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Sleep Correlates of Cognition in Early Course Psychotic Disorders

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Abstract

Background—Slow waves and sleep spindles, the main oscillations during non-rapid eye movement sleep, have been thought to be related to cognitive processes, and are impaired in psychotic disorders. Cognitive impairments, seen early in the course of psychotic disorders, may be alterations in these oscillations, but few studies have examined this relationship.

Method—Twenty seven untreated patients with a recently diagnosed psychotic disorder had polysomnographic sleep studies and neuro-cognitive testing.

Results—Reduced power in the sigma range, which reflects spindle density, was associated with impaired attention, and reasoning, but not intelligence quotient (IQ). Slow wave sleep measures were not significantly associated with any cognitive measures.

Conclusions—Impairments in sleep spindles may be associated with cognitive deficits in early course of psychotic disorders. These observations may help clarify neuro-biologic mechanisms of cognitive deficits in psychotic disorders such as schizophrenia.

Keywords

Sleep; Spindles; Slow waves; Cognition; Schizophrenia; Psychosis

1. Introduction

Cognitive dysfunction is part of the core pathology of psychotic disorders such as schizophrenia (Elvevag and Goldberg, 2000, Mesholam-Gately et al., 2009, Kalkstein et al., 2010) which are also characterized by significant alterations in sleep architecture (Keshavan et al., 1990, Monti and Monti, 2005, Cohrs, 2008). Cognitive impairments which are strong determinants of functional outcome in schizophrenia (Green, 1996) do not consistently respond to currently available antipsychotic treatments (Hill et al., 2010). An improved understanding of the relationship between sleep and cognition in health as well as in disease may therefore be critical for developing better approaches to treat these deficits.

Converging data suggest that sleep is critical to a number of cognitive processes such as information processing and memory consolidation (Maquet et al., 2000, Crick and

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Mitchison, 1983). Furthermore, different components of sleep, i.e. Rapid Eye Movement (REM) sleep and non-REM sleep (Schabus et al., 2007, Diekelmann and Born, 2010) seem to have distinct roles in memory consolidation processes (Maquet et al., 2000, Gais et al., 2000, Stickgold et al., 2000). Slow waves, a hallmark of NREM sleep (also called delta sleep), increase after motor learning in direct correlation with the improvement in post-sleep performance on the learning task (Huber, 2007). Similarly, a second hallmark of the NREM sleep, the 12-15 Hz rhythms in the the sigma band commonly referred to as sleep spindles, increase after training on a declarative learning task (Gais et al., 2002). Sleep spindles have been associated with verbal memory consolidation (Goder et al., 2008). Decreases in delta sleep are associated with impairments in visuospatial memory (Goder et al., 2004), declarative memory (Goder et al., 2008), attention/ cognitive flexibility (Goder et al., 2006) and consolidation of declarative memory (Plihal and Born, 1999). Since cognitive deficits and sleep disturbances are both part of the core pathology in schizophrenia (Elvevag and Goldberg, 2000, Keshavan et al., 1998), elucidating the relationship between cognitive deficits, delta and spindle sleep changes in psychotic disorders is likely to shed light on the pathophysiology of this illness.

Unfortunately, much of the research on cognition and sleep in schizophrenia has been conducted in chronic patients, with some exceptions (Taylor et al., 1992, Forest et al., 2007) and is potentially confounded by the use of current or past medications, and disease chronicity. Herein, we present the results of a study of cognition and sleep architecture in patients with early course psychotic disorders. We hypothesized that two components of sleep architecture i.e. sleep spindles and delta sleep, correlate with performance on tasks involving multiple domains of cognition.

