9

The Effects of Sleep-Related Breathing Disorders on Waking Performance

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1. Introduction

Sleep is a necessary and reversible behavioural state of perception, cognition, psyche and physical conditions. Abnormal sleep behaviours may include e.g. difficulties in falling asleep, breathing difficulties such as different kinds of apneas, sleep paralysis, hypnagogic hallucinations, sleep onset-REM, leg movements, sleepwalking, sleep talking, tooth grinding and other physical activities. These anomalies involving sleep processes also include sleep itself, dream imagery or muscle weakness.

Within sleep there are two separate states, non-rapid eye movement (NREM) and rapid eyes movement (REM). REM sleep is defined by EEG activation, muscle atony, and episodic bursts of rapid eye movement. NREM (non-REM) sleep is subdivided into four stages (stages 1, 2, 3 and 4 – Rechtschaffen & Kales) or three stages (N1, N2 and N3 – AASM), which are defined by the electroencephalogram (EEG). The NREM stages are parallel to the depth of sleep continuum (lowest in stage 1 and highest in stage 4 sleep).

NREM sleep and REM sleep continue to alternate through the night in cyclically. REM sleep episodes become longer across the night, stages 3 and 4 become shorter across the night.

Sleep disorders have an impact on the structure and distribution of sleep. A distinction is important in diagnosis and in the choice of treatments. There are three very important sleep disorders: Insomnia, Narcolepsy and Sleep Apnea Syndrome.

Altogether, in Western Europe already suffer more than 10 % of the population from *Sleep-Awake-Disturbances* which has to be treated urgently; 800,000 from Sleep Apnea Syndromes and 25,000 from Narcolepsy (PETER et al. 1995).

1. *Insomnia* is a sleeplessness and includes a decreased total sleep time, a poor sleep efficiency too little and a poor sleep quality caused by one or more of the following: trouble falling asleep (delayed sleep latency), waking up a lot during the night with trouble returning to sleep, waking up too early in the morning, and/or having un-refreshing sleep/not feeling well rested (even after sleeping 7 to 8 hours at night). Under this criterion the frequency is in the western industrial countries between 20-30 % in which about 10-15 % suffer under a very severe illness and 40 % of all depressions may be preceded by insomnia first.
2. *Narcolepsy* is a genetic disorder and characterized by sleep onset REM sleep, hypnagogic hallucinations, sleep paralysis, cataplexy and excessive daytime sleepiness.

The exact prevalence of the general population is unknown. Great differences exist in its appearance frequency. So the frequency of Japan is 0.16 % and of Israel 0.0002 %. Central Europe (0.006 %) and the USA (0.06-0.1 %) are located in the middle.

3. *Sleep Apnea Syndromes* (SAS) are common disorders, which are characterized by repeated oropharyngeal occlusions occurring during the sleep time (sleep-related breathing problems, intermittent hypoxemia) and may be associated with suppression of SWS sleep (disrupted and fragmentized sleep architecture). Due to intermittent hypoxemia and disrupted sleep architecture, SAS leads to impaired daytime functioning in various (neuro)psychological and affective domains and has been associated with increased morbidity and mortality, principally from adipositas, cardiovascular and neurological diseases.
   The prevalence of moderate SAS (AHI >15/h) is 9% in male and 4% in female, respectively. 25-30 % Sleep Apnea Syndromes were described at patients with hypertension and 35-45 % with patients with on the left heart-failure. The SAS frequency increases with an advancing age and reaches their peak at the age from 50 to 70 years. 80% of the patients suffer under excessive daytime sleepiness and a reduced sustained attention. Resulting from this it comes to performance losses both professional and in the ability to drive motor vehicles.

Fragmentation of sleep and *increased frequency of arousals* occur in association with this three disorders and a number of other sleep disorders as well as with medical disorders involving physical pain or discomfort.

In this chapter, the author will describe neuropsychological dysfunctions/courses and neuropsychiatric syndromes due sleep disorders which were characterized by

1. excessive daytime sleepiness
2. attention deficit,
3. memory dysfunction,
4. executive dysfunction,
5. driving difficulties,
6. motivation and emotional deficits,
7. psychiatric consequences (e.g. depression, anxiety) and
8. lack of ability to recognize the effects of behaviour.

There are wide varieties of difficulties in assessment, treatment and rehabilitation for cognitive impairment, psychiatric disorders and behavioural disability after sleep disorders.

In our studies we used neuropsychological and neuropsychiatric methods in different patient groups in a sleep laboratory. Over the past five years we have been testing and treating more than 2000 patients with different sleep disorders and more than 5000 neurological patients.

During admission to the clinic, all patients were selected according to their clinical diagnosis (ICD-10) and were examined neurologically, (neuro)psychologically, psychiatrically and medically. The test persons must not suffer from any severe psychiatric disorders. The study was carried out involving randomly selected patients with sleep disorders.

2. Excessive daytime sleepiness in patients with Sleep Apnea Syndrome

2.1 State of research

2.1.1 Sleep Apnea Syndromes and neuropsychological disorders

In addition to nocturnal Sleep Apnea Syndrome symptoms there are a lot of daytime symptoms. It is assumed that the reduced sleep quality, arising out of deep sleep or REM-

suppression, resulting in increased nocturnal arousal responses, or constantly occurring waking or a reduced relaxation function (Weeß et al. 1998a/b) and cognitive damage caused by intermittent hypoxia (Montplaisir et al. 1992). As the main symptom is excessive daytime sleepiness (EDS) is considered.
It is also assumed that the OSAS accompanying Insomnia and sleepiness influence cognitive functions (Jennum et al. 1993). As reported by Schwarzenberger et al. (1987) that patients with EDS have complaints and problems in situations of physical rest and during prolonged monotonous concentration tasks. A study by Kales (1985) showed that 76% of OSAS patients have cognitive deficits in the areas of thinking, learning ability, memory, communication and the ability to learn new information. Naëgelé et al. (1995) were able to establish in Sleep Apnea Syndrome patients that they were reduced at executive functions when these tasks involve the acquisition of information to memory processing. Another study by Cassel et al. (1995) showed that Sleep Apnea Syndrome patients have a reduced non-verbal performance and processing speed. Regarding the central nervous system activation (*alertness*), selective attention and sustained attention in Sleep Apnea Syndrome patients Kotterba et al. (1998) found, that they were impaired, and that they have a reduced vigilance (Barbè et al. 1998).
The cause of cognitive and neuropsychological deficits in the EDS itself, the sleep fragmentation and arousals and nocturnal hypoxemia are discussed (Findley et al. 1986, Greenberg et al. 1987, Guilleminault et al. 1988, Colt et al, 1991, Bédard et al. 1991, Roehrs et al. 1995).

2.1.2 Causes of neuropsychological deficits (Büttner 2001, 2009)

Two concepts play a central role, first, the hypoxia and the other the disturbed sleep architecture in the causes of the neuropsychological and/or cognitive deficits in Sleep Apnea Syndrome patients.
Both factors appear usually occur together, so that it is hardly possible to separate the two. Several studies confirm the link between *nocturnal oxygen desaturation* and neuropsychological deficits. Greenberg et al. (1987) showed, for example, that the nocturnal hypoxia is the cause of the neuropsychological deficits and daytime sleepiness. In another study conducted by Findley et al. (1986) showed that there is a correlation between hypoxia during sleep and wakefulness with the degree of cognitive impairment, but not between sleep fragmentation and the cognitive functions. In a study of Kotterba et al. (1998), various neuropsychological parameters correlate with the degree of hypoxia, but not with the arousal index and AHI. Montplaisir et al. (1992) describe the nocturnal hypoxia as the best predictor for both daytime alertness as well as daytime sleepiness.
For other investigators, the cause of the neuropsychological deficits such as those of daytime sleepiness exist in the *disruption of sleep patterns* or *sleep fragmentation*, accompanied by a reduction in the proportion of REM and slow wave sleep. According to Bonnet et al. (1985) healthy persons' sleep fragmentation leads to neuropsychological impairment. Other researchers such as Telakivi et al. (1988) and Guilleminault et al. (1988) find that sleep fragmentation has an important impact on neuropsychological deficits. This allowed Guilleminault et al. (1988) to conclude in a study that the sleep fragmentation would be the best predictor of the occurrence of daytime fatigue is, and that there is no relationship between daytime sleepiness and respiratory parameters such as RDI or oxygen desaturations. This could confirm also by Colt et al. (1991) in a study. Nocturnal hypoxias were induced during a night under nCPAP therapy and, no effect on daytime sleepiness

could be found. So it was adopted by this study that the day's fatigue does not caused by a decrease of intermittent nocturnal oxygen saturation, but rather by the sleep fragmentation.
Bédard et al. (1991) suggested it was an *interaction of both factors*; both sleep fragmentation and nocturnal hypoxia were of great importance in the emergence of decreased vigilance or neuropsychological deficits, with the hypoxia seemingly playing a larger role in severe cases. In addition, the *daytime sleepiness* itself is responsible for the cognitive deficits (Roehrs et al. 1995).
Other assumptions are that neither the disturbed sleep architecture nor nocturnal hypoxias play a role for the neuropsychological deficits in OSAS. Thus Ingram et al. (1994) showed that there are no differences in vigilance between OSAS patients and normal subjects. The reduction of vigilance could be determined by age. Research of Kotterba et al. (1998) and Büttner et al. (2004b) were able to contradict these suggestions, as they found differences of vigilance between OSAS patients and healthy individuals, but no age differences. Severity of OSAS, as measured by the AHI or RDI, or nCPAP compliance may also play a role (Cassel et al. 1989, Engleman et al. 1993, John (et al.) 1991, 1992, 1993).

