Prologue
Deep slow wave sleep is a normal physiological phenomenon, while absence epilepsy is regarded as a brain disturbance. Nevertheless, both phenomena share common characteristics and the decrease in consciousness is most striking. In this paper the similarities between the two brain states are shown, whereby data of humans as well as rats are taken into consideration.

The lowering of consciousness
Consciousness is decreased during sleep. This is expressed by a lack of a response towards an external stimulus. This does not exclude that sleep can be terminated by stimuli and two factors play a role in awakening: the strength of the stimulus and its relevance. While waking threshold for auditory stimuli is dependent on the stage of sleep, awakening starts by stimuli of about 57 till 60 dB. However, from classical experiments it is well-known that the threshold for awakening can be much lower for a relevant stimulus than for a physical identical but neutral stimulus. Obviously, evaluation of incoming stimuli still takes place during sleep and the putative relevance can even be established. This common sense phenomenon was investigated by Westerhuis et al (1996) by measuring waking thresholds in rats. They compared the arousal reaction to relevant and irrelevant stimuli during slow wave sleep, during the presence of a spike-wave discharge (the electrophysiological manifestation of a seizure characterising generalised absence epilepsy) and during REM sleep. They found that rats were more often aroused after the presentation of a conditioned stimulus than after an unconditioned stimulus, irrespective of the behavioural condition. This suggests that the information flow through the brain is never stopped, even not during the highly synchronised epileptiformic activity. Westerhuis et al (1996) also noticed a lower awakening threshold for spike-wave discharges.
than for sleep (taken light and deep slow wave sleep together), suggesting that there are gradients in what the brain is able to do in the various states. In concordance with sleep it is shown that during the occurrence of a spike-wave discharge the evaluation of incoming stimuli is still possible. When physically identical stimuli with differential impact, induced by previous conditioning, are offered during the presence of a spike-wave discharge, the relevant stimulus terminates this activity more frequently than the less relevant one. This not only means that during this aberrant state, just as during sleep, some sensory information reaches the sensory cortex, but also that the brain still has the ability to evaluate this activity. This despite the lowering in consciousness, as indicated by the fact that no abortion of a spike-wave discharge occurs on a neutral stimulus, unless this stimulus is powerful enough (Drinkenburg et al, 1996).

**Time estimation**
The general feeling of the course of time during sleep is that the time stands still. Brief lapses in time also occur during absences in which the patient is unable to maintain contact with the environment. When a patient is counting this counting is stopped when an attack begins, but continues correctly when the absence is finished. To study this in more detail an experiment was performed with children suffering from absence epilepsy and the same experiment was achieved in epileptic WAG/Rij rats. All these rats show abundantly spike-wave discharges of the absence type. Children were asked to press a button when they thought that a fixed period of time had elapsed. The performance of the subjects in trials with and without spike-wave discharges was compared. Brief discharges, shorter than 3 seconds, prolonged the duration of the estimated time period, while longer ones reduced its duration. The prolongation was longer than could be anticipated from the duration of the spike-wave discharge. Moreover, it seemed that after long discharges patients behave differently and were perhaps more severely disturbed. The duration of misperception of the interval after the short discharges was larger than could be predicted from the duration of the paroxysms, which seem to contrast with the view that cognitive impairments are only limited to the period of the epileptic phenomena. Correspondingly, it was studied in epileptic rats whether differences in timing could be noticed in the estimation of a fixed time period with and without spike-wave discharges. Rats were extensively trained to press a lever for food in a fixed interval task until a stable response pattern emerged. The time the rats waited till they made a response, the post-reinforcement pause, lasting about half of the interval. During the task, the post-reinforcement pause was significantly enhanced in trials with spike-wave discharges compared to trials without discharges, indicating a clear change in perform-
The difference in pause was about 15 seconds, while the absence lasted about 5 seconds. Again it was found that the duration of the misperception was longer than the duration of the EEG paroxysm. This result shows that the rat does not count the time of the spike-wave, and even more, indeed suggests that the time stands still during an absence. This is fully comparable to that what happens in epileptic children when they have short lasting absences (van Luijtelaar et al, 1991a, 1991b).

**Underlying neuronal activities**

The EEG of deep slow wave sleep in humans is characterised by large amplitude, low frequency, irregular (delta) waves, while waking is associated with high frequency, low amplitude (beta) waves. This is also true for rats. The ‘tonic’ or ‘relay’ firing mode of wakefulness explains the EEG characteristics during waking. Numerous thalamo-cortical neurones spontaneously show a high neuronal firing during waking. This is caused by depolarised cells which polarisation voltage is near the threshold. This also implies that information can easily pass the thalamic nuclei on the way to the higher cortical areas. The high spontaneous activity together with a low synchronisation between thalamic and cortical cells causes the low amplitude, high frequency waves. How different is the situation during slow wave sleep! Thalamo-cortical cells are then firing in the so-called ‘burst’ mode. Extended populations of neurones fire rather synchronously with short bursts, interspersed with prolonged pauses. This firing mode is the substrate of the high voltage, low frequency and irregular waves characterising deep slow wave sleep. During this firing mode sensory information from the sensory receptors in the periphery through the thalamus on the way to the cortex is largely blocked and does not reach the higher perceptual cortical centres. This process is called ‘sensory gating’ (Coenen, 1995, 1998). The EEG associated with human generalised absence epilepsy also shows large amplitude waves, but this activity is quite regular with 3 Hz spike-wave activity. In rats also spike-wave activity is present during an attack of absence epilepsy. Instead of 3 Hz the frequency in rats is fluctuating around 8 Hz. This difference is considered as a not well understandable species difference.