2. Methods

2.1 Participants

Twenty seven patients newly diagnosed with psychosis (18 males and 9 females) were recruited from among inpatient and outpatients of Western Psychiatric Institute and Clinic, Pittsburgh. The subject's age was in the range of 18 and 44 years (mean 27.2 ± 7.3). The duration of psychosis was 100.6 weeks (S.D =91.33 weeks), consistent with our previously published data in the larger sample (mean 95.7 weeks; Keshavan et al 2003).. Approaches to determination of illness duration, and other clinical characteristics of this sample are detailed elsewhere (Keshavan et al., 2003). All of the 27 patients were antipsychotic-naïve at the time of their sleep study and neuropsychological testing. Diagnoses were confirmed following structured clinical interviews for DSM diagnoses (SCID) interviews (First et al., 2002) by experienced clinicians using DSM-IV criteria. Diagnoses included schizophrenia (15), schizoaffective disorder (2), psychotic disorder, not otherwise specified (n=1); bipolar disorder with psychotic features (n=2); major depression with psychotic features (n=4) and delusional disorders (n=3). The Scales for the Assessment of Positive and Negative Symptoms, respectively (SANS) (Andreasen, 1990, Andreasen, 1989) were used to estimate levels of psychopathology. None of the subjects had any significant medical illness, history of head injury with loss of consciousness >30minutes, or mental retardation (IQ <75). All subjects gave written informed consent to the study which was approved by the University of Pittsburgh Institutional Review Board.

2.2 Sleep studies

Subjects underwent at least two nights of sleep EEG studies on consecutive nights. They were discouraged from napping during the day, to avoid confounding effects of naps on cognition (Seeck-Hirschner et al., 2010). A few days prior to the sleep studies, the subjects were requested to maintain a diary of their sleep wake patterns to estimate the usual time at

which the subjects were to be woken up in the morning. The subjects chose the time to retire to bed. Electrodes for polysomnographic (PSG) recording were placed about one hour before bedtime. PSG was recorded on two nights to control for adaptation effect to the sleep lab. The second night of sleep was used in these analyses.

PSG was conducted using Grass Telefactor M15 bipolar Neurodata amplifiers and locally-developed collection software. The recording montage consisted of bilateral central EEG leads referenced to A1+A2; right and left electro-oculogram referenced to A1+A2; and bipolar electromyogram. Sleep stages were scored in 60-second epochs according to standard criteria (Rechtschaffen and Kales, 1968) by trained raters blind to clinical data. For the analyses in this study, we used the percent spent in visually scored delta (stage 3+4) sleep.

Methods for automated sleep analysis have been previously published (Doman et al., 1995). Briefly, EEG signals were digitized at a rate of 256 Hz. The raw digitized data were bandlimited to 64 Hz using a low pass finite impulse response (FIR) filter, then decimated to 128 Hz for quantitative analyses. Low frequency artifacts were excluded by eliminating epochs scored as wakefulness or movement time. High frequency EEG artifacts were identified and excluded in 4-second bins with a previously validated and published algorithm that uses a moving window threshold. Basically, this algorithm excludes 4-second bins whose power in the frequency range of 26.25-32 Hz exceeds the power in adjacent bins by a factor of 4 or greater. Power spectral analysis was used to quantify the frequency content of the sleep EEG from 0.25-50 Hz (Doman et al., 1995, Vasko et al., 1997, Brunner et al., 1996). Non-overlapping 4-second epochs were weighted with a Hamming window, and periodograms were then computed for these epochs using the Fast Fourier transform (FFT). EEG spectra for each artifact-free 4-second epoch were then aligned with 60-second visually-scored sleep stage data to exclude epochs scored as awake or REM sleep. EEG power values from artifact-free 4-second epochs at 0.25 Hz resolution were averaged into 0.5 Hz bins prior to analysis, to provide adequate resolution of frequencies while limiting the number of statistical comparisons. For this analysis, we used the frequency band from 13.5 to 15 Hz to measure the spindle density. It is to be noted that this frequency range corresponds to the sigma activity (Aeschbach and Borbely, 1993, Landolt et al., 1996) which comprises the spindles. Spectral power in the sigma range typically reflects spindle density, though these terms are not synonymous (De Gennaro and Ferrara, 2003). One study has shown that sleep spindle waveforms are sensitive to learning while quantified EEG sigma activity is not (Gais et al., 2002).

Using Period amplitude analyses (Doman et al., 1995, Tekell et al., 2005), the number of delta “counts” (the number of half-waves above and below the baseline at 0.5-2 Hz, 75-200- μ V activity) per minute were measured with a zero-crossing half-wave detector. For analyses in this study, we used average delta counts per minute of NREM sleep, thus controlling for differences in non-REM period length.

2.3. Neuropsychological testing

Each subject also underwent neuropsychological testing within 1-2 days of sleep studies, including tasks of attention and psychomotor speed (trials B errors and time; (Reitan and Wolfson, 1992) reasoning and conceptual flexibility (Wisconsin card test) (Heaton and Pendleton, 1981) and intelligence quotient (the Ammond’s quick IQ) (Otto and McMenemy, 1965).