2.1.3 Daytime sleepiness, fall asleep and driving performance (Büttner 2001, 2009)

The ability to drive safely and without accident needs sustained attention and alertness (Guilleminault et al. 1978, Bradley et al. 1985, Podszus et al. 1986, Findley et al. 1988a/b, 1989b, 1990, 1991, 1995, He et al. 1988, Mitler et al. 1988, Lamphere et al. 1989, Roehrs et al. 1989, Bédard et al. 1991, Cassel et al. 1991a/b, 1993, 1996, Kribbs et al. 1993a/b, ATS 1994, Martin et al. 1996, Gerdesmeyer et al. 1997, Krieger et al. 1997, Randerath et al. 1997, 1998, Weeß 1997, Weeß et al. 1998a/b).
Increased daytime sleepiness is one of the most common causes of road accidents. Driver fatigue is the cause in up to 25% of highway accidents (Langlois et al. 1985, Pack et al. 1994, Horne et al. 1995). A study of 67 671 non-alcohol-related car accidents in France in the years 1994-1998 showed that the risk of accidents involving fatalities or serious injuries in fatigue-related accidents is increased as compared to non-fatigue-related accidents significantly (Philip 2000). An analysis of fatal accidents on highways in Bavaria in 1991 showed that 49 of 204 accidents (24%) caused by falling asleep at the wheel (Langwieder et al. 1994). Obstructive Sleep Apnea Syndrome is again one of the most common causes of daytime sleepiness is increased (American Thoracic Society 1994, McNicholas, 1999).
Reliable data on sleepiness-related causes of accidents due to the German data protection regulations is not available and caused on it the published data's are very inconsistent: According to Seko et al. (1986) 45% of all fatal road accidents were caused by falling asleep at the wheel or a micro-sleep, but declared by the Federal Statistical Office at Wiesbaden (1988) only 0.5% of all traffic accidents (Seko et al. 1986, Federal Statistical Office Wiesbaden 1988, Cassel et al. 1993). A study of Zulley et al. showed that 38% in all traffic accidents on Bavarian highways were due vigilance reduction and 24% of all serious accidents (Zulley et al. 1995).
The sleep-related vigilance and sustained attention losses were intensified, especially exacerbated by the effects of biological rhythms (Hildebrandt et al. 1974, Hildebrandt 1976, Mitler 1991, Cassel et al. 1991c, 1993, Zulley 1995).
As early as 1955 Prokop and Prokop discussed regarding traffic safety and the importance of fatigue and falling asleep, but without to discuss the sleep-related aspects or causes (Prokop & Prokop 1955, Cassel et al. 1993). At first in 1978 Guilleminault et al. showed a possible increased risk for patients with sleep-disordered breathing (Guilleminault et al. 1978, Cassel et al. 1991a/b).

George et al. (1987) took up this assumption and investigated the accident probability of 27 suspected OSAS patients. In 93% of patients were entered injuries in the accident register of *Motor Vehicle Branch* of Manitoba (Canada), but only 54% of the control group participants. Unfortunately, in seven patients, the polysomnographic confirmation of the diagnosis and the information on the period of specified accidents are missing (George et al. 1987, Cassel et al. 1991a/b, Weeß 1997, Weeß et al. 1998 a/b). Findley et al. (1988b) found that 29 OSAS patients (AHI> 5) a three-fold increased probability of accidents compared to all license holders of Virginia (USA), and even a seven-fold increased compared to a control group (n = 35). However, Findley et al. didn't give the information whether the OSAS diagnosis was already known in the survey (Findley et al. 1988b, Cassel et al. 1991a/b, Weeß 1997, Weeß et al. 1998 a/b). Later studies and studies by Cassel et al. (1991a/b, 1996), the ATS (1994) and Krieger et al. (1997) confirmed these findings. Thus, patients with Sleep Apnea Syndrome seem increasingly to suffer from severe fatigue and falling asleep while driving (see also George et al. 1987, 1996b, Findley et al. 1988b). With increasing impairment of those affected persons by the symptoms of Obstructive Sleep Apnea are also accumulated self-inflicted, sustained attention-related injuries (Cassel et al. 1991a/b, 1996, ATS 1994, Kruger et al. 1997).

According to Young et al. (1997), the relative risk of an accident within five years, causing increased for men with sleep-related breathing disorders by factor of 3. Several studies show a minimum of a 2-fold to 3-fold, up to 7-fold increased risk of accidents (George et al. 1987, 1999, Findley et al. 1988, 2000, Horne & Reyner 1995, Wu & Yan-Go 1996, Young et al. 1997, Barbé et al. 1998, Terán-Santos et al. 1999, Horstmann et al. 2000, LLoberes et al. 2000, Sharma & Sharma 2008). For example, George et al. (1999) investigated the relationship between accident rates and the number of traffic offenses in OSAS patients, with the result that the frequency of accidents and the number of traffic violations during a period of five years was significantly higher compared to a control group.

A special group in this context represent professional drivers, bus and truck drivers, because they spend a lot of professional time on the road and also with some larger vehicles usually dangerous cargo or other people, so that probably occur in an accident caused considerable damage and injury. These people have to suffer through their work and the associated lifestyle at increased risk of interference with OSAS. Thus for example truck drivers have a very irregular sleep-wake rhythm (Stradling 1989, Stoohs et al. 1995). In 1994 Stoohs et al. researched the influence of sleep-disordered breathing (SDB) and obesity among commercial drivers of large trucks. Drivers with SDB cause twice as many accidents per 1000 driven miles, than that without SDB, and obesity, the accident rate still increased. Accidents caused by overtiredness-related un-roadworthy and related offenses are likely among professional drivers having accepted a level that is comparable to the drunken crime (Meyer 1990).

The diagnosis of central nervous system stimulation as well as the diagnosis of daytime sleepiness has therefore central importance in the sleep medical field. Thus, the daytime sleepiness is on the one hand understood as an important symptom of non-restorative sleep, but on the other hand can also be closed due to their expression on the severity of this sleep disorder. Ultimately, their diagnostic evaluation is also an important criterion for therapy evaluation.

The sleepiness-related medical history or diagnosis is used to assess the clinical and social impact of daytime sleepiness. In particular, the severity and the social and medical risk will be assessed. It can also be used as parameters of the differential diagnosis of fatigue. This anamnesis can be supported by the use of orienting processes or by the method of screening.

It is used especially in the assessment of type and of frequency about the tendency to fall asleep, micro-sleep episodes and monotony intolerance at work (especially in monitoring activities) and to capture the possibility of active participation in road traffic and other social situations (Walsleben 1992, Weeß 2011).
The *Epworth Sleepiness Scale* (ESS), the *Stanford Sleepiness Scale* (SSS), the *Multiple Sleep Latency Test* (MSLT) and the *Maintenance Wakefulness Test* (MWT) are among the methods that are most widely used for the investigation of daytime sleepiness in sleep disorders. The ESS reflects the global and subjective severity of daytime sleepiness in eight different situations and activities of daily living. The SSS is, however, to capture subjective circadian fluctuations of daytime sleepiness. To objective capture electrophysiological and standardized tests are often, such as the MSLT and the MWT used to determine the degree of alertness on the basis of tonic activation.
If, on the basis of questionnaire data and medical history of sleeping on the basis of suspicion that a pathological daytime sleepiness (Table 1) exists, then objective analysis methods can be used to measure sleepiness-related functions.

