

## Neural Correlates of human cognitive abilities during sleep

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## ABSTRACT

1 Inter-individual differences in sleep spindles are highly correlated with “Reasoning” abilities  
2 (problem solving skills; i.e., the ability to employ logic, identify complex patterns), but not Short  
3 Term Memory or Verbal abilities. Simultaneous electroencephalography and functional  
4 magnetic resonance imaging (EEG-fMRI) have revealed brain activations time-locked to  
5 spindles (e.g., thalamic, paralimbic, and motor cortical areas)—yet the functional significance of  
6 inter-individual differences in spindle-related brain activation remains to be investigated. Using  
7 EEG-fMRI during sleep, we identified, for the first time, the neural activation patterns time-  
8 locked to spindles that are correlated with cognitive abilities. Similar to previous studies,  
9 activations time-locked to spindles were observed in thalamocortical circuitry and basal ganglia  
10 regions. Importantly, spindle-related activation in a subset of these regions were specifically  
11 related to inter-individual differences in Reasoning, but not STM or Verbal abilities. These  
12 results may help elucidate the physiological mechanisms which support the function of sleep  
13 for the capacity for reasoning.

14 **Keywords:** sleep, spindles, cognitive abilities, simultaneous EEG-fMRI

## 15 INTRODUCTION

16 The sleep spindle is the only known spontaneous neural oscillation that has been identified  
17 as an electrophysiological marker of cognitive abilities and aptitudes, that are typically assessed  
18 by intelligence quotient (**IQ**) tests (for review, see Fogel & Smith, 2011). As one of the defining  
19 features of Stage 2 non-rapid eye movement (**NREM**) sleep, spindles are traditionally defined  
20 as neural oscillations between 11 and 16 Hz (Iber et al., 2007), lasting up to ~3 sec in duration  
21 (Rechtschaffen & Kales 1968). Spindles are remarkably stable from night-to-night, but vary  
22 considerably from one individual to another, and have even been suggested to be an  
23 “electrophysiological fingerprint” (De Gennaro et al., 2005) because of the trait-like nature of  
24 spindles (Silverstein & Michael Levy, 1976). Previous studies have revealed that interindividual  
25 differences in spindle characteristics are related to the capacity for reasoning (i.e., the ability to  
26 identify complex patterns and relationships, the use of logic, existing knowledge, skills, and  
27 experience to solve novel problems (Fogel & Smith, 2007; Fogel & Smith, 2006; Nader & Smith,  
28 2001, 2003). Moreover, the relationship between spindles and cognitive abilities is specific to  
29 the capacity for Reasoning, over-and-above Verbal abilities and short-term memory (Fang et al.,  
30 2017; Fogel et al., 2007). These studies have provided insight into the electrophysiological  
31 correlates of Reasoning abilities, insofar as to suggest that efficient functioning of the neural  
32 substrates that support spindle generation (e.g., thalamocortical circuitry) may be related to the  
33 capacity for these cognitive skills. Interestingly, spindle production is reduced with age (Carrier  
34 et al., 2001; Fogel et al., 2014; Fogel et al., 2017), and abnormal in developmental disorders,  
35 such as Autism (Limoges et al., 2005), learning disabilities (Shibagaki et al., 1982) and in  
36 schizophrenia (Wamsley et al., 2012). Thus, a better understanding of the neural basis of the  
37 relationship between spindles and cognitive abilities may ultimately help to better understand  
38 the significance to a variety of normal and abnormal cognitive functioning in healthy individuals

39 and in neurological conditions. This may eventually lead to novel interventions to precisely  
40 target cases where spindle production is abnormal or non-optimal. However, it is necessary to  
41 first understand the physiological correlates of the relationship between spindles and  
42 Reasoning abilities in healthy individuals, which is the principle aim of the current study.