2.4 Statistical analyses

Pearson correlations and where the data were non-normally distributed, Spearman correlations were used to examine relationships between sleep and cognitive parameters. Partial correlations were also examined to examine these relationships after covarying the effect of age. Two-tailed tests were used for significance.

3. Results

Spindle power did not correlate with age, duration of the psychotic symptoms or the severity of SANS positive and SANS negative symptoms (all correlation coefficients $< .25$ and $p > .2$). Similarly, delta power did not correlate with duration of symptoms or severity of positive and negative symptoms. However, there was trend towards decreased delta sleep ($r = -.38$; $p = .052$), delta power ($r = -.32$; $p = .1$) and spindles ($r = -.27$; $p = .16$) with age, which was consistent with previous studies of declines in sleep and age (Keshavan et al., 1995). Age correlated positively with percent perseverative error ($r = 0.49$, $p = 0.01$) and Trail B time ($r = 0.47$, $p = 0.015$). There were no differences between genders for cognitive or sleep measures. Delta sleep correlated non-significantly with spindle power ($r = .36$; $p = .06$).

Spindle power correlated inversely with trails B errors and time, and Wisconsin card sort perseverative errors (Table 1), but not with IQ. When these correlations were examined with diagnosis as a categorical covariate, the results remained significant. The correlation between spindle power and trails B errors survived Bonferroni correction for multiple inference testing.

Automated average delta counts had a trend for a correlation with IQ (partial $r = .38$; $p = .055$) but did not correlate with any other cognitive measure. Visually scored delta sleep showed a negative trend-worthy correlation with WCST perseverative errors (partial $r = -.34$; $p = .09$) but not with any other cognitive measure.

4. Discussion

Reduced sleep spindle power was associated with impaired attentional and executive function measures in patients with early course psychotic disorders. This deficit was unrelated to reduced general cognitive ability. This observation is consistent with prior evidence that spindle activity is related to the learning potential of an individual (Bodizs et al., 2005, Schabus et al., 2007). Our findings are also consistent with and expand on an earlier small study of neuroleptic naïve patients with schizophrenia ($n=8$) showing a negative correlation between reaction time on the selective attention task and sleep spindle density and the duration of the delta sleep (Forest et al., 2007). In the absence of an appropriately matched-control group, we could not examine whether the spindle activity is reduced in patients with treatment naïve psychosis, but this is a key question to be addressed in future studies. In a study of medicated schizophrenia patients, Ferrarelli et al (2007, 2010) observed reduction in spindle activity. The effect of antipsychotics on spindles remains unclear with no effects (Ferrarelli et al., 2007, Ferrarelli et al., 2010) and reductions with olanzapine being observed (Goder et al., 2008). Contrary to some earlier observations (Huupponen et al., 2002), we did not see a gender effect on spindle parameters, perhaps due to the relatively small sample size in this study.

Our data suggest that cognitive deficits may be related to spindle activity reductions in both schizophrenia and non-schizophrenia psychotic disorders. Decreased spindle activity has been observed across a range of disorders, including autism (Godbout et al., 2000), Alzheimer's (Prinz et al., 1982), normal aging (Nicolas et al., 2001), paramedian thalamic stroke (Hermann et al., 2008), and depression (Lopez et al., 2010). It is possible that

reductions in spindle activity cuts across a number of conditions – physiological and pathological- and may reflect impairments in neuroplasticity across these conditions.

Examining spindle measures in early course psychosis patients is of importance to investigate developmental alterations that may characterize the early phases of these disorders. Induction of long term potentiation appears to increase spindles; synchronous neuronal activation during spindles may contribute to learning-related synaptic plasticity (Werk et al., 2005). Spindle activity decreases progressively with age (from teenage to the high sixties) (Nicolas et al., 2001), perhaps as a function of decreasing plasticity.. Since cognitive function also declines during prodromal phase of schizophrenia (Seidman et al., 2010), follow-up sleep studies during the prodromal phase may further elucidate the psychobiology of transition to schizophrenia. Spindles have been shown to increase neocortical neuroplasticity (Steriade et al., 1993, Steriade, 1999).