Central nervous system activation
Vigilance
Selected Attention
Divided Attention

Table 1. Sleepiness functions

2.2 Epworth Sleepiness Scale (ESS)

The Epworth Sleepiness Scale (ESS) of Johns (1991) is very often used as a screening method for detecting the global daytime sleepiness and fall asleep in sleep disorders, especially used in hypersomnias. It is asked retrospectively, how high is the probability to fall asleep in eight everyday situations. The scale has a 4-step response format, in which values between 0 and 3 (0 = never to 3 = strongly agree) must be marked and results are added up a total maximum value of 24.
Following Johns (1991, 1992, Johns & Hocking 1997) a cut-off value ≥ 11 indicates a pathological daytime sleepiness. Standardization studies for the German-speaking countries were presented by Büttner et al. (2004c) and Sauter and colleagues (2007). The study found that 85% of healthy persons achieved a total value < 10, which corresponds to the calculated cut-off values in other studies (Johns 1991, Johns & Hocking 1997). The test-retest reliability of the ESS was calculated by Johns (1994) and based on a survey after five months in 87 healthy medical students. It was r_{tt} = .82 (p <.001), even the quality of internal consistency was confirmed (Cronbach's alpha = .88 (p <.001).
The ESS has in spite of it being subjective and a global assessment of daytime sleepiness (Johns 2000) has a very good validity. At a cut-off value > 10 it shows a high sensitivity of 93.5% and - high specificity 98.4%. The ESS is thus a highly reliable and valid procedure. The short implementation time and simple evaluation makes it very economical and cost effective. In addition, it can also be used for measuring the effectiveness of nCPAP therapy.
Nevertheless the ESS does not lend itself to capture gradually different levels of sleepiness (Sangal et al. 1997b) and that four of the eight items have very low selectivity (Rühle et al. 2005).

2.3 Stanford Sleepiness Scale (SSS)

The Stanford Sleepiness Scale (SSS) of Hoddes et al. (1973) is a scale on which momentary alertness can be assessed on a grading of 1 to 7 and thus serves to assess the circadian variations in daytime sleepiness. The scale describes gradual gradations of awareness; it varies between very alert and drowsy conditions. The alertness descriptions are also described, each with typical sensations (e.g. *some slack*, *slows*, *woozy*) characterized. Studies on the sensitivity of the scale showed that ratings in 15-minute intervals represent discrete changes in the degree of alertness. According to the response ratings point values are assigned for each time interval, which are then summated.

2.4 Multiple Sleep Latency Test (MSLT)

The Multiple Sleep Latency Test by Carskadon and Dement (1977) recorded the sleep latency lying down and is recommended for the investigation of daytime sleepiness in OSAS patients in the ICSD-2. The MSLT is based on the assumption that a strong physiological sleepiness can reduce the sleep latency (Arand et al. 2005).

For a long time the MSLT has been considered a gold standard for the investigation of daytime sleepiness (Carskadon et al. 1986). The MSLT (as well as the Maintenance of Wakefulness Test (MWT)) is often used to determine the alertness with expert's investigations, e.g. to assess the driving ability (Poceta et al. 1992). Five times a day electrophysiological recordings (C3/A2, C4/A1, EOG, EMG) are performed in 2-hour intervals. The first time of measurement should be from 1.5 to 3 hours after waking. The patient lies in a darkened room and is asked to fall asleep. During the test procedure, the patient is monitored with a video recording.

A pathological fall asleep exists, when the medium sleep latency is < 5 minutes (Richardson et al. 1982). The gray area is between 5-10 minutes and > 10-20 minutes is a normal finding. But are also divergent standard values of 5-8 minutes; thereby establishing of normal values is equivalent to a kind of "rule of thumb" (Guilleminault et al. 1994, van den Hoed et al. 1981, Johns 2000). Although the MSLT perform and should be evaluated strictly according to objective criteria and standardized, it seems to have low implementation objectivity, because the results of individual tests vary greatly (Danker-Hopfe et al. 2006). As other reasons for the inconsistent individual test results Thorpy (1992) describes the different day times and measuring times and not objectified sleep deprivation and sedative or stimulating effects of drugs. In spite of these influences, however satisfactory test-retest reliabilities of r_{tt} = .65 to .97 (van den Hoed et al. 1981, Zwyghuizen-Doorenbos et al. 1998) have been found.

Another problem of MSLT is the limited external generalization of daytime sleepiness in everyday situations (Johns 1994). The assumption that the MSLT describe daytime sleepiness - as reflection of everyday life - Johns (2000) keeps being wrong. As a predictor of MSLT is therefore not own, regardless how strict standards and criteria were met. In considering of the relationship between ESS and MSLT are unsatisfactory correlation of r = .27 ($p < .001$) or on those that are not significant (Mitler et al 1998.). Reasons for the inconsistent correlations are different: Either there are satisfactory (significant) correlations when all patients fell asleep in all MSLT times or when the patients rarely slept or not fell asleep (Chua et al. 1998).

2.5 Maintenance of Wakefulness Test (MWT)

The Maintenance of Wakefulness Test of Poceta et al. (1992) examines the ability to stay awake in a sleep-inducing situation. The patient sits in a darkened room on a comfortable

chair or on the bed and will be asked to refrain movements (e.g., grimacing, shaking), which may prevent falling asleep to refrain (Hartse et al. 1982, Mitler et al. 1982). Three to four times a day electrophysiological recordings (C3/A2, C4/A1, EOG and EMG) are recorded in 2-hour intervals of 20 minutes. The earliest start of the first test procedure should be scheduled two hours after waking. As with the MSLT test history is filmed with a video camera. Evaluated will be the sleep latency from the moment "light off" until the onset of the first two epochs of sleep stage 1 or 2.
In various standardization studies, inconsistent cut-off values were found from 13.5 to 18 minutes (Banks et al. 2004, Rühle 2005). Reasons for the different standard values according to Shreter et al. (2006) are that the test exercises have a significant influence on occasion staying awake in the test situation. So they provided proof that the sleep latency on the MWT was deliberately suppressed because the OSAS patients were afraid to get the license revoked. In considering the relationship between the MWT and ESS were calculated a satisfactory correlation of $r = .48$ ($p < .001$), with the common variance of the two devices was only 23% (Sangal et al. 1997b).

2.6 Pupillography (Fig. 1)

The Pupillograph Sleepiness Test (PST) from Amtech (Weinheim) reflects the fatigue waves of the pupil described by Löwenstein. Normally, the pupil size will be constant in normal central nervous system activation in the dark for a long time. However, occur with increased daytime sleepiness after a few minutes spontaneous fluctuations (oscillations) on the pupil, which are recorded with infrared videography. Cause of fluctuations in pupil size is a mechanism of the autonomic nervous system. With reduced central nervous system activating two divisions acting simultaneously, which inhibit the Edinger-Westphal nucleus. This leads to instability of the central sympathetic activation and consequently fluctuating in an inhibition of parasympathetic activity and the Edinger-Westphal nucleus (Löwenstein et al. 1963, Yoss et al. 1970).

Fig. 1. Experimental setup for the pupillography. The patient wears an infrared protective goggle, has propped his chin on a device and looks toward the infrared camera.

Evaluation

The average Pupil Unrest Index (PUI) is the average pupil size fluctuations in millimetres per second over a period of 11 minutes. Higher PUI values indicate a clinically significant

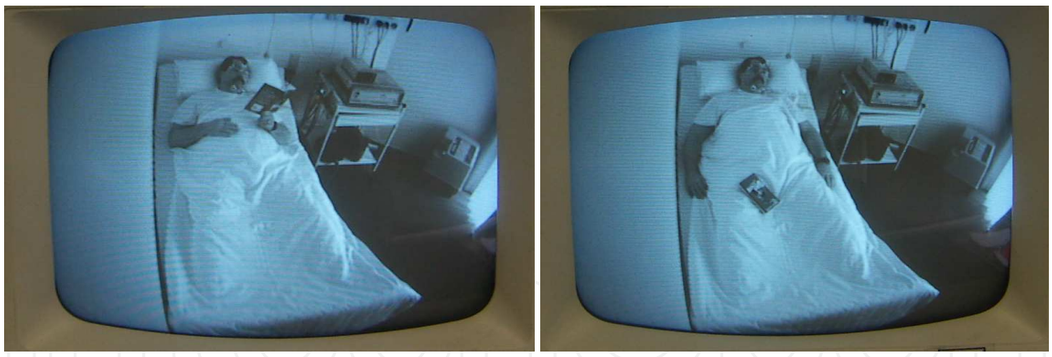
daytime sleepiness in (Table 2). In a normal population (n = 349) between 20 and 60 years, was found a mean value for ln PUI of 1.50 ± 0.39 mm/min. Thus, abnormal values are obtained from ln PUI > 1.89 and pathological values from ln PUI > 2.28. The cut-off value of > 6.64 was found for 84.1% of a healthy sample (Wilhelm et al 2001), which was established that this is independent of gender and age (r = .85 to .94). The PUI correlated low, but significantly with the subjective estimates of daytime sleepiness in SSS (r = .29, p < .010). The implementation objectivity and evaluation objectivity seem to be sufficiently given, because the change in pupil size can be deliberately manipulated. The reliability was tested in healthy control subjects and is satisfactory (r = .64, p < .001) (Weeß et al. 2000).

Value range	**Mean-2SD**	**Mean-SD**	**Mean**	**Mean+SD**	**Mean+2SD**
ln PUI (mm/min)	0.73	1.11	1.50	1.89	2.28
Percentile	2.3%	15.9%	50.0%	84.1%	97.7%
PUI (mm/min)	2.07	3.05	4.50	6.64	9.80

Table 2. Percentile of the normal reference range for ln PUI and PUI

2.7 Reading test (Fig. 2)

In the first version of the *Reading test*, it was up to the patients and healthy controls, to select a passage according to their interests. Therefore, it was possible that the individual level of activation of OSAS patients may have influenced the excitement level of the books. For this reason, the story "One day, maybe one night" by Arnold Stadler (2003) was selected. This is a retrospective narrative. Due to the low excitement level of the narrative it was assumed that the degree of tonic activation would remain constant.