43 The association between sleep spindles and individual differences in cognitive abilities has  
44 been well documented. For example, Nader and Smith (Fogel & Smith, 2006; Nader & Smith,  
45 2001, 2003) found that both the number of sleep spindles and sigma power (12–14 Hz) uniquely  
46 correlated with Performance IQ scores, over-and-above Verbal IQ (Fogel et al., 2007).  
47 Consistently, Bodizs and colleagues (Bódizs et al., 2005) found that spindle density was  
48 correlated with Reasoning abilities (i.e., “fluid intelligence”) measured by the Raven’s  
49 Progressive Matrices (Raven, Court, and Raven 1976). Similar studies identified a positive  
50 correlation between right-parietal fast spindles and visuospatial abilities assessed by the Rey–  
51 Osterrieth Complex Figure test (Bódizs et al., 2008), and a positive correlation between  
52 spindles and the intellectual abilities measured by the Cattell Culture Fair Intelligence Test,  
53 specifically in woman but not in men (Ujma et al., 2014). Although, a relationship in men was  
54 subsequently identified by the same group in daytime sleep (Ujma et al., 2015). Most recently,  
55 Fang and colleagues (Fang et al., 2017) used the Cambridge Brain Sciences (**CBS**) test battery  
56 (Hampshire et al., 2012) to explore if the relationship between sleep spindles and intellectual  
57 ability was a direct relationship, or whether this could be partially (or fully explained) by other  
58 spindle-related factors such as sleep quality or circadian chronotype. They found that, indeed,  
59 the relationship between spindles and Reasoning abilities was independent of sleep quality and  
60 circadian chronotype. Taken together, these studies support the notion that sleep spindles are  
61 an electrophysiological marker of cognitive abilities, and specifically, the ability to solve

62 problems using logic and reasoning. However, the brain regions supporting the relationship  
63 between the sleep spindles and cognitive abilities are still unknown.

64 Only a small number of studies have employed simultaneous electroencephalography and  
65 functional magnetic resonance imaging (**EEG-fMRI**) to explore brain activations time-locked to  
66 spindles (Andrade et al., 2011; Caporro et al., 2012; Laufs et al., 2007; Schabus et al., 2007;  
67 Tyvaert et al., 2008). Spindle-related activations have been consistently found in the thalamus  
68 and the temporal lobe, for both fast spindles and slow spindles (Andrade et al., 2011; Caporro  
69 et al., 2012; Laufs et al., 2007; Schabus et al., 2007; Tyvaert et al., 2008), and activation of the  
70 cingulate cortex and motor areas have been reported to be associated with sleep spindles  
71 during NREM sleep (Andrade et al., 2011; Caporro et al., 2012). Interestingly, activation of the  
72 putamen has also been found to be correlated with spindle events (Caporro et al., 2012; Tyvaert  
73 et al., 2008) and Andrade et al. (2011) found a strong interaction between sleep spindle  
74 occurrence and hippocampal formation functional connectivity. In addition, by directly  
75 comparing fast spindles vs. slow spindles, Schabus et al. (2007) observed that slow spindles  
76 increase activations in the superior temporal gyrus while fast spindles recruit activations in the  
77 sensorimotor area, mesial frontal cortex, hippocampus, and cerebellum. Not surprisingly, given  
78 the methodological complexities and limitations of EEG-fMRI recordings during sleep, most of  
79 these studies used relatively small sample sizes ( $n < 15$ ), suggesting that additional studies  
80 investigating the neural correlates of sleep spindles in a larger sample is warranted.  
81 Nonetheless, taken together, the extant literature intriguingly suggest that brain activations  
82 associated with the action of sleep spindles involve well-known spindle-generating regions (e.g.,  
83 thalamic and cortical regions), as well as regions which subserve cognitive functioning and  
84 memory (e.g., hippocampal, striatal, prefrontal, motor cortical and cerebellar regions).