Single unit measurements of cells in thalamus and cortex reveal that these neurones are firing during absences in the burst mode, with short bursts underlying the spikes and the pauses underlying the waves (Inoue et al, 1993). There is a heavy synchronisation between cells, causing the sharp spikes. This implies again that the neuronal characteristics of slow wave sleep and absence epilepsy are rather identical, although the amount of regularity and synchronisation is different. The bursting mode of firing during an absence also means that the incoming afferent information is blocked to a certain degree. The fact, however, that a relevant stimulus can easily abort a spike-wave discharge im-
plies that also during this aberrant brain activity incoming information is, just as during sleep, evaluated.

**Figure**

An evoked potential study to the characteristics of the brain states was performed in WAG/Rij rats. Visual evoked potentials (VEP) were constructed during active and passive wakefulness, during deep slow wave sleep and REM sleep and during the occurrence of spike-wave discharges (see figure) (Meeren et al, 1998). In general two types of evoked potentials were recorded. The first type was seen during active wakefulness and REM sleep, while the second type was recorded during deep slow wave sleep and spike-wave discharges. The VEP of passive wakefulness takes a middle position. VEP's recorded during active wakefulness and REM sleep are smaller in amplitude and are more detailed and complex, compared to those registered during deep slow wave sleep and spike-wave discharges. In the latter VEP's larger components can be seen and the shape is less detailed. Obviously this is related to the electrophysiological state of the brain. Active during alertness and REM sleep, and less active but bursting during the two other states. This finding again underlines the comparable aspects of neuronal activities during slow wave sleep and absence epilepsy.

**Epilogue**

From neuropsychological studies it is concluded that the physiological phenomenon of deep slow wave sleep shares common characteristics with the aberrant state of absence epilepsy. Most pronounced is a relatively comparable lowering in consciousness. This is expressed in an unresponsiveness to external stimuli, but both states can be terminated by strong stimuli. Another correspondence is the fact that unconscious stimulus evaluation is still possible. Relevant stimuli can terminate both slow wave sleep and absence attacks much
easier than neutral stimuli. Thus, the process of sensory gating is still intact during absences. All phenomena can be related to the underlying neuronal mechanisms. In both the sleep and the absence state neurones are firing in the ‘burst’ mode. Single unit studies in rats as well as evoked potential studies reveal this firing mode. A difference is the regular and spiky character of the spike-wave discharges, contrasting the large irregular sleep waves. This is due to the even stronger burst mode during absences. Perhaps this can also explain the small differences in behavioural aspects. During absences small muscle twitches of eyes and extremities can often be seen, which is not the case during slow wave sleep. To uncover this difference is a matter of future research.

References


Functional assessment and treatment of sleeping problems in developmentally disabled children: case studies

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Sleeping problems of children with developmental disabilities are highly prevalent as well as persistent. Such problems can be distinguished as settling difficulties (e.g., prolonged sleep latencies, disruptive behaviors at bedtime, co-sleeping with parents) and waking up frequently during the night or early morning and disturb the parents or siblings (e.g., calling out, crying, co-sleeping). Recent prevalence studies show that the prevalence of sleeping problems among children with biologically determined intellectually handicapping disorders such as Prader-Willi syndrome, Angelman syndrome, Smith-Magenis syndrome, Rett syndrome or autism, is particularly high compared to children without such syndromes. The mechanisms causing phenotypic features like sleeping problems remain for most of the syndromes largely unknown.

Disruptive sleep patterns are of considerable concern for several reasons, the first being the adverse effects on the child. For example, results from a small number of studies indicate that there is a strong correlation between chronic sleeping problems and daytime behavioral difficulties. Next to this, chronic and severe sleeping problems may place enormous stress on the family.

There are several factors that may be related to the emergence and maintenance of sleeping problems in our target group. Medical factors encompass apnea (of central origin or caused by upper airway obstruction), nighttime seizure activity, pain as a result of e.g., otitis media and/or discomfort due to e.g., exzema, asthma or nocturnal enuresis/encopresis. A disordered sleep-waking cycle may be due to visual impairments. Psychological factors include inconsistent bedtime rules of parents and positive reinforcement of abnormal sleeping behavior by parental attention. Sleeping problems may also be related to traumatic events experienced by the child. Finally, factors pertaining to the physical environment may be related to the level of light and noise and opportunities of toy play.

Only a few studies have documented the effectiveness of treatment of chronic sleeping problems of our target group. A number of treatment modalities have been developed and validated. Behavioral procedures encompass (graduated)