A B

Fig. 2. In 2A is seen as the patient reads in a semi-recumbent position, the modified form of the story "One day, maybe one night" by Arnold Stadler (Fischer paperback 2003). In the face of the electrodes are glued EOG, EEG and the EMG and its right to recognize a polysomnography. In **2B**, the patient is asleep and the book has resigned.

The text was justified, typed in the font "Times New Roman" and the size 12. The pages were not numbered and included 36 lines with 11 cm length. A lamp (40 watts) was used for lighting, placed at a distance of one meter above the patient's head. At the beginning of the *Reading test*, the patient was informed by a verbal instruction, to read the text as possible in the normal reading speed and without interruptions. Patients were asked to keep the book at a distance of 40 cm. Lack of vision and of reading ability has been excluded by

spontaneous, aloud reading of few sentences, if the patient was able to read 3-5 sentences correctly and fluently. About the intention and the period of reading, the patients were not informed in order to allay apprehensions and expectations.

Evaluation

The reading movements are simultaneous eye movements, which are characterized by either internal or external amplitude deflections in the EOG. It occurs while reading a specific rhythm EOG, as the eyes "jump" at the end of the line to the next line start. The reading movements can be distinguishing well visually by small and big eye movements (Fig. 3). All reading movements were counted that occurred after a minimum interval of 3 seconds.

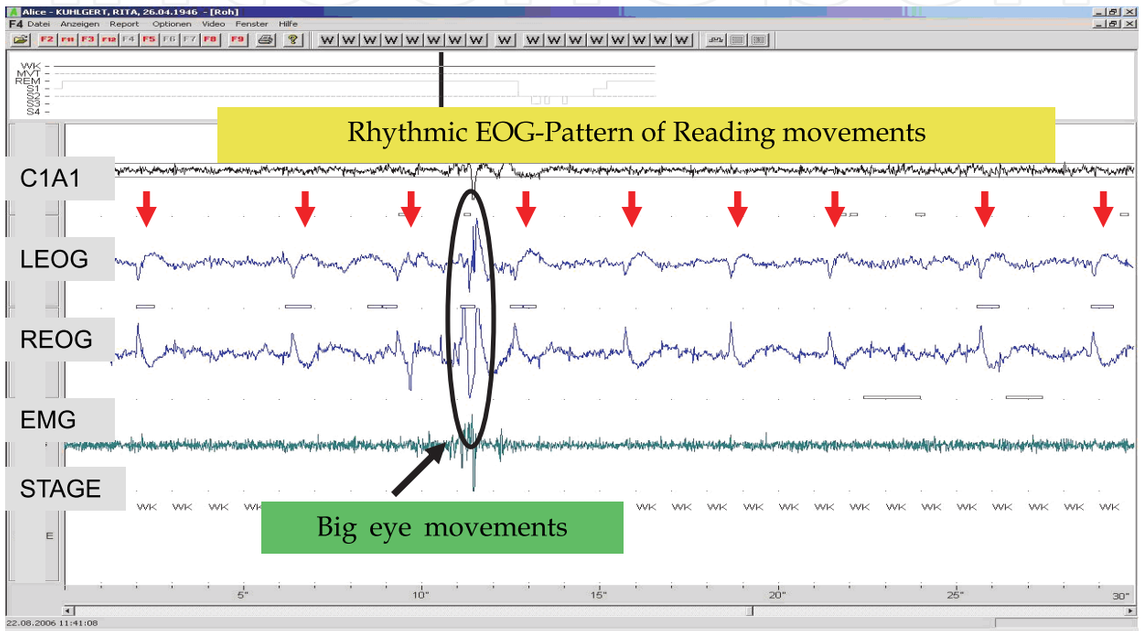


Fig. 3. On display are the reading movements of the left and right eye (LEOG and REOG) as a rhythmic, blue wave pattern. The reading movements occur during reading, when the eyes "jump" at the line end of the text (right) to line beginning (left). Large eye movements (e.g. view movements) are characterized by large amplitude fluctuations.

In the present study, the following variables were used and calculated: the average, the highest and the lowest reading frequency (read line per epoch), sleep latency (in minutes) and the number of read pages.

Results

The average reading rate of the patients (n = 75) was 7.0 +/- 3.5 lines per epoch. In healthy volunteers (n = 16) it was 9.4 +/- 4.0 lines per epoch. All healthy subjects were evaluated for daytime sleepiness than normal, since neither sleep onset tendencies nor decreasing reading frequencies were observed. In 32 of the 70 OSAS patients (45.5%), however, sleep latency was found within 60 minutes. Also the reading frequency decreased over time. Rühle and colleagues calculated for the first time, the sensitivity and specificity of the *Reading test*, finding a cut-off value of greater than 11 for a pathological daytime sleepiness (Rühle et al. 2007). The standardized *Reading test* achieved a sensitivity of 76.2% and a specificity of 66.7% (Erle et al. 2009).

2.8 Conclusion

2.8.1 Effect size analysis of the Epworth Sleepiness Scale

Rühle and colleagues (2005) researched into an effect size analysis of the ESS the question, if daytime sleepiness could be investigated through a situation. Therefore, the authors analyzed the effect sizes of the eight items. From methodological considerations, it was reasonable to imagine, to come across items with good to very good discriminatory power, because the ESS has a good to very good reliability and validity.

In the study, which took place in the sleep laboratory of the Helios Clinic in Hagen-Ambrock, 209 male OSAS patients and 164 healthy subjects participated. To calculate the effect sizes for each item the difference between of the two item means (of patients and healthy subjects) was divided by the standard deviation of the normal population. Rühle et al. received low to very good effect sizes (ES) between 0.19 to 1.50 The best effect sizes were found for the situation "in reading" (ES = 1.50), "watching TV" (ES = .90), "sit and be passive" (ES = .85) and for "traffic-related stopping" (ES = .61). Similarly, there was an increased mean effect size of ES = .88 for the four selected items, compared to a mean effect size of ES = .68 for the total scale. Some situations of ESS was associated with both healthy subjects and OSAS patients with a high propensity for sleep, e.g. to "lie down to rest" (ES = .19), as a "passenger" (ES = .22) and "talk with someone sitting" (ES = .24). For the development of everyday life and job-related tests - as it had been suggested by Johns (2000), the reading activity was an important characterisation of daytime sleepiness, because it discriminates at the best between OSAS patients and healthy individuals in comparison to the other ESS items.

2.8.2 MSLT and MWT criticism

Although MWT and MSLT are often used in practice, since years there is the assumption that its operationalization does not correspond to the tonic activation. Johns (1998) excludes that the MSLT is suitable as a predictor of daytime sleepiness in everyday situations, regardless how strict are implementation and evaluation standards. Although have the sleep latency on both tests satisfactory correlations as Sangal and colleagues (1992, 1997a) showed in subjects with various sleep disorders ($r = .41$, $p < .001$) and in Narcolepsy patients ($r = .52$, $p < .001$). However, the tests clarify maximum of 20-25% of common variance, indicating that the test methods measure different constructs of daytime sleepiness. Reasons for the average correlations according to Sangal et al. (1992) are that patients with pathological MSLT values were able to stay awake in the MWT, while others who fell asleep in the MWT were able to stay awake in the MSLT.

In addition, Johns described measurement error as reasons for the variability of individual test results. It argues that the measurements are depended on the situation character, internal attitude and physical condition of the patient. Kotterba and colleagues (2007) reported that the sleep latency of the MSLT corresponds to the individual property to switch off quickly. In the opinion of John (2000) was the MLST least suitable and is no longer regarded as the gold standard.

In handling the tests are very time-consuming and labour intensive (because of multiple tests during the day) as well as it is uneconomical. This would be calling in question the use of the method (Danker-Hopfe et al. 2006, Johns 2000). Because the claim of a standardized implementation and evaluation it could also be performed only by professionally-equipped sleep laboratories (Randerath 1997). Daytime sleepiness can be measured more easily and possibly more effectively with the ESS (Johns 2000).

2.8.3 Summary and outlook

Although the MSLT and MWT have been used frequently, in many studies was found evidence that the reliability and validity of the procedures are unsatisfactory. In addition, the two test methods don't correspond to any real life situation (Johns, 2000). Even if it is objective and standardized measuring instruments, have been repeatedly confirmed weaknesses in the implementing objectivity of the individual tests as well as their generalization ability (Danker-Hopfe et al. 2006). John's criticism is that the reliability and validity verification of MWT and MSLT were not gone in any way according to objective and standardized criteria. The ESS compared to the MSLT and MWT has good reliability and validation criteria, sensitivity and specificity measures. Its only drawback lies in the fact that the subjective assessments are based on individual perception and trust and the honesty of the patient.