We have previously reported decreased delta sleep in early course schizophrenia (Keshavan et al., 1998). There is also evidence for a correlation between decrements in delta activity and attentional impairment in schizophrenia (Orzack et al., 1977). Furthermore, striking similarity between age related changes in delta activity and synaptic density has led to a view that these two are related (Tononi, 2009, Feinberg, 1982). However, in the present study, we observed only a weak, non-significant relation between cognitive performance and delta sleep. These differential correlations for spindle activity and slow wave sleep (with cognition) may reflect differences in the physiological substrate between these two sleep oscillations. For instance, slow oscillations are primarily generated by the cortex, while sleep spindles are generated by thalamo-cortical circuits (Ferrarelli et al., 2010). It is also possible that delta sleep reductions are seen only in a subgroup of schizophrenia and their relationship to cognitive deficits is subtle and may have not reached significance. The evidence that thalamocortical gamma- amino butyric acid (GABA)ergic activity has a role in spindle generation (Pangratz-Fuehrer et al., 2007) may mean that the observed relationship between spindles and cognitive abilities in the present study supports the theory of GABA dysfunction in schizophrenia (Gonzalez-Burgos et al., 2010). This view is consistent with the view that alterations in selective attentional processes in schizophrenia may be mediated by thalamocortical circuits (Trenado et al., 2009, Crespo-Facorro et al., 2007).

A significant strength of our study was inclusion of treatment naïve patients with early course psychosis. The difficulty in recruiting these patients in sleep studies affected our chances of working with a more homogenous group. Limitations of our study include the lack of an appropriately matched control group, the absence of visual scoring of spindles, and the use of 60 second epochs that may have limited resolution for quantification of the sleep data. Further studies are needed to document the effect of individual antipsychotic medications on sleep spindles and activity. Prospective studies throughout the course of the illness can be expected to further enhance our understanding of schizophrenia.

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References

- Aeschbach D, Borbely AA. All-night dynamics of the human sleep EEG. *J Sleep Res.* 1993; 2:70–81. [PubMed: 10607074]
- Andreasen NC. The Scale for the Assessment of Negative Symptoms (SANS): conceptual and theoretical foundations. *Br J Psychiatry Suppl.* 1989;49–58. [PubMed: 2695141]