85            Interestingly, some of the regions activated during spindle events, are thought to support  
86 human cognitive abilities. For example, the thalamocortical circuitry, one of the most important  
87 neural substrates related to spindle generation (Steriade, Contreras et al.,1993; Steriade,  
88 McCormick, & Sejnowski, 1993), has been observed to be involved in reasoning abilities  
89 assessed by Raven’s Progressive Matrices test (Gray et al., 2003), the Wechsler Adult Scale  
90 of Intelligence (WAIS-III) (Wechsler, 1997), and other reasoning ability-related tasks, especially  
91 with regard to the prefrontal cortex and the thalamus (Bugg et al., 2006; Kroger, 2002; Melrose,  
92 Poulin, & Stern, 2007; Waltz et al., 1999). In addition, the basal ganglia region, especially the  
93 striatal areas (i.e. caudate and putamen), which are recruited during spindle events (Caporro  
94 et al., 2012; Tyvaert et al., 2008), have also been found to be related to cognitive functions,  
95 including reward-based learning (O’Doherty, 2004), planning (Elsinger et al., 2006), motor  
96 execution (Monchi et al., 2006), and reasoning (Melrose et al., 2007; Rodriguez-Moreno &  
97 Hirsch, 2009). Recently, Hampshire et al. (2012) employed the Cambridge Brain Sciences  
98 cognitive test battery to identify and distinguish the brain networks that support distinct cognitive  
99 abilities (e.g., Reasoning, Verbal, and Short Term Memory). It was found that the inferior frontal  
100 sulcus, the inferior parietal cortex, and the dorsal portion of the anterior cingulate /  
101 supplementary motor area activations related to Reasoning abilities and were disassociated  
102 from brain regions that related to Verbal abilities and Short Term Memory. While it is intriguing  
103 that a subset of regions which support Reasoning abilities are also regions activated with the  
104 occurrence of sleep spindles, it remains to be investigated whether spindle-related activations  
105 in these areas are correlated with interindividual differences in Reasoning abilities.

106            Thus, it is clear that spindle characteristics are linked to Reasoning abilities, however, the  
107 neural correlates of this relationship remain unknown. Therefore, here, using a large sample of  
108 simultaneous EEG-fMRI recordings during sleep, we sought to identify, for the first time, the

109 neuroanatomical function correlates of the relationship between sleep spindles and Reasoning  
110 abilities. We hypothesized that the neural activation patterns, time-locked to spindles would be  
111 related to distinct cognitive abilities whereby consistent with previous cognitive and  
112 electrophysiological studies, spindle-related brain activations would be correlated with  
113 Reasoning but not STM or Verbal abilities. This will provide insight into the neural basis of the  
114 functional correlates of sleep spindles.

## 115 **RESULTS**

### 116 **Cognitive abilities: Cambridge Brain Sciences Trials**

117         Based on previous literature (Hampshire et al., 2012), the raw scores from each of the  
118 12 subtests were Z-score normalized using the mean and standard deviation of each subtest  
119 from a large population (N = 44,600). Each test item was then weighted according to the factor  
120 loadings from Hampshire et al. (Hampshire et al., 2012) and then the respective sub-tests were  
121 averaged to create the Reasoning, STM and Verbal sub-scores and transformed to a mean of  
122 100 and a SD of 15, so that test scores were readily comparable to results from similar studies  
123 that employed test batteries tapping into Reasoning and Verbal abilities, such as the  
124 Multidimensional Aptitude Battery - II (Fogel et al., 2007; Fogel & Smith, 2006) and other  
125 commonly used batteries of cognitive abilities (e.g., Wechsler Adult Intelligence Scale). The  
126 descriptive statistics of each subtest are shown in **Table 1**.

**Table 1.** Descriptive statistics of the 3 CBS Trials subscales (Reasoning, Short-term memory (STM) and Verbal abilities).

<b>IQ Measures</b>	<b>Range</b>	<b>Mean <math>\pm</math> SD</b>	<b>Median</b>
<b>Reasoning</b>	78.84 - 108.17	95.65 $\pm$ 7.20	96.46
<b>STM</b>	84.38 - 115.33	101.60 $\pm$ 6.77	102.30
<b>Verbal</b>	88.51 - 110.92	99.62 $\pm$ 5.12	99.52

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128 **Sleep Architecture:**

129 Participants slept, on average, a total of 44.20 (SD=23.84) minutes in the scanner during  
130 the experimental sleep session (**Table 2**). All N=29 participants experienced NREM2 sleep,  
131 N=20 had SWS sleep, and N=8 had rapid eye movement (REM) sleep. Given the focus of the  
132 current investigation, we did not analyze REM data. Participants had on average, a total of  
133 334.74 (SD=212.29) total bandwidth sleep spindles at Cz during NREM sleep. Spindle  
134 parameters for all spindles at Cz (11-16 Hz), slow spindles at Fz (11-13.5 Hz) and fast spindles  
135 at Pz (13.5-16 Hz) during NREM sleep are shown in the **Table 2**.

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**Table 2.** Sleep architecture and sleep spindle parameters for spindles at Fz, Cz and Pz during NREM sleep from EEG-fMRI recording sessions.