Johns (2000) emphasizes the need to find an objective test, such as the ESS is valid and able to quantify the alertness in various everyday situations. Such a test would represent a true gold standard. Result of this strong criticism and of the clinical relevance of developing a new measuring method, Rühle et al. (2005) analyzed the effect sizes of the ESS. They pursued the goal, to detect the daytime sleepiness of life situation as objective, reliable and valid as possible. The analysis of the ESS and its implications led to the experimental derivation, design and construction of the *Reading test* (pilot study: Rühle et al. 2007, main study: Erle et al. 2009).

2.8.4 Conclusion of the reading test

Both the pilot study and the main study, the alertness impairments in OSAS patients with the reading activity, a simple spiritual activity were operationalized. In contrast to the MSLT and MWT daytime sleepiness was not measured in an experimental laboratory situation, but in an everyday clinical situation. The *Reading Test* is suitable for the determination of daytime sleepiness, because it probably produces a low level of attention. The reading activity will be documented and monitored continuously by EOG. Therefore, the non-reading phases can be observed, e.g. at the beginning of sleep, movement and looking around of the patient. In addition, the behaviour spectrum of patients are also detected in the EMG, as unwanted movements (facial grimacing and head movements), which can prevent sleep. This aspect would be particularly relevant in experiments.

3. Vigilance and attention in patients with Sleep Apnea Syndrome

3.1 State of research (Fig. 4)

Attention underlies performance of intellectual and everyday tasks. Depending on requirement character, novelty, intensity and level of activity, different components of attention are required.

The central nervous system activation (*alertness*) reflects the degree of general alertness and represents a kind of basic activation and general responsiveness. It is unconscious, and affected by the autonomic nervous system and the physiological diurnal state of the organism. Two variants of the central nervous system activation are described. The *tonic activation* is the stable level of attention over a long period of time. A disruption in tonic activation is manifested by a slowing of cognitive and motor processes. The tonic activation can be measured with the Multiple Sleep Latency Test *MSLT* (Carskadon & Dement 1977, Carskadon et al. 1986), the Maintenance of Wakefulness Test *MWT* (Poceta et al. 1992) or the

Pupillography (company Amtech, Weinheim, Wilhelm et al. 1998, 2001). A newer method to quantify the tonic activation is the *Reading test* (Erle et al. 2009).
The *phasic activation* is manifested in stimulus situations, in which short-term increases of the activation in the resting state are required. Limitations of the phasic activation can result in delayed reaction rapidities up to omitted reactions. The phasic activation may be tested for example in the kind of reaction time measurements, e.g. with the test battery of Zimmermann and Fimm (TAP / 1994), event-related EEG deductions or on the basis of the heartbeat rate or skin conductivity.

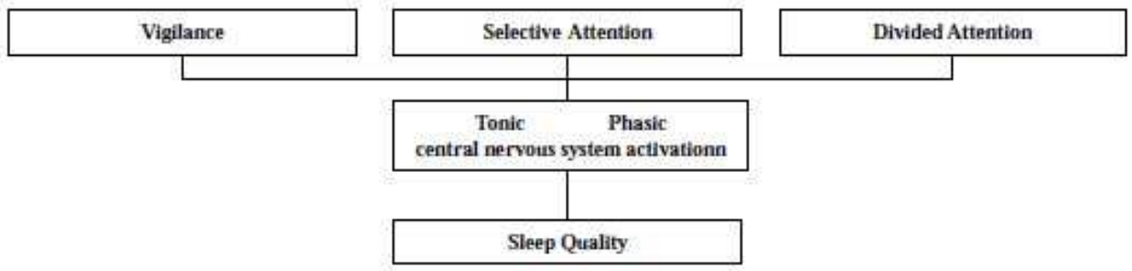


Fig. 4. Proposed relationship between sleep quality and sleepiness-related restrictions during the day

Sustained attention is the ability to direct attention over a long period to one or more randomly occurring stimuli and to respond to minimal stimuli changes (Davies, Jones and Taylor 1984). *Vigilance*, which is a variant of sustained attention, requires long-term attention performance in minimally and irregularly occurring stimuli. As reliable indicators false (i.e. incorrectly or delayed) and omitted responses as well as reaction times can be measured as an expression of sustained attention and vigilance. Furthermore, particularly in the field of sleep medicine the *Clock Test* by Mackworth (1948), modified by Quatember and Maly (Sturm und Büssing, 1993), and the *vigilance test* "*Carda*" by Randerath et al. (1997, 2000) and Gerdesmeyer et al. (1997) and the *sustained attention test* "*Carsim*" by Büttner et al. (2000a/b, 2001) have been used to test the vigilance and sustained attention.
Selective attention is also the ability to focus on specific relevant stimuli and to suppress simultaneously occurring irrelevant stimuli. The kind of attention function can be investigated by choice-reaction tasks or orienting responses, e.g. based on the subtest "*Selective attention*" to the *TAP*[1].
Divided attention describes the capacity for serial and parallel information processing and the flexibility of selecting to switch back and forth at least two different sources of information (Sturm and Zimmermann 2000). Relevant stimuli can each occur in one or two sources of information to which the person have to respond as quickly as possible. Divided attention can be measured with dual-task activities (e.g. using the subtest "*Divided attention*" of the *TAP*).
As with many sleep-related disorders, such as hypersomnias and dyssomnias, the victims suffer from, in addition to their nocturnal symptoms, increased daytime sleepiness and the tendency to fall asleep (Büttner et al. 2004b). These difficulties are in turn associated with attention-related deficits and limitations (including Gerdesmeyer et al. 1997, Müller et al. 1997, Randerath et al. 1997, 1998, Weeß 1997, Weeß et al. 1998a/b, Büttner et al. 2003b, 2004b).

[1] TAP = German: **T**estbatterie zur **A**ufmerksamkeits**p**rüfung; English translation: Test battery for Attentional Performance

Consequence of this reduced performance include an increased risk of accidents at work and in traffic and thus a higher socio-medical risk (e.g. Bradley et al. 1985, Podszus et al. In 1986, He et al. 1988, Mitler et al. 1988, Lamphere et al. 1989, Roehrs et al. 1989, Bédard et al. 1991, Kribbs et al. 1993a/b, Gerdesmeyer et al. 1997, Randerath et al. 1997, 1998, Weeß 1997, Weeß et al. 1998a/b, Büttner et al. 2000a/b, Büttner 2001).

To explore the difficult relationship between sleep, daytime fatigue and physical and mental performance is based mainly on three conditions (Johnson 1982, Weeß 1997, Weeß et al. 1998a/b). Thus, the three mentioned above parameters will be affecting through a variety of other variables, for example by the motivation of the healthy subjects or patients, or the daily and weekly rhythm. Furthermore, daytime fatigue and performance as well as their underlying attention-related processes are complex constructs. This analysis will be complicated also by the lack of standard term uses in the medical and psychological literature (Johnson 1982, Weeß 1997, Weeß et al. 1998a/b).

There are, both in the medical and especially in sleep medicine research, a number of different research approaches and definitions regarding the attention and attention-driven processes (Rützel 1977, Rapp 1982, Brickenkamp & Karl 1986, Posner & Rafal, 1987, Säring 1988, Posner & Petersen, 1990, Posner 1995), which accentuate different characteristics and aspects of the daytime performance (James 1890, Head 1926, Mackworth JF 1956, Mackworth N 1958, Schmidtke 1965, Norman 1973, Bäumler 1974, Harnatt 1975, Rützel 1977, Brickenkamp & Karl 1986, Posner & Rafal, 1987, Säring 1988, Posner & Petersen, 1990, Rollet 1993, Schmöttke & Wiedl 1993).

Currently, in the sleep medicine literature, mainly the concept of Posner and Rafal (1987) will be used (Keller et al. 1993, Weeß 1997, Weeß et al. 1998a/b).

Also problematic are the very diverse conducted empirical analysis of attention and its components and the varying quality of the validation test procedures and instruments. Thus, inter alia vigilance covered by inappropriate (Stephan et al. 1991), too complex (Bédard et al. 1993) or timely too short (Bédard et al. 1991, 1993) test requirements (Weeß 1997, Weeß et al. 1998a/b).

To capture the tendency to fall asleep in Obstructive Sleep Apnea is conducted usually by the MSLT (Multiple Sleep Latency Test) (Poceta et al. 1992), because it correlated most strongly with the subjective state/mood of OSAS. However, through it the attention and vigilance will be detected only indirectly (Denzel et al. 1993).

For this purpose researched Denzel et al. (1993) for more suitable methods and examined in this context, two computerized neuropsychological test procedures, a vigilance and a attention test, in which the attention test was checked under three experimental conditions (visual, auditory, combined). In both the dual-task-task as well as the vigilance testing was found significant differences before and after nCPAP therapy (Denzel et al. 1993).