- Andreasen NC. Methods for assessing positive and negative symptoms. *Mod Probl Pharmacopsychiatry*. 1990; 24:73–88. [PubMed: 2336066]
- Bodizs R, Kis T, Lazar AS, Havran L, Rigo P, Clemens Z, Halasz P. Prediction of general mental ability based on neural oscillation measures of sleep. *J Sleep Res*. 2005; 14:285–92. [PubMed: 16120103]
- Brunner DP, Vasko RC, Detka CS, Monahan JP, Reynolds CF 3rd, Kupfer DJ. Muscle artifacts in the sleep EEG: automated detection and effect on all-night EEG power spectra. *J Sleep Res*. 1996; 5:155–64. [PubMed: 8956205]
- Cohrs S. Sleep disturbances in patients with schizophrenia : impact and effect of antipsychotics. *CNS Drugs*. 2008; 22:939–62. [PubMed: 18840034]
- Crespo-Facorro B, Roiz-Santianez R, Pelayo-Teran JM, Rodriguez-Sanchez JM, Perez-Iglesias R, Gonzalez-Blanch C, Tordesillas-Gutierrez D, Gonzalez-Mandly A, Diez C, Magnotta VA, Andreasen NC, Vazquez-Barquero JL. Reduced thalamic volume in first-episode non-affective psychosis: correlations with clinical variables, symptomatology and cognitive functioning. *Neuroimage*. 2007; 35:1613–23. [PubMed: 17395492]
- Crick F, Mitchison G. The function of dream sleep. *Nature*. 1983; 304:111–4. [PubMed: 6866101]
- De Gennaro L, Ferrara M. Sleep spindles: an overview. *Sleep Med Rev*. 2003; 7:423–40. [PubMed: 14573378]
- Diekelmann S, Born J. The memory function of sleep. *Nat Rev Neurosci*. 2010; 11:114–26. [PubMed: 20046194]
- Doman J, Detka C, Hoffman T, Kesicki D, Monahan JP, Buysse DJ, Reynolds CF 3rd, Coble PA, Matzzie J, Kupfer DJ. Automating the sleep laboratory: implementation and validation of digital recording and analysis. *Int J Biomed Comput*. 1995; 38:277–90. [PubMed: 7774987]
- Elvevag B, Goldberg TE. Cognitive impairment in schizophrenia is the core of the disorder. *Crit Rev Neurobiol*. 2000; 14:1–21. [PubMed: 11253953]
- Feinberg I. Schizophrenia: caused by a fault in programmed synaptic elimination during adolescence? *J Psychiatr Res*. 1982; 17:319–34. [PubMed: 7187776]
- Ferrarelli F, Huber R, Peterson MJ, Massimini M, Murphy M, Riedner BA, Watson A, Bria P, Tononi G. Reduced sleep spindle activity in schizophrenia patients. *Am J Psychiatry*. 2007; 164:483–92. [PubMed: 17329474]
- Ferrarelli F, Peterson MJ, Sarasso S, Riedner BA, Murphy MJ, Benca RM, Bria P, Kalin NH, Tononi G. Thalamic dysfunction in schizophrenia suggested by whole-night deficits in slow and fast spindles. *Am J Psychiatry*. 2010; 167:1339–48. [PubMed: 20843876]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured clinical interview for DSM-IVTR Axis I disorders, research version, patient edition. Biometrics Research, New York State Psychiatric Institute; New York: 2002.
- Forest G, Poulin J, Daoust AM, Lussier I, Stip E, Godbout R. Attention and non-REM sleep in neuroleptic-naïve persons with schizophrenia and control participants. *Psychiatry Res*. 2007; 149:33–40. [PubMed: 17141330]
- Gais S, Molle M, Helms K, Born J. Learning-dependent increases in sleep spindle density. *J Neurosci*. 2002; 22:6830–4. [PubMed: 12151563]
- Gais S, Plihal W, Wagner U, Born J. Early sleep triggers memory for early visual discrimination skills. *Nat Neurosci*. 2000; 3:1335–9. [PubMed: 11100156]
- Godbout R, Bergeron C, Limoges E, Stip E, Mottron L. A laboratory study of sleep in Asperger's syndrome. *Neuroreport*. 2000; 11:127–30. [PubMed: 10683843]
- Goder R, Aldenhoff JB, Boigs M, Braun S, Koch J, Fritzer G. Delta power in sleep in relation to neuropsychological performance in healthy subjects and schizophrenia patients. *J Neuropsychiatry Clin Neurosci*. 2006; 18:529–35. [PubMed: 17135379]
- Goder R, Boigs M, Braun S, Friege L, Fritzer G, Aldenhoff JB, Hinze-Selch D. Impairment of visuospatial memory is associated with decreased slow wave sleep in schizophrenia. *J Psychiatr Res*. 2004; 38:591–9. [PubMed: 15458855]
- Goder R, Fritzer G, Gottwald B, Lippmann B, Seeck-Hirschner M, Serafin I, Aldenhoff JB. Effects of olanzapine on slow wave sleep, sleep spindles and sleep-related memory consolidation in schizophrenia. *Pharmacopsychiatry*. 2008; 41:92–9. [PubMed: 18484550]

