in the focused attention task). The instructions in fact emphasized accuracy. In the NG, RT showed a positive relationship to errors (other hand: $r=0.79$, $p=0.0001$, same hand: $r=0.41$, $p=0.08$), i.e., patients with longer RTs also made more errors. This speaks against a speed-accuracy trade off in this group and indicates that patients tried to compensate for difficulties in this task by taking more time. Nevertheless, their quality of performance was below that of the CG. Thus, the reduced quality of performance indicates that there is a specific deficit in flexible attention. A deficit in flexible attention also points to a deficit in the attentional control.

Patients with narcolepsy did not show any memory deficits in the current study. This result is in line with previous studies using the AVLT or other verbal memory test.^{23,26,27} However, two other studies, which employed similar procedures, found deficits.^{11,24} Nevertheless, it does not seem likely that the negative results are due to insufficient power; ESs in the verbal memory test range from 0.04 to 0.14, which is quite small. Thus, effects are virtually non-existent. The fact that patients complain about memory problems,²³ but tests usually do not detect any deficits, might be due to the patients developing an inaccurate assessment of their memory abilities (which are supposed to be intact) because of a lowered self-efficacy for memory performance.³⁶ Another possibility is that the attentional requirement of the memory task in our study, and probably of the tasks in other studies as well, was mainly focused attention, which is not impaired in patients with narcolepsy. If one would increase requirements on attentional capacity, e.g., by increasing the rate of stimulus presentation, a memory deficit might occur.

Does it matter whether attention has to be paid to visual or auditory stimuli? Although the performance of patients starts to deteriorate in the third block of the AL task, the performance deterioration becomes more manifest in the fourth. The critical factor for this performance decrement might be the disappearance of the warning signal. The tone may have had a wakefulness-sustaining function, and, as soon as it disappeared, performance declined rapidly. In the divided attention task, the difference between the groups was larger for visual than for auditory stimuli. We hypothesize that auditory attention might be less prone to fluctuations than visual attention. Normal performance of the NG in the memory test, which was auditory verbal, might also be explained this way.

What are hypotheses about the mechanisms responsible for performance deficits? Many authors assume that information processing is impaired on a temporal (not long sustaining, low temporal consistency) but not on the functional level.^{5,6} According to this view, patients do not have a real impairment of cognitive functions but are not able to sustain a performance level and show variable performance from moment to moment. Our results do support the notion that there are disturbances on the temporal level of information processing in patients with narcolepsy. However, temporal disturbances of information processing cannot account for all of the observed deficits. Specific deficits seem to appear here in divided attention and flexible attention. Those cannot solely be explained by slowed or variable information processing, but, instead,

Table 5—Memory indexes of the narcolepsy (NG) and the control group (CG).

	NG M (SD)	CG M (SD)	ES
Total score (sum 1st to 5th)	51.9 (8.6)	52.9 (8.9)	0.11
Immediate recall (list A, 1st)	6.9 (2.1)	6.9 (1.8)	-0.05
Immediate recall: other material (list B)	5.9 (1.9)	6.1 (1.9)	0.05
Maximum score (list A, 5th)	12.4 (1.9)	12.6 (2.1)	0.1
Free recall after disruption (list A, 6th)	10.8 (2.6)	10.9 (2.9)	0.04
Recognition	13.9 (1.4)	13.8 (1.5)	-0.14

Note. A negative value of the ES indicates numerically better performance of the NG.

attention capacity and attention control problems seem likely. Other factors, apart from temporal disturbance, that have been suggested to play a role in attention deficits in patients with narcolepsy are a disturbance in time resolution of stimulus input³⁷ or dysfunctional processing of relevant stimulus properties.¹¹ Specifically, it was suggested that performance deficits in narcolepsy could be due to deficits in a) perceptual encoding, b) the time to execute appropriate motor responses, and / or c) perceptual-motor integration.¹¹ A deficit in the time to execute motor responses was ruled out because participants performed as well as controls on a finger oscillation test.¹¹ A perceptual-motor integrative deficit cannot be totally discarded; however, a perceptual-encoding deficit seems to be more likely.¹¹ Although our study was not designed to test that hypothesis, it might give insights to this issue. The VS was the only task that did not require a reaction as soon as a stimulus appeared but first required a visual search. This means that the motor component plays only a minor role in the RT, and thus, if the deficit of the patients would be only perceptual-motor, patients should not be slowed in this task. However, here, like in all the other tasks, they showed slower RTs. Therefore a perceptual-encoding deficit is likely and a perceptual-motor deficit unlikely, which is in accordance with previous suggestions.¹¹