Similar results – i.e. a significant improvement of vigilance under nCPAP – were found already by Kesper-Schwarzenberger et al. (1991), Cassel et al. (1991) and George et al. (1997; *DADT*)

As important criteria was found the standardization of experimental conditions (Horn et al. 1983, Denzel et al. 1993) and the design of the experimental setup (the author). Thus showed, inter alia, that an immediate auditory feedback about the correctness improved the occurred reactions improved the motivation of the patients, thereby obscuring the effects of sleep deprivation and their resulting poor performance (Wilkinson 1961, Steyvers & Gaillard 1993, Weeß 1997, Weeß et al. 1998a/b).

3.2 Vigilance test *Carda* (Fig. 5)

The Ambrock vigilance test "Carda" by Randerath et al. (1997) recorded the vigilance performance over a period of 30 minutes. The patient sits in a semi-darkened room in front of a black computer screen and look at the picture of a street with a running road median and the lateral lane boundaries. They are asked to respond within one second of a with a computer keyboard button on stimuli (white flashing rectangles), which occur in time and space for 20 ms randomly. In each 10-minute interval 100 stimuli appearing, in the total period 300 will be shown. After a brief instruction and a short practice the test is started via a menu driven DOS computer program.

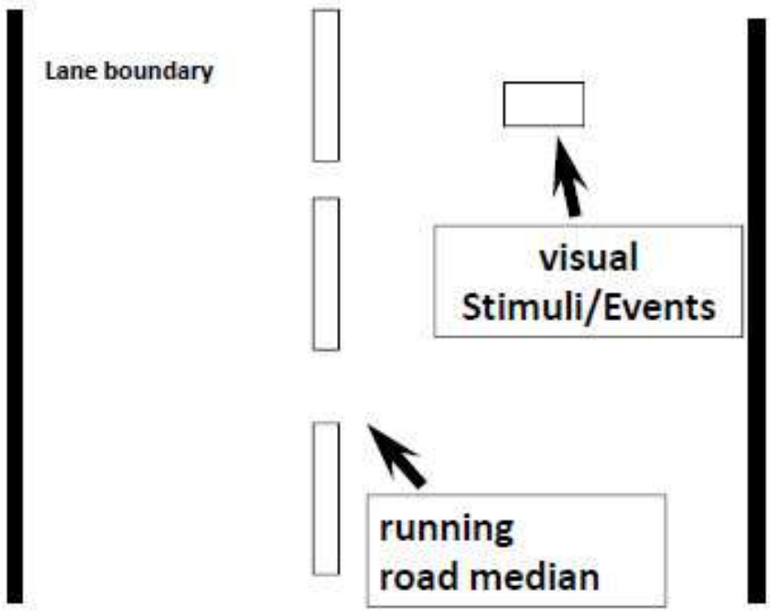


Fig. 5. Driving Simulator *Carda* by Gerdesmeyer et al. 1997, Randerath et al. 1997, 1998

Evaluation

Right and false reactions are calculated in relation to the presented events (in percentage), the latter being registered as an error. The unfounded (delayed) reactions are given in absolute numbers. The age-and gender-independent cut-off value for the error is 5.75% (SD = 11.3%) after a standardization study with healthy volunteers of Randerath and colleagues (2000). For the unfounded responses and response times are currently no cut-off values. Measurements for the reliability and validity are pending.

3.3 Sustained attention test *Carsim* (Fig. 6)

The Ambrock sustained attention test "Carsim" by Büttner et al. (2000a/b, 2001) recorded its performance over a period of 30 minutes. The image with a road median and lane boundary is simulated polychrome. On the right side of the road obstacles (in the kind of no entry signs) can be presented, which are only briefly visible in each case (e.g. for 200 ms). Their appearance is timely random, in which a fixed number of events can be adjusted with a 5-minute section. The patient now has the task to keep up with the help of

a steering wheel in his lane the ideal track (*tracking*) and by using of two buttons (both same function), which are located on the steering console, to respond on appearing obstacles (*visual search*).

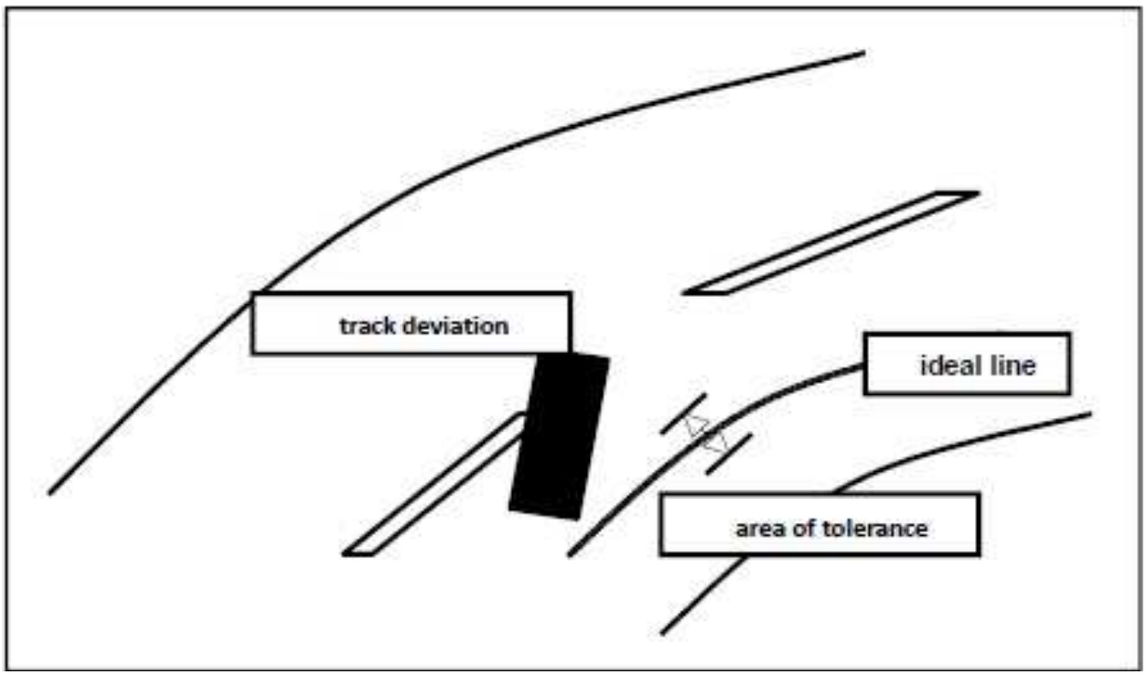


Fig. 6. Driving Simulator *Carsim* by Büttner et al. 1999, 2000

Evaluation

Depending on the steering wheel movements, the position of the vehicle on the road will be recalculated and visualized on-line. The program records the time deviation from the ideal line (*tolerance deviation time*) and of the lane (*tracking deviation time*) and the right, the missing, the unfounded reactions and the reaction time (Büttner et al. 2000a/b, Büttner 2001). Tolerance or track deviation is the number of tracking errors, which in absolute terms described, exceeds the tolerance and lane width in the test. By converting the number of pixels we obtain the time in seconds, which was driven outside the tolerance range or beyond the roadway.

Standardization and quality criteria

The average error of the tracking deviation time was 2.3 ± 4.5 s in the calibration sample, the limit of the track deviations of healthy persons in a 95% confidence interval was < 13.2 s, 98% of healthy individuals have had values between 0 to 150 track deviations. The mean error of tolerance deviation time was 96.0 ± 177.0 s in the healthy person's, the limit of tolerance deviations of the calibration sample in a 95% CI was < 450.4 s (Büttner et al. 2000a/b, Büttner 2001).

The verification of the *reliability* using the *Cronbach alpha* was for the tracking component r = .9785, for the visual search r = .9666 and for the reaction time = .8943. The verification of the *test-retest reliability* (after 3 days) was for the tracking component r_{tt} = .9855, for the visual search r_{tt} = .9447 and for the reaction time r_{tt} = .9211 (Büttner et al. 2000a/b, Büttner 2001).

3.4 Sustained attention test *Quatember & Maly* (Fig. 7)

With the computerized sustained attention "Clock test" of Quatember and Maly (Wiener Testsystem TM, Schufried, Austria 1994; modified for Task force *Vigilance* and *SIESTA group* of DGSM[2]) the sustained attention will be evaluated under monotone conditions and the processing diligence will be measured in the kind of errors and reaction times over a period of 60 minutes. There are two types of errors: missed and incorrect (delayed) responses reactions. Patients are instructed to press a key on the computer keyboard when the "moving point" in a points circle one point skips. At the beginning of the test will be started shortly to introduce the circular arrangement of points. During implementation, the patients sit in a relaxed position ca. 60-80 cm in front of the screen in a semi-darkened room.

Evaluation

The average reaction rate (in milliseconds), the degree of right, incorrect and omitted responses were recorded at Q&M-sustained attention test.Danker-Hopfe, Sauter and Popp (2006) determined in a standardization study with healthy volunteers cut-off values of more than 3 for omitted responses, more than 4 for incorrect responses and longer than 498 milliseconds for the response times of subjects. Standard values for OSAS patients are not yet available.

