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Research report

Sleep-related cognitive function and the K-complex in schizophrenia

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HIGHLIGHTS

- Increasing density of K-complexes is related to enhanced problem solving performance in schizophrenia.
- Increasing age is related to decreased overnight improvement in problem solving performance in schizophrenia.
- Longer SWS is related to shorter duration of completing the problem solving task.

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ABSTRACT

Sleep parameters have been reported to be related to cognitive function in a variety of ways. Problem solving and procedural learning were found to be improved after sleep but training also affected subsequent sleep and some parameters were related to cognitive trait variables, e.g. IQ. Additional to rapid-eye-movement (REM) and slow wave sleep (SWS), micro-architectural features such as spindle activity and K-complexes have recently been the focus of interest. The study aimed at investigating the relationship of neuropsychological variables, problem solving and procedural learning with sleep parameters in stably medicated schizophrenia patients.

Twenty schizophrenia out-patients participated in the study. Learning and testing occurred over a randomly balanced waking and sleep interval. The tasks were the Tower of London (ToL) and mirror tracing. Sleep EEG was analysed together with spindle activity and K-complexes.

Performance improved with regard to both tasks from learning to testing irrespective of type of interval. Increasing density of K-complexes was related to a higher number of solved ToL tasks pre and post night whereas longer SWS was related to faster completion of the ToL. A higher age was related to less overnight improvement in regard to number of solved ToL tasks.

K-complexes are thought to indicate intra-cortical activity paving the way for the uptake of new information. As ToL is considered a test of executive function, K-complexes appear to be linked to this domain, deficits of which are thought to be a core feature of schizophrenia.

1. Introduction

Cognitive function was found to be related to sleep in a variety of ways. Sleep is thought to play an important role in offline memory reprocessing [10,47,50] and the beneficial effect of sleep on cognitive function was investigated repeatedly in healthy volunteers [e.g. 6]. Learning has also been shown to have an effect on the pattern of subsequent sleep [4,48] and some sleep features are related to cognitive function in a trait-like manner [18,25,50]. There is, however, less agreement as to the particular sleep stages which promote performance.

Procedural learning was assessed using visuomotor [20,27] or motor sequence tasks [52]. It was variably found to be improved after enhanced rapid-eye-movement (REM) sleep [16] and after longer duration slow wave sleep (SWS) [27]. Other authors reported performance to be improved after enhanced stage-2 duration [52,38,17]. Yet other authors found improvements in procedural learning to be due to recovery from fatigue, circadian confounds or initial skill level instead [38,43].

Problem solving was more rarely investigated but has also been found to benefit from sleep. Wagner et al. [51] presented a task which could be solved more rapidly with knowledge of the underlying hidden rule. Twice as many participants gained insight into the hidden rule after sleep than after a day-time interval or sleep deprivation. Sleep also benefited relational [12] and category learning [11]. Napping especially when combined with REM sleep improved problem solving in a remote associates task [7].

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Recently, spindle activity has received increased attention in sleep research. Sleep spindles are brief bursts of synchronous neural firing. Employing simultaneous EEG and functional magnetic resonance imaging (fMRI) [1], spindle activity during stage-2 sleep could be shown to be related to activation of the functional connectivity between the hippocampal formation and neocortex. It is thought that memories initially encoded in the hippocampus are transferred to the neocortex for long-term storage [46]. Consistent with this model, performance was shown to be improved after enhanced stage-2 duration and spindle activity [17,38,52]. Spindle activity has also been found to be increased due to procedural learning before the night [4,48]. Furthermore, increased spindle activity appears to be a trait feature. Schabus et al. [44] reported increased spindle activity in high-IQ participants independently of learning and Fogel et al. [18] reported this to be case in performance but not verbal IQ.

So far, K-complexes have, to our knowledge, not been directly investigated in relation to cognitive function. They are characterised by a large surface-negative complex followed by positivity and arise within cortical networks [2,3]. Originally thought to occur during SWS, it has now been shown that they predominate during stage 2 [8]. K-complexes are assumed to suppress – or indicate the suppression of – cortical arousal evoked by stimulation [50]. With regard to the latter function, K-complexes are proposed to be correlated to memory consolidation during sleep in that they are assumed to represent synaptic downscaling which paves the way for subsequent processing of new information [8]. Research on this feature has so far been restricted to sleep studies in animals and investigations of neurological disorders without the study of concomitant cognitive function.

There are still only few investigations of the effect of sleep on cognition in schizophrenia [24,32]. The disorder is associated with altered sleep patterns in unmedicated patients [9] and antipsychotic medication has shown to normalise sleep parameters [23,30]. But even medicated patients exhibited reduced spindle activity compared to healthy volunteers [14] and depressed patients [13]. Consistent with this finding, there was no evidence of significant overnight improvement of performance in schizophrenia patients [19,31,32]. Notwithstanding, there is considerable variability among patients in regard to the relationship between performance and different sleep stages. Göder et al. [19] reported a significant correlation between decreased SWS and impairment in a visuospatial memory task after sleep. Manoach and Stickgold [32] confirmed that enhanced SWS but also increased stage-2 sleep during the last quarter of the sleep led to improved performance in a motor task. Finally, Keshavan et al. [25] reported elevated spindle activity to be related to elevated performance in tests of attention and executive function in unmedicated psychosis patients.