- Gonzalez-Burgos G, Hashimoto T, Lewis DA. Alterations of cortical GABA neurons and network oscillations in schizophrenia. *Curr Psychiatry Rep.* 2010; 12:335–44. [PubMed: 20556669]
- Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia? *Am J Psychiatry.* 1996; 153:321–30. [PubMed: 8610818]
- Heaton RK, Pendleton MG. Use of Neuropsychological tests to predict adult patients' everyday functioning. *J Consult Clin Psychol.* 1981; 49:807–21. [PubMed: 7309951]
- Hermann DM, Siccoli M, Brugger P, Wachter K, Mathis J, Achermann P, Bassetti CL. Evolution of neurological, neuropsychological and sleep-wake disturbances after paramedian thalamic stroke. *Stroke.* 2008; 39:62–8. [PubMed: 18048862]
- Hill SK, Bishop JR, Palumbo D, Sweeney JA. Effect of second-generation antipsychotics on cognition: current issues and future challenges. *Expert Rev Neurother.* 2010; 10:43–57. [PubMed: 20021320]
- Huber R. Memory formation: sleep enough before learning. *Curr Biol.* 2007; 17:R367–8. [PubMed: 17502091]
- Huupponen E, Himanen SL, Varri A, Hasan J, Lehtokangas M, Saarinen J. A study on gender and age differences in sleep spindles. *Neuropsychobiology.* 2002; 45:99–105. [PubMed: 11893867]
- Kalkstein S, Hurford I, Gur RC. Neurocognition in schizophrenia. *Curr Top Behav Neurosci.* 2010; 4:373–90. [PubMed: 21312407]
- Keshavan MS, Haas G, Miewald J, Montrose DM, Reddy R, Schooler NR, Sweeney JA. Prolonged untreated illness duration from prodromal onset predicts outcome in first episode psychoses. *Schizophr Bull.* 2003; 29:757–69. [PubMed: 14989413]
- Keshavan MS, Reynolds CF 3rd, Haas G, Miewald JM, Montrose DM. Sleep EEG changes in psychotic disorders: gender and age effects. *Neuropsychobiology.* 1995; 32:1–8. [PubMed: 7566516]
- Keshavan MS, Reynolds CF 3rd, Miewald MJ, Montrose DM, Sweeney JA, Vasko RC Jr. Kupfer DJ. Delta sleep deficits in schizophrenia: evidence from automated analyses of sleep data. *Arch Gen Psychiatry.* 1998; 55:443–8. [PubMed: 9596047]
- Keshavan MS, Reynolds CF, Kupfer DJ. Electroencephalographic sleep in schizophrenia: a critical review. *Compr Psychiatry.* 1990; 31:34–47. [PubMed: 2404658]
- Landolt HP, Dijk DJ, Achermann P, Borbely AA. Effect of age on the sleep EEG: slow-wave activity and spindle frequency activity in young and middle-aged men. *Brain Res.* 1996; 738:205–12. [PubMed: 8955514]
- Lopez J, Hoffmann R, Armitage R. Reduced sleep spindle activity in early-onset and elevated risk for depression. *J Am Acad Child Adolesc Psychiatry.* 2010; 49:934–43. [PubMed: 20732629]
- Maquet P, Laureys S, Peigneux P, Fuchs S, Petiau C, Phillips C, Aerts J, Del Fiore G, Degueldre C, Meulemans T, Luxen A, Franck G, Van Der Linden M, Smith C, Cleeremans A. Experience-dependent changes in cerebral activation during human REM sleep. *Nat Neurosci.* 2000; 3:831–6. [PubMed: 10903578]
- Meshulam-Gately RI, Giuliano AJ, Goff KP, Faraone SV, Seidman LJ. Neurocognition in first-episode schizophrenia: a meta-analytic review. *Neuropsychology.* 2009; 23:315–36. [PubMed: 19413446]
- Monti JM, Monti D. Sleep disturbance in schizophrenia. *Int Rev Psychiatry.* 2005; 17:247–53. [PubMed: 16194796]
- Nicolas A, Petit D, Rompre S, Montplaisir J. Sleep spindle characteristics in healthy subjects of different age groups. *Clin Neurophysiol.* 2001; 112:521–7. [PubMed: 11222974]
- Orzack MH, Hartmann EL, Kornetsky C. The relationship between attention and slow-wave sleep in chronic schizophrenia [proceedings]. *Psychopharmacol Bull.* 1977; 13:59–61. [PubMed: 860001]
- Otto W, Mcmenemy RA. An Appraisal of the Ammons Quick Test in a Remedial Reading Program. *Journal of Educational Measurement.* 1965; 2:193–198.
- Pangratz-Fuehrer S, Rudolph U, Huguenard JR. Giant spontaneous depolarizing potentials in the developing thalamic reticular nucleus. *J Neurophysiol.* 2007; 97:2364–72. [PubMed: 17251370]
- Plihal W, Born J. Effects of early and late nocturnal sleep on priming and spatial memory. *Psychophysiology.* 1999; 36:571–82. [PubMed: 10442025]