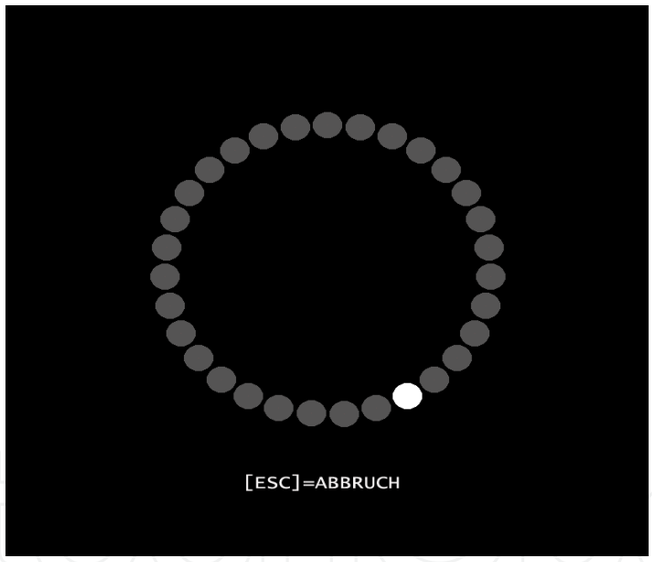


Fig. 7. Sustained attention test by Quatember and Maly (1994)

3.5 Conclusion

The driving simulator *Carda*, similar to the test developed by Findley, does not fulfil the requirements that are important on a real tracking test. It is rather a reaction test, which describes the attention and the vigilance.

Krieger et al. (1997) were able to demonstrate by means of questionnaires that the accident rate in OSAS patients was often caused by sleepiness and that both the rate of accidents and

[2] DGSM = Deutsche Gesellschaft für Schlafforschung und Schlafmedizin (engl.: German Society of Sleep Research and Sleep Medicine)

nearly accidents could be reduced with nCPAP therapy. A test for assessment of accident risk would therefore be helpful.
Findley was found a correlation between the number of accidents and the error rate in a driving simulator test using *Steer Clear* and data's of *Accidents Authority* Virginia/USA. He also had verified a certain connection between accident rate and Sleep Apnea Syndrome and a dependence on the severity of the disease (Findley et al. 1989, 1995, 1999, 2000). Tests of this kind should be used only with great caution on the question of driving ability, because it detected only a few aspects.
Due to the simple construction *Steer Clear* and *Carda* offer also some advantages, because the technical effort is relatively low and even restricted patients can understand the task very well. However, the tests can only evaluate the response to nCPAP treatment in cases with much higher error rate and can control it course.

	Carda	**Carsim**
Monotony	**(+)**	**+++**
Continuity	**-**	**++**
Interactivity	**-**	**+++**
Usability	**+++**	**++**

Table 3. Design and properties of the two simulation programs

The severity of sleepiness, as assessed by the ESS, didn't correlate with the results of driving simulators. Sleepiness/drowsiness describes the degree of alertnes and will be influenced by central nervous system activation (Weeß et al. 2000). Because the test situation, the sleepiness is often compensated in moderate limitations (ESS < 13) – in our patients, the ESS score was on average = 11.0 – so that the error rate or track deviation showed no relevant dependence. However, in OSAS patients with profound sleepiness (ESS score > 13) a higher number of errors were found in *Carda* reached a higher (Randerath et al. 2000). Under the testing with *Carsim*, the number of patients who have had a pathological deviation is much higher. The complex task of interactive driving simulation recorded thus patients with reduced performance, special with difficulties in the divided attention and interactive activities. This could be proven, to persons whose driving performance was checked after alcohol administration with a driving simulator. In OSAS capacity was similar limited to persons with a blood alcohol of 95 ± 25 mg/dl (George et al. 1996a).
Studies, which correlate the laboratory results of tracking tests with the real frequency of accidents, are still missing. It would be therefore desirable to obtain objective data on road authorities to characterize better any risk patients with this sensitive instrument. A tracking-driving simulator has a higher reality character than a reaction test, because it realized better the task, i.e. the reflection of driving situation (George 2000). Yet here, too, it is important to be sceptical about its evidence power, because the driving performance is dependent of many factors (e.g. responsible acting), which cannot be detected alone by simulation tests. A driving simulator test should be used only as one of several components in the complex assessment of driving ability.
The interactive driving simulator test *Carsim*, designed by the Ambrock task force, can also be used for further questions: In OSAS patients may be improve due to different treatment modalities several sub-components of attention (such as selective attention, divided

attention, sustained attention, processing speed) (Büttner et al. 2000a/b, Büttner 2001). An interactive driving simulator should reflect several of these changes and should be a more suitable instrument, because tracking tasks reflect more components of the limited capabilities in comparison to reaction tests (*Carda*).
We could demonstrate that an interactive driving simulator (e.g. *Carsim*) describes the disorder of OSAS patients more sensitive. It is used, therefore, specifically in clinical trials for the assessment of treatment effects to attention increase (e.g., nCPAP or theophylline (Büttner et al. 1999 or 2003a, 2004a)).Due the easy use also *Carda* will continue to be a suitable method to detect neuropsychological disorders and demonstrate treatment effects in clinical routine.

4. Memory processes in patients with Sleep Apnea Syndrome

4.1 State of research

Jenkins & Dallenbach (1924) could show for the first time that learning tasks which are presented before sleep could be keep better than tasks that are presented before wakefulness. This was confirmed in other studies (Hennevin et al. 1995, Smith 1996). The discovery of REM sleep (Dement & Kleitman 1957) was the start for a more specific research program in which certain stages of sleep each were assigned specific roles for the memory processes. As follow on one hand, REM sleep, was attributed partly memory-favouring effects because of its particular physiological changes, on the other hand, as well as the Slow Wave Sleep (SWS) was attributed the same effects (Hobson & McCarley 1977, Crick 1983, Wilson & McNaughton, 1994, Karni et al. 1994, Squire & Alvarez 1995).
One of the studies on cognitive deficits in the thinking, memory, communication and the ability to learn new information in OSAS patients comes from Kales (1985). In this study 76% of OSAS patients show cognitive deficits in all these areas. A study by Naëgelé et al. (1995) showed that the executive functions, which are important for the acquisition of information during memory processing in OSAS patients, were impaired.
It is assumed that in sleep disorders the often found reduced sleep quality leads, as a result of Slow Wave Sleep or REM suppression, increased nocturnal arousal responses or prolonged awakenings to a reduced recovery function of night sleep (Weeß et al. 1998a/b). According to Jennum et al. (1993), Insomnia and sleepiness affect cognitive functions. Patients with excessive daytime sleepiness complaints have special problems in situations of physical relaxation and during long monotonous concentration tasks (Schwarzenberger-Kesper et al. 1987).
Cassel et al. (1989) were able to detect in Sleep Apnea patients a reduced cognitive performance and a decreased non-verbal processing speed. In this connection they were able to detect a reduced cognitive processing speed on ZVT in OSAS patients. Also Kotterba et al. (1997) detect in 32 of 40 OSAS patients abnormal results on the ZVT. In another study of Kotterba et al. (1998), they found in OSAS patients an impairment of the central nervous system activation (*alertness*), of the selective attention and of the sustained attention. Barbé et al. (1998) verified in Sleep Apnea patients a decreased vigilance.

4.2 Number-connection test (ZVT)

The number-connection test is composed from four number matrices. Each matrix contains 90 unsorted numbers. It must be connected according to the statement by lines from 1 to 90. For estimating the test processing time, the experimenter uses a stopwatch.

The test is used to measure the basal, all intelligence performances underlying, largely milieu independent and genetically related cognitive performance speed. It corresponds with those ability bundles, which in literature will be called as "*liquid*" intelligence, "*perceptual speed*" or "*processing speed*" are. The test has a wide range of applications. It can apply from 8th years up for all age levels; from the special school to high school and universities (for all levels of education). It is very economical and can be use on an individual or group test. For the processing of the tests the subjects require 5 to 10 minutes (Oswald and Roth, 1987).

The high reliability of the test (test-retest reliability between r_{tt} = .84 and r_{tt} = .97[3]; parallel test reliability between r = .95 and r = .98) is largely independent of age and educational level of the subject. The correlations with various intelligence techniques (PSB, HAWIE, IST-70, RAVEN, CFT-3) are between r = .40 and r = .83. For the individual experiments exist currently standards for 8th to 60th years (n > 2,000), standard values for the group version of the ZVT are available for the age range from 9 to 16 years. The mean of the norm sample (16-60 years) is a **T-value** of 50 ± 10.The Sleep Apnea patients achieved before therapy a T-value of **39.82 ± 10.73**, under a only 3-day-CPAP therapy, there was a significant improvement (T-value: **43.08 ± 10.50**) (Büttner et al. 2007).

