CPs ($p < 0.10$). Although the SPs spent less time in REM sleep ($p < 0.05$), further REM sleep parameters, including REM latency and REM density, were not altered.

In conclusion, our findings in drug-naive patients with a first episode of a schizophrenic disorder are in favour of an arousal linked disturbance at the beginning of the night sleep resulting in a delayed sleep onset and a disturbed build-up of SWS. On the other hand, we did not observe changes in REM latency or REM density in these patients.

VI.4

CSF LEVELS OF DIAZEPAM BINDING-INHIBITOR CORRELATE WITH REM LATENCY AND SLOW WAVE SLEEP IN SCHIZOPHRENIA

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Based upon the sleep inducing and potential antipsychotic effects of benzodiazepines (BZDs), and the relationships between negative schizophrenic symptoms and rapid eye movement sleep (REM) latency and slow wave sleep, we studied CSF diazepam-binding inhibitor-like immunoreactivity (DBI-LI) and polysomnography in schizophrenic patients. Twenty eight drug free male schizophrenic patients (DSMIIIR), underwent a three night polysomnography evaluation and a lumbar puncture. CSF DBI-LI correlated positively with REM latency and stage 4 percent-sleep; while CSF DBI-LI correlated negatively with Stage 1 percent-sleep and REM density. CSF DBI-LI did not correlate significantly with duration of sleep or sleep latency. Negative symptoms also correlated negatively with CSF DBI-LI. CSF DBI-LI did not correlate significantly with sleep EEG measures during haloperidol treatment in 17 of the patients who were evaluated on medication as well. While there were positive relationships between CSF DBI-LI and sleep measures, the relationships between CSF DBI-LI and schizophrenic behavior were negative. The results of this first study of the relationship between endogenous DBI and sleep in humans suggest a different physiological role for DBI than concluded from pharmacological studies. However, the absence of similar sleep data in normals precludes us from establishing a specific relationship between DBI and sleep in schizophrenia.

VI.5

CHOLINERGIC STIMULATION AND REM SLEEP IN DEPRESSION AND SCHIZOPHRENIA

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Altered distribution of REM sleep i.e. shortening of REM latency, is assumed to be specific for sleep in depression. It was demonstrated that stimulation with cholinergic agonists, for example RS 86, prior to sleep provokes significantly shorter REM latencies in depressives than in controls, supporting the theory of a muscarinic supersensitivity in depression. In the present study the influence of cholinergic stimulation on REM sleep is investigated comparatively in healthy subjects, depressed patients and schizophrenic patients.

We investigated 36 healthy subjects, 39 patients with major depression and 39 patients with schizophrenia. All patients were drug free for at least 7 days and after an adaptation night in the sleep laboratory the patients were given placebo/1.5 mg RS 86 in a randomized double-blind order prior to sleep on the next two nights.

RS 86 had the strongest impact on REM latency in depressed patients compared to the two other groups. In depression mean REM latency was shortened from 47 to 19 min after RS 86 and in schizophrenic subjects REM latency was shortened from 67 min to 43 min. Although depressed patients and schizophrenic subjects differed significantly, an unexpected high number of extremely shortened REM latencies in schizophrenic patients occurred. The results support the hypothesis that muscarinic supersensitivity may be implied in the pathophysiology of a subgroup of schizophrenic patients.

VI.6

CHOLINERGIC MECHANISMS AND REM SLEEP ABNORMALITIES IN SCHIZOPHRENIA

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Polysomnographic abnormalities in schizophrenia are poorly characterized and the underlying mechanisms and clinical correlates of such abnormalities are poorly understood. To address these issues, we recorded EEG sleep in 20 drug-naive schizophrenics, 20 drug-free but previously medicated schizophrenics, and 20 matched normal controls. Drug-naive and previously

medicated patients both had significantly greater impairment of sleep continuity and shorter REM latency when compared to controls. REM latency was inversely correlated with the severity of negative symptoms ($r = -0.52$, $p < 0.001$) but unrelated to depressive symptoms. Considering the role of dopaminergic and cholinergic mechanisms in the regulation of sleep measures, these findings are consistent with the model of concomitant increases in dopaminergic and cholinergic activity in schizophrenia. To further evaluate the cholinergic contribution to these sleep findings, we studied the effects of 6 and 10 mg of biperiden (an anticholinergic agent) on REM sleep measures in 20 schizophrenic patients (10 patients at each dose) and matched normal controls. 6 mg of biperiden produced a smaller increase in REM latency in schizophrenic patients; 10 mg of biperiden produced an equal increase in REM latency in both groups. Both doses of biperiden produced a greater reduction in REM density in the schizophrenic group. Considering that REM latency is predominantly regulated by the cholinergic system and REM density by the balance between cholinergic and catecholaminergic systems, these findings provide further support for the hypothesis of concomitant increases in dopaminergic and cholinergic activity in schizophrenia.

VI.7

SLEEP DISTURBANCES IN SCHIZOPHRENIA: EFFECTS OF HALOPERIDOL

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Sleep disturbances have been noted in relapsed and residual schizophrenic patients. Only recently some patterns have emerged such as shortened overall sleeping time, fragmented sleep, decreased slow wave sleep and REM latency. Antipsychotic treatment tends to normalize some of these findings. However, the lack of consistency across studies of sleep abnormalities in schizophrenia may be explained by methodological problems such as lingering after-effects of neuroleptic treatment and uncertain clinical state. The authors will present sleep EEG data on 25 physically healthy male schizophrenic patients (DSMIIIR), ages 25–49, who were studied before and after haloperidol withdrawal at varying times drug free. Sleep EEG was significantly different in the drug free patients who relapsed versus those who did not. Haloperidol withdrawal was associated with decreased total sleep, sleep efficiency and maintenance; decreased REM latency, and overall decreases in stages 1 through 3 and delta sleep. Relapsers had less total sleep and lower sleep efficiency than nonrelapsers in the drug free state. Reports examining sleep in schizophrenic patients should include information on time drugfree before testing and the clinical condition (e.g. relapsed, clinically stable).