- Prinz PN, Peskind ER, Vitaliano PP, Raskind MA, Eisdorfer C, Zemcuznikov N, Gerber CJ. Changes in the sleep and waking EEGs of nondemented and demented elderly subjects. *J Am Geriatr Soc.* 1982; 30:86–93. [PubMed: 7199061]
- Rechtschaffen, A.; Kales, A. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. P., N., editor. U.S. Government Printing Office, Department of Health Education and Welfare; Washington, D.C: 1968. p. 204
- Reitan RM, Wolfson D. Conventional intelligence measurements and neuropsychological concepts of adaptive abilities. *J Clin Psychol.* 1992; 48:521–9. [PubMed: 1517447]
- Schabus M, Dang-Vu TT, Albouy G, Balet E, Boly M, Carrier J, Darsaud A, Degueldre C, Desseilles M, Gais S, Phillips C, Rauchs G, Schnakers C, Sterpenich V, Vandewalle G, Luxen A, Maquet P. Hemodynamic cerebral correlates of sleep spindles during human non-rapid eye movement sleep. *Proc Natl Acad Sci U S A.* 2007; 104:13164–9. [PubMed: 17670944]
- Seek-Hirschner M, Baier PC, Sever S, Buschbacher A, Aldenhoff JB, Goder R. Effects of daytime naps on procedural and declarative memory in patients with schizophrenia. *J Psychiatr Res.* 2010; 44:42–7. [PubMed: 19559446]
- Seidman LJ, Giuliano AJ, Meyer EC, Addington J, Cadenhead KS, Cannon TD, McGlashan TH, Perkins DO, Tsuang MT, Walker EF, Woods SW, Bearden CE, Christensen BK, Hawkins K, Heaton R, Keefe RS, Heinssen R, Cornblatt BA. Neuropsychology of the prodrome to psychosis in the NAPLS consortium: relationship to family history and conversion to psychosis. *Arch Gen Psychiatry.* 2010; 67:578–88. [PubMed: 20530007]
- Steriade M. Coherent oscillations and short-term plasticity in corticothalamic networks. *Trends Neurosci.* 1999; 22:337–45. [PubMed: 10407416]
- Steriade M, McCormick DA, Sejnowski TJ. Thalamocortical oscillations in the sleeping and aroused brain. *Science.* 1993; 262:679–85. [PubMed: 8235588]
- Stickgold R, Whidbee D, Schirmer B, Patel V, Hobson JA. Visual discrimination task improvement: A multi-step process occurring during sleep. *J Cogn Neurosci.* 2000; 12:246–54. [PubMed: 10771409]
- Taylor SF, Goldman RS, Tandon R, Shipley JE. Neuropsychological function and REM sleep in schizophrenic patients. *Biol Psychiatry.* 1992; 32:529–38. [PubMed: 1445969]
- Tekell JL, Hoffmann R, Hendrickse W, Greene RW, Rush AJ, Armitage R. High frequency EEG activity during sleep: characteristics in schizophrenia and depression. *Clin EEG Neurosci.* 2005; 36:25–35. [PubMed: 15683195]
- Tononi G. Slow wave homeostasis and synaptic plasticity. *J Clin Sleep Med.* 2009; 5:S16–9. [PubMed: 19998870]
- Trenado C, Haab L, Strauss DJ. Corticothalamic feedback dynamics for neural correlates of auditory selective attention. *IEEE Trans Neural Syst Rehabil Eng.* 2009; 17:46–52. [PubMed: 19211323]
- Vasko RC Jr. Brunner DP, Monahan JP, Doman J, Boston JR, El-Jaroudi A, Miewald J, Buysse DJ, Reynolds CF 3rd, Kupfer DJ. Power spectral analysis of EEG in a multiple-bedroom, multiple-polygraph sleep laboratory. *Int J Med Inform.* 1997; 46:175–84. [PubMed: 9373779]
- Werk CM, Harbour VL, Chapman CA. Induction of long-term potentiation leads to increased reliability of evoked neocortical spindles in vivo. *Neuroscience.* 2005; 131:793–800. [PubMed: 15749334]

Figure 1. Scatterplot showing the partial correlation between spindle power and trails B errors in first episode psychosis patients.

Table 1

Partial correlations (with age partialled out) between cognitive and sleep measures.

	Spindle power Partial r (p)	Delta power Partial r (p)
Trails B time	-.45 (.01)	-.24 (.23)
Trails B errors	-.56 (.0038)	-.18 (.36)
WCST PE %	-.48 (.014)	-.27 (.18)
IQ	.12 (.53)	.38 (.055)