4.3 Benton Test

The *Benton Visual Retention Test* is one of the best known and most widely used tests of immediate remembering for visual-spatial stimuli. The test consists of three parallel series, each with 10 geometric stimulus cards. The test person or the patient is shown one stimulus card for a short time (10 seconds), the figure of the card is to be draw directly after showing or after a short delay as accurately as possible. Further testing variations allow a shorter presentation time from 5 seconds, direct copying or simply selecting/choosing of a seen template from four alternatives. The *drawing form* allows evaluating, especially in children, the assessment of the draw ability, whereas the *electing/choosing form* evaluates the memory without the drawing component. The German edition follows the fifth American edition of 1992. It contains a simplified scoring system, additional evaluation examples, advanced standard values and a summary with new findings (Benton test at the onset of dementia). The German Benton also contains, in contrast to the U.S., the election form. The numerous new German-published studies for the Benton test were specifically considered. The test is used in adults until an old age and in children older than 7 years (Benton 1974).

Retest reliability for the *drawing form* is r_{tt} = .85[4]. The relationship between *drawing form* and *electing/choosing form* is relatively low (r = .55). There are numerous studies, especially in the

[3] This retest reliability has been verified by the authors of the following sources:

1. http://www.google.de/search?q=cache:5m0-sgoxY1AJ:wt.fb3.uni-wuppertal.de/fachschaft/psychologie/studi_hilfen/files/Hauptstudium/Diagnostik/Zahlen-Verbindungs-Test_(ZVT).doc++reliabilit%C3%A4t+zvt+test+&hl=de&lr=lang_de&ie=UTF-8: (r_{tt} = .81) and
2. http://www.testraum.ch/Serie%204/ZVT.htm: (r_{tt} between .81 and .97).

Learning effects of the ZVT may thus be concluded in clinical trials.

[4] This retest reliability has been verified by the authors of the following sources:

1. http://www.testzentrale.de/tests/t0300401.htm: Retest reliability for the *drawing form* was r_{tt} = .85
2. http://www.unifr.ch/ztd/lernsystem/tb/benton.html#Testentwicklung: Retest reliability for the *drawing forms* C, D and E is given as average of r_{tt} = 0.85.

Learning effects of the Benton test may thus be concluded in clinical trials.

evaluation of brain damage.The mean of **correct reproductions** of the 15-44-year old persons was 8 (IQ score of 95-109). In contrast, the mean of the OSAS patients was **6.76** before therapy (IQ score: 70-79), after a 3-day treatment with nCPAP it was **7.84** (IQ score: 80-94).The mean of **error numbers** of 15-39-year-old persons was three (IQ score of 95-104). The error mean of the study patients was **4.46** before therapy (IQ score: 90-94), after 3-day treatment with nCPAP it was **2.66** (IQ score: 105-109) (Büttner et al. 2007).

4.4 Conclusion

As mentioned above, in several studies could be demonstrated neuropsychological and cognitive deficits in OSAS patients (Bédard et al. 1991, Naëgelé et al. 1995, Gresel et al. 1996, Engleman et al. 2000). This allowed finding inter alia differences between healthy subjects and OSAS patients in the assessment of cognitive processing speed and of performance speed (ZVT) (Cassel et al. 1989, Kotterba et al. 1997, Büttner et al. 2007). Also in the Benton test to record the performance of visual memory the OSAS patients showed – compared with healthy subjects – significantly worse results in the number of errors. None significant results were found for the number of correct reproductions. This may have resulted through the sample composition or sample size. On the other hand, it could be that the increased error number and the nearly normal number of correct responses is a criterion or a feature for the detection of neurocognitive deficits in OSAS patients (Büttner et al. 2007).

Conclusion

It can be said that OSAS patients differ from healthy individuals with respect to cognitive skills. These differences can be verified both the memory processes (Benton) and in cognitive processing speed and performance speed (ZVT). These impairments can have serious consequence, if or as long as they remain untreated.

4.4.1 CPAP therapy and its effect

In various studies improved performance under nCPAP therapy have be determined regarding to changes in neuropsychological parameters and/or test performance. Lamphere et al. (1989) could be shown that after one therapy night there was a significant improvement of the attention, which normalized after 14 days of nCPAP. In several studies it could be detected also a reduction in both subjective and objective daytime sleepiness (Montplaisir et al. 1992, Engleman et al. 1993, 1994, Douglas et al. 2000 – according to Schwarzenberg-Kesper et al. (1987) is the improvement of daytime sleepiness an essential motif for a good therapeutic compliance of the patients). Sforza et al. (1995) found after one year of nCPAP treatment an objectively reduced daytime sleepiness, which increased again after a night of therapy interruption. In several studies could be verified also improved further neuropsychological deficits. Kotterba et al. (1998) reported a significant improvement in the simple attention as well as the divided attention, in the cognitive performance and the processing speed. The latter could be replicated also by Büttner et al. (2007). Even an improvement of vigilance or sustained attention, and various cognitive deficits due to the nCPAP therapy was described many times (Denzel et al. 1993, Engleman et al. 1994, Randerath 1997, 2000, Büttner 1999).

Other studies have shown, however, that the cognitive and neuropsychological deficits don't increase or only improving in certain areas, which could indicate an irreversible hypoxic damage of the CNS (Montplaisir et al. 1992, Bédard et al. 1993, Kotterba et al. 1998) and thus point up the importance of early diagnosis and treatment of OSAS underscores.

Conclusion

The difference or the improvement after effective nCPAP therapy suggests the need to use this therapy in OSAS patients, possibly to avoid serious impairment in the memory processes and in cognitive performance or to allow the patient not to suffer under the daytime consequences of Sleep Apnea Syndrome.

5. Summary

In the western and eastern industrial countries, the number of sleep disturbed subjects increased over the time. Undiagnosed and untreated, sleep disorders caused on one hand often by subjective suffering among those affected individuals and on the other hand, due to decreased attention and increased daytime fatigue or daytime sleepiness, to an increased risk of accidents in road traffic and workplace (e.g. Peter et al. 1995, Gerdesmeyer et al. 1997, Randerath et al. 1997, 1998, Büttner et al. 2000a/b).

Sleep Apnea syndromes are common disorders. 1-5% of the population is affected by it (men are about ten times more affected than women). In particular, patients with OSAS suffer in addition to their symptoms often also on a multitude of sequelae, including excessive daytime sleepiness (Büttner et al. 2004e), vigilance decrease (Büttner et al. 2003b, 2004c) and memory disorders (Büttner et al. 2003c/d).

These performance restrictions or impairments affect the affected subjects, both professionally and in their ability to drive motor vehicles (Findley et al. 1988a/b, 1989b, 1990, 1991, 1995, Mitler et al. In 1988, Cassel et al. 1991a/b, 1993, 1996 , ATS 1994, Gerdesmeyer et al. 1997, Krieger et al. 1997, Randerath et al. 1997, 1998, 2000, Weeß 1997, Weeß et al. 1998a/b, Büttner et al. 2000a/b, Büttner 2001). Consequences of this reduced performance are therefore often accidents or nearly accidents by falling asleep at the wheel. However, other cognitive and mental functions and the quality of life can be affected by sleep disorders (Sleep Apnea Syndrome, Insomnia and/or Narcolepsy).

In summary therefore, can be said that sleep disorders and/or sleep diseases are complex disorders which human beings can affect in his totality and in his whole personality. It can therefore affect all physical, mental and spiritual processes. It can lead to lower physical and mental performances; reduce vigilance, impaired attention and concentration. It can affect the quality of life, reduce, limit and/or prevent social contacts and competencies skills, and cause in other psychiatric[5], neurological[6] and organic[7] diseases.

A detailed sleep diagnostics and possibly therapy of previously known sleep disorders and/or sleep diseases is therefore essential to prevent complications and comorbidities, to prevent treatment resistance with respect to other physical and mental diseases and to provide effective medical treatment.

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[7] such as hypertension, heart disease / heart infarction

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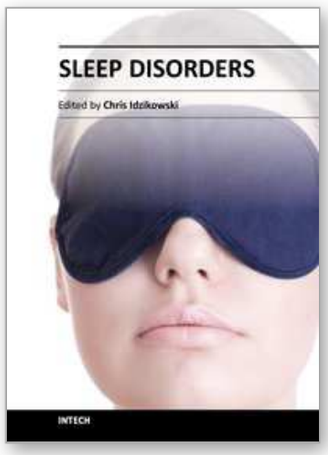

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For progress to be maintained in a clinical field like sleep medicine, unimpeded, unrestricted access to data and the advances in clinical practice should be available. The reason why this book is exciting is that it breaks down the barriers to dissemination of information, providing scientists, physicians, researchers and interested individuals with a valuable insight into the latest diverse developments within the study of sleep disorders. This book is a collection of chapters, which can be viewed as independent units dealing with different aspects and issues connected to sleep disorders, having in common that they reflect leading edge ideas, reflections and observations. The authors take into account the medical and social aspects of sleep-related disorders, concentrating on different focus groups, from adults to pregnant women, adolescents, children and professional workers.

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