	<b>M</b>	<b>SD</b>
<b>Sleep Architecture</b>		
<b>Wake (min)</b>	26.87	20.25
<b>NREM1 (min)</b>	5.84	4.38
<b>NREM2 (min)</b>	23.87	14.50
<b>SWS (min)</b>	14.77	17.17
<b>NREM (min)</b>	39.29	19.33
<b>REM</b>	17.80	10.76
<b>Total Sleep</b>	44.20	23.84
<b>Total bandwidth (11-16 Hz) spindles at Cz</b>		
<b>Number</b>	334.74	212.29
<b>Duration (sec)</b>	0.49	0.05
<b>Amplitude (<math>\mu</math>V)</b>	27.21	6.43
<b>Density</b>	8.22	2.34
<b>Slow spindles (11-13.5 Hz) at Fz</b>		
<b>Number</b>	249.41	179.40
<b>Duration (sec)</b>	0.38	0.06
<b>Amplitude (<math>\mu</math>V)</b>	42.71	9.44
<b>Density</b>	6.00	2.20
<b>Fast (13.5-16 Hz) spindles at Pz</b>		
<b>Number</b>	92.48	69.66
<b>Duration (sec)</b>	0.38	0.08
<b>Amplitude (<math>\mu</math>V)</b>	21.53	6.01
<b>Density</b>	2.50	1.80

*Abbreviations: non-rapid eye movement sleep (NREM); stage 1 sleep (NREM1); stage 2 sleep (NREM2); slow wave sleep (SWS); rapid eye movement sleep.*

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144

145 **Relationship between sleep spindles and cognitive abilities**

146 Standard multiple linear regression revealed that, taken together, Reasoning, Short Term  
147 Memory and Verbal abilities significantly accounted for variability in spindle amplitude ( $F(3, 25)$   
148  $= 4.884$ ,  $r^2 = 0.370$ ,  $p = 0.008$ ), but not duration ( $F(3, 25) = 0.531$ ,  $r^2 = 0.060$ ,  $p = 0.665$ ) or  
149 density ( $F(3, 25) = 2.522$ ,  $r^2 = 0.232$ ,  $p = 0.081$ ) at Cz during NREM sleep (**Table 3**). Similar to  
150 previous studies (Fang et al., 2017; Fogel et al., 2007), inspection of the semipartial coefficients  
151 revealed that Reasoning ability ( $t(25) = 2.191$ ,  $r = 0.401$ ,  $p = 0.038$ ; **Figure 1**) uniquely  
152 accounted for variability in spindle amplitude over and above STM ( $t(25) = 0.314$ ,  $r = 0.063$ ,  $p$   
153  $= 0.756$ ) and Verbal ( $t(25) = 0.972$ ,  $r = 0.191$ ,  $p = 0.341$ ) abilities. The same regression analyses  
154 were conducted for slow spindles at Fz and fast spindles at Pz, however, we did not observe  
155 any significant relationship between spindles and cognitive abilities.

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**Table 3.** Multiple regression analyses of the relationship between Cambridge Brain Sciences Trials and 11-16Hz spindles at Cz during NREM sleep. See **Figure 1**.