In sum, performance deficits cannot solely be explained by impairments on the temporal level of attention, but other functions like attentional capacity and attentional control are impaired as well. The question is whether the obtained deficits are specific to narcolepsy or whether they reflect general aspects of performance change due to sleepiness. This question cannot be answered by our investigation. It might be that deficits resemble those of normal sleep-deprived participants, or vary only quantitatively, but it might also be that other aspects of narcolepsy may lead to a qualitatively different performance.²³ One important question for future research on attention deficits in patients with narcolepsy might be the neurophysiological basis for those. Recent work suggests the existence of several anatomically different, nevertheless interacting, attentional networks.^{12,16} One of those networks is the "vigilance network," another one is the "executive attention network".^{12,16} There seems to be no doubt of an impairment in the vigilance network in patients with narcolepsy. Our results also point to an impairment in the executive attention network.

To conclude, this study has shown that patients with narcolepsy show attentional deficits, which cannot solely be explained by impairment of the temporal level of information processing. Patients showed a normal phasic alertness reaction and were not impaired in focused attention; however, deficits were apparent in divided and flexible attention. No memory deficit was found in this study. As a practical consequence, this means that a more extensive diagnostic process of attention is necessary to be able to evaluate patients' attention deficits and to specify them. A single test of vigilance, as is common practice in most hospitals, is not enough. In addition, after a patient is medicated, it should be controlled whether an improvement of performance shows up in all impaired attentional areas.

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APPENDIX

Performance of the medicated narcolepsy participants was slightly better than that of unmedicated narcolepsy participants in some of the tests but still worse than that of healthy controls. Moreover, the overall performance pattern of medicated patients was similar to the pattern of unmedicated patients. Therefore, medicated and unmedicated patients were not considered separately. The results of the subgroup analysis are presented in the following passages in more detail. Not all results are reported, but those relating to the central and most interesting effects in

the tasks. The following abbreviations are used: NG-M=narcolepsy group, medicated participants (N=6), NG-UM, narcolepsy group, unmedicated participants (N=13), NG=narcolepsy group total (N=19), CG=control group (N=20), RT= reaction time.

Auditory Verbal Learning Test: there were no differences between the NG-M and the NG-UM.

Alertness: RT of the medicated participants is comparable to that of controls in the first block; the NG-M shows the same effect as the NG-UM, namely a decrease in RT from the first to the fourth block, whereas controls actually improved their RT. This was the central and most interesting effect in this task. The decrease in RT from the first to the fourth block was (in ms); NG-UM: -59 ms, NG-M: -32 ms and CG: +20 ms gain.

Focused Attention: Apart from slower and more variable RTs, no specific deficits of the NG were found in the original analysis. This is also true for medicated and unmedicated in the NG. The means of RT for critical trials were: NG-UM: 3514, NG-M: 3207, CG: 2532, and the SD means of RT for critical trials were: NG-UM: 1844, NG-M: 1509, CG: 1241.

Divided attention: Again, the NG-M performs better than the NG-UM but is still slower and more variable than the CG. The main argument for a divided attention deficit was an increase in omissions in the NG in the dual task condition. This is the case both for the NG-UM and the NG-M; the means of omissions (added for the auditory and visual condition) are: NG-UM single task: 2.44, dual task: 3.23; NG-M single task: 0.84, dual task: 1.83; CG single task: 1.0, dual task: 1.05.

Flexible attention: The NG-M shows even longer and more variable RTs than the NG-UM. Error rates, which were important for the argument of a flexible attention deficit, are (averaged across the two conditions): NG-UM: 4.8%, NG-M: 5.7%, OG: 1.7%.

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