In the present study, tests of cognitive function and learning of a problem solving (Tower of London – ToL) [45] and a visuomotor task (mirror tracing), were investigated in relation to sleep in schizophrenia patients. A day/waking interval was compared with that of a sleep/night interval, during which polysomnographic records were obtained. Apart from analysing sleep stages, attention was given to spindle activity and K-complexes. We expected a significant relationship between spindle activity and performance.

2. Methods and materials

2.1. Participants

Twenty out-patients (8 m, 12 f; mean age 41.25 (8.7)) with a DSM-IV diagnosis of schizophrenia and a mean duration of illness of 13.4 (8.4) years took part in the study. Exclusion criteria were substance abuse or dependence, diagnosed sleep or neurological disorders and benzodiazepine use at the time of the study. Inclusion criteria were an age of 18–55 years, fluency in German, an IQ > 70 and stable medication for the last 2 weeks. Patients were administered the Structured Clinical Interview for DSM-IV (SCID, German version) [53] and the Positive and Negative Syndrome Scale (PANSS) [22]. Thirteen patients had a diagnosis of paranoid schizophrenia, two of the residual type and five of schizoaffective disorder. Fifteen patients took atypical, one typical and four took both kinds of antipsychotics. Additional six patients were not included in the study (two because of equipment malfunction and four terminated their participation prematurely).

Informed written consent was obtained from each participant. The study was approved by the ethics committees of the Universities of Wuppertal and Düsseldorf. Patients were paid to participate.

2.2. Experimental design

All participants took part in a waking interval and a sleep interval condition and were randomly allocated to either the day ($N = 11$) or the night interval first ($N = 9$). The two occasions were separated by one week. During the waking interval condition, learning occurred in the morning and testing approximately 8 h later ($M = 7.9$ h, SD = .3) in the evening. Patients were instructed not to sleep or have a nap during the day of testing. During the sleep interval condition, learning occurred in the evening and testing 8 h later in the morning. Combining the waking and sleep intervals respectively across the two orders resulted in a Condition (waking vs. sleep interval) × Pre-post (learning vs. testing) design.

2.3. Experimental tasks

2.3.1. Tower of London (ToL) [45]

In this computerised test participants are shown coloured spheres arranged on poles. Displayed are a start and a goal position and participants are informed of the least number of moves possible for rearranging the spheres to attain the goal position. The task is to be carried out as fast as possible. If it is not completed within the least number of moves it is registered as unsolved. Participants were given an initial practice task to familiarise themselves with the apparatus. There were 15 tasks with increasing difficulty. Performance measures were number of solved tasks and total time taken. Two versions of the test were used.

2.3.2. Mirror tracing

Participants used a stylus to trace either a square or a triangle which they saw in a mirror. Deviations from the track were recorded as error. Performance measures were the total time to complete the task, number of errors and percentage of error time.

2.4. Polysomnography

Prior to retiring to the sleep laboratory, participants were wired for standard polysomnographic sleep recordings. Central EEG leads C3, C4 to A1 with an earth electrode at Fp1 were placed according to the International 10/20 system [21]. EOG leads were placed 1 cm above and lateral to the outer canthus of the left and right eye. Finally, EMG electrodes were placed under the chin. A 16-channel polygraph (Biopac-MP150; Biopac Systems, Inc.) was used for data acquisition together with the companion Acqknowledge 3.9.1 software for analysis. EEG data were sampled at 1000 Hz and band-pass filtered between 1 and 35 Hz for analysis. EOG data were sampled at 1000 Hz and band-pass filtered between .05 and 35 Hz and EMG data at 1000 Hz with band-pass filters of 10 and 500 Hz. Additionally, a 50-Hz filter was applied. Data were manually scored twice by two of the authors who were unaware of the performance of the participant. Each 30-s epoch was scored for sleep stages according to standard criteria [40]. Additionally, in accordance with recently reported results [33] number of spindle activities, of K-complexes and stage-2 duration during the last quarter of sleep (S2q4) were evaluated. As duration of stage-2 sleep may have a confounding effect on number of K-complexes, density of K-complexes (i.e., number of K-complexes per minute of stage-2 sleep) was also computed. Sleep variables are displayed in Table 2.

2.5. Neuropsychological tests

(1) IQ estimate: Multiple Word Recognition Test (MWT-B) [29]. It consists of 37 increasingly more difficult items with five word creations only one of which is meaningful. (2) Digit Symbol Test: a simplified version by Oswald and Fleischman [35] was used. (3) Controlled Oral Word Association Test (COWAT) [5]. During this test of verbal fluency participants are asked to produce as many words as possible starting with F, A, and S. The performance score is the sum of correct words. (4) Trail-Making-Test A and B [42]. In version A, digits distributed over a page have to be linked in ascending order as fast as possible and in version B, the digits are interspersed with letters.

2.6. Procedure

Patients were administered the standardised interviews and gave their written informed consent. Within the following week they entered either the waking or the sleep interval condition. For the sleep interval condition participants spent two consecutive nights at the sleep laboratory of the Department of Clinical Psychology, University of Düsseldorf. Only the data of the second night were analysed. The