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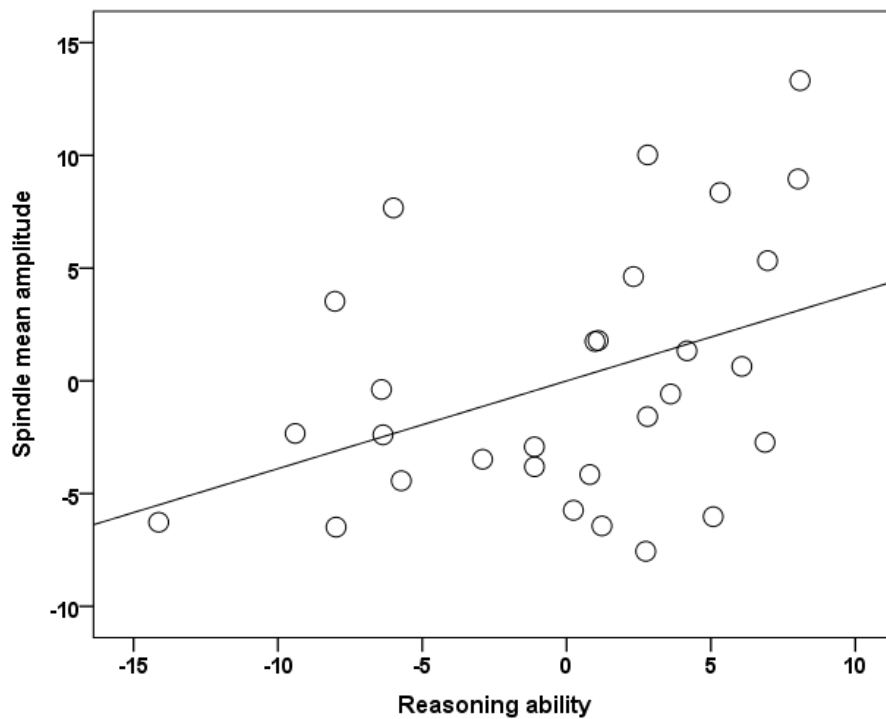
<b>Overall regression effect</b>			
<b>Sleep Spindle parameter</b>	<b><math>r^2</math></b>	<b><math>F(3,25)</math></b>	<b>p</b>
<b>Amplitude</b>	0.37	4.884	0.008*
<b>Duration</b>	0.060	0.531	0.665
<b>Density</b>	0.232	2.522	0.081
<b>Post-hoc effects analyses</b>			
<b>CBS measures</b>	<b>Semipartial r</b>	<b><math>t(25)</math></b>	<b>p</b>
<b>Reasoning</b>	0.401	2.191	0.038*
<b>Verbal</b>	0.191	0.972	0.341
<b>STM</b>	0.063	0.314	0.756

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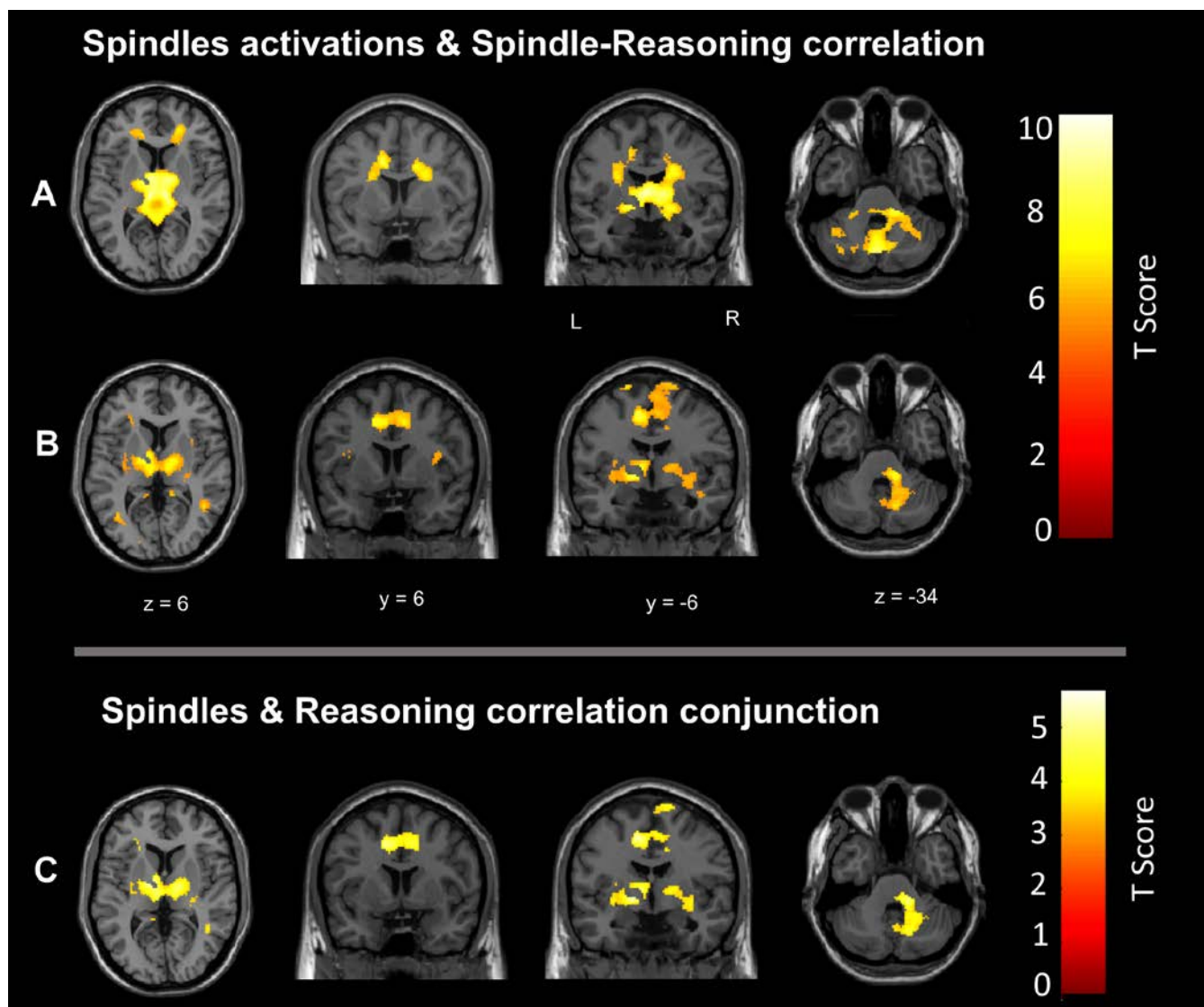
159

160 **Figure 1.** The unique relationship (i.e., semipartial correlation,  $r(29) = 0.401$ ,  $p = 0.038$ ) between  
161 Reasoning ability, over-and-above STM and Verbal abilities with spindle amplitude during NREM2.

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### 163 **Activation of brain regions time-locked to spindles during NREM sleep**

164 As shown in **Figure 2A**, activations time-locked to all spindles (11-16 Hz) at Cz during  
165 NREM sleep, were observed in the thalamus/midbrain, the bilateral striatum (putamen/globus  
166 pallidum and caudate), the medial frontal cortex, cerebellum, and the brain stem (cluster-level  
167 FWE corrected  $p < 0.05$ , **Table 4**). These results were statistically robust, as it is worth noting  
168 that even when a conservative whole-brain voxel-wise FWE statistical threshold correction ( $p$   
169  $< 0.05$ ) was used, activations remained statistically significant in the thalamus/midbrain, the  
170 brainstem, the cerebellum, and the right putamen.



171

172 **Figure 2. Cerebral activation time-locked to sleep spindles and correlation between spindle-related**  
173 **activation and Reasoning abilities. A.** Activations time-locked to sleep spindles per se during NREM sleep. **B.**  
174 Spatial correlation maps between activations time-locked to sleep spindles and Reasoning abilities. **C.**  
175 Conjunction between A and B.

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177 Given the two physiologically distinct spindles types (fast and slow), we also explored  
178 the brain activations time-locked to fast (13.5-16 Hz) spindles and slow (11-13.5 Hz) spindles  
179 during NREM sleep. As shown in **Figure S1**, activations time-locked to fast spindles at Pz  
180 (**Figure S1A**) and slow spindles at Fz (**Figure S1B**) were very similar in most brain regions,  
181 including the thalamus, the precuneus, and the cerebellum. There were no significant  
182 differences between fast spindle and slow spindle-related activations.

**Table 4.** Statistically significant activations time-locked to 11-16Hz sleep spindles at Cz during NREM sleep (see **Figure 2A**).

Hemisphere	Region	MNI Coordinate			Peak z score	FWE corrected p-value
		X	Y	Z		
Right	thalamus	10	-22	12	6.47	< 0.001
Left	thalamus	-12	-26	16	6.00	<0.001
Left	caudate	-14	12	12	6.07	<0.001
Left	putamen/pallidum	-18	-2	-4	4.22	0.001
Right	putamen/pallidum	18	-4	-4	5.32	<0.05
Bilateral	cerebellum	2	-62	-10	5.88	<0.001
Left	anterior cingulate	-16	32	18	5.16	0.001
Right	anterior cingulate	12	22	28	3.94	0.001
Middle	middle cingulate	0	24	32	4.53	0.001

**Note:** Significant brain responses after Family Wise Error (FWE) correction  $p < 0.05$  at the cluster-level.

183

## 184 **Correlation between cognitive abilities and brain activations time-locked to spindles**

185 To examine the neural correlates of the relationship between sleep spindles and cognitive  
186 abilities, we conducted whole-brain spatial correlation analyses between brain activation maps  
187 time-locked to all spindles at Cz and the scores on the three cognitive factors (Reasoning, STM,  
188 and Verbal abilities) assessed by the Cambridge Brain Sciences tests. As shown in **Figure 2B**,  
189 Reasoning ability was significantly correlated with spindle-related activation maps in the  
190 thalamus, bilateral putamen, brainstem/pons anterior cingulate cortex, the middle cingulate  
191 cortex, the paracentral lobe, the posterior cingulate cortex, the precuneus, and bilateral  
192 temporal lobe (see **Table 5**).

193

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**Table 5.** Whole brain correlations between Reasoning ability and 11-16Hz spindle-related activations at Cz during NREM sleep. (see **Figure 2B**)

Hemisphere	Region	MNI Coordinate			Peak z	FWE corrected
		X	Y	Z	score	p-value
Left	paracentral lobe	-12	-32	58	5.01	<0.001
Middle	anterior cingulate	-6	12	26	4.44	<0.001
Middle	middle cingulate	-8	10	40	4.07	<0.001
Left	Precuneus	-14	-58	32	5.12	<0.001
Left	putamen/pallidum	-16	-6	-2	4.39	<0.001
Right	putamen	32	-6	-8	3.38	<0.001
Left	thalamus	-12	-10	6	4.18	< 0.001
Right	thalamus	16	-10	8	4.03	< 0.001
Right	cerebellum	14	-64	-34	3.80	< 0.001
Left	temporal lobe	-42	-58	-2	4.30	<0.05
Right	temporal lobe	48	-52	-4	4.24	<0.05

**Note:** Significant brain responses after Family Wise Error (FWE) correction  $p < 0.05$  at the cluster-level.

195

196 Since Reasoning ability was highly inter-correlated with Verbal ability ( $r = 0.596$ ,  $p =$   
197  $0.001$ ), and marginally correlated with STM ability ( $r = 0.357$ ,  $p = 0.058$ ), to ensure that the  
198 relationship between Reasoning ability and the spindle-related activations was not accounted  
199 for by Verbal or STM abilities, we also examined the correlations between spindle-related  
200 activations and Short Term Memory, and also Verbal abilities, respectively. However, no  
201 significantly correlated activations were observed between Short Term Memory or Verbal  
202 abilities and the spindle-related activations. This demonstrates that a subset of spindle-related  
203 activations was specifically related to Reasoning abilities, but not to Short Term Memory or  
204 Verbal abilities. This is consistent with, and provides physiological support for the current and  
205 previous studies (Bódizs et al., 2005; Fang et al., 2017; Fogel et al., 2007; Schabus et al., 2006;  
206 Ujma et al., 2014, 2015), demonstrating that Reasoning abilities are uniquely correlated to sleep

207 spindles. The same whole-brain spatial correlation analyses were conducted for fast spindle  
208 and slow spindle activation maps, however, we did not observe significant correlations between  
209 any cognitive ability and the activation maps for each individual spindle type.

210 From **Figure 2**, we can see that there were several overlapping regions between the  
211 spindle activation maps (**Figure 2A**) and the maps that show activations time-locked to spindles  
212 that were correlated with Reasoning abilities (**Figure 2B**). The conjunction (at  $p < 0.001$  using  
213 the conjunction null) between the spindle activation maps and the Reasoning-related spindle  
214 correlation maps (**Figure 2C**), show several regions were consistently high and jointly activated  
215 in both the spindle and Reasoning-spindle correlation maps, including the thalamus, medial  
216 frontal cortex, bilateral putamen, and the cerebellum (**Table 6**).

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**Table 6.** Conjunction between the spindle-related activation maps and the spindle-related activations correlated with reasoning abilities maps. (see **Figure 2C**)

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Hemisphere	Region	MNI Coordinate			Peak z score	FWE corrected p-value
		X	Y	Z		
Middle	anterior cingulate	-8	12	26	4.10	<0.001
Middle	middle cingulate	-14	5	42	4.17	<0.001
Left	putamen/pallidum	-16	-6	-2	4.39	<0.001
Left	putamen	-32	-10	-4	3.75	<0.001
Left	thalamus	-12	-10	6	4.18	< 0.001
Right	thalamus	12	-10	8	4.00	< 0.001
Right	cerebellum	14	-64	-34	3.80	< 0.001

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**Note:** Significant brain responses after Family Wise Error (FWE) correction  $p < 0.05$  at the cluster-level.

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218 Finally, to ensure that activations time-locked to spindles were specific to spindles per se,  
219 and not to some general epiphenomena of NREM sleep, a separate analysis investigated  
220 activations time-locked to the same number of randomly distributed onsets during NREM sleep,

221 instead of onsets aligned to spindles events. The results revealed only a small single cluster at  
222 the left frontal lobe (peak coordinate: -28, -2, 68; uncorrected  $p < 0.005$ ), which did not overlap  
223 with the activations time-locked to spindles (**Figure S2**), and did not survive correction for  
224 multiple comparisons, suggesting that this activation is non-specific to NREM sleep, and likely  
225 spurious. No correlation was observed between Reasoning ability and the uncorrected random  
226 onsets map. This suggests that the reactivations reported here, are specifically related to  
227 spindle events, and not simply to NREM sleep in general.

228

## 229 **DISCUSSION**

230 Sleep supports normal human cognitive performance, such as attention, language,  
231 reasoning, decision making, learning and memory (for review, see Alhola & Polo-Kantola 2007;  
232 Diekelmann 2014; Diekelmann & Born 2010; Goel et al. 2009; Harrison & Horne 2000).  
233 Previous EEG studies have identified sleep spindles as a biological marker of cognitive abilities,  
234 and in particular, reasoning abilities (Bódizs et al., 2005; Fang et al., 2017; Fogel et al., 2007;  
235 Fogel & Smith, 2011; Schabus et al., 2006; Ujma et al., 2014, 2015). Only a few EEG-fMRI  
236 studies have explored the brain activations correlated with sleep spindles (Andrade et al., 2011;  
237 Caporro et al., 2012; Laufs et al., 2007; Schabus et al., 2007; Tyvaert et al., 2008). Interestingly,  
238 some of these regions are also known to support reasoning abilities. However, the  
239 neuroanatomical functional correlates of the relationship between spindles and Reasoning  
240 abilities are unknown. Here, we identified the neural activation patterns time-locked to spindles  
241 that are correlated to cognitive abilities. Using a large sample of simultaneous EEG-fMRI sleep  
242 recordings, the results of the present study support three main findings: (1) similar to previous  
243 studies (Fang et al., 2017; Fogel et al., 2007), spindles detected at Cz (11-16Hz) during NREM  
244 sleep were related to Reasoning but not Short Term Memory or Verbal abilities, (2) similar to



245 previous studies (Andrade et al., 2011; Caporro et al., 2012; Laufs et al., 2007; Schabus et al.,  
246 2007; Tyvaert et al., 2008), activations time-locked to spindles were observed in the thalamus,  
247 bilateral striatum, middle cingulate cortex, and cerebellum, and (3) Reasoning abilities were  
248 correlated with spindle-related activations in a subset of these regions including the thalamus,  
249 bilateral striatum, medial frontal gyrus, middle cingulate cortex, and precuneus. These results  
250 are specific to spindles *per se*, and cannot be attributed to some epiphenomena during NREM  
251 sleep; given that these results were not observed when random onsets during NREM sleep  
252 were used instead of onsets time-locked to spindle events. Altogether, our results identified for  
253 the first time, the neural correlates of the relationship between spindles and Reasoning abilities.

#### 254 **Spindle-related activation of thalamocortical circuitry**

255 Consistent with previous EEG-fMRI studies of spindle-related activations (Andrade et al.,  
256 2011; Caporro et al., 2012; Laufs et al., 2007; Schabus et al., 2007; Tyvaert et al., 2008), our  
257 results identified and confirmed the brain regions associated with spindle events during NREM  
258 sleep in both cortical (including the media prefrontal, anterior cingulate cortex, and middle  
259 cingulate cortex), and subcortical areas (including the thalamus and bilateral caudate, putamen,  
260 and pallidum), indicating the role of cortico-thalamic-basal ganglia circuitry in spindle generation.  
261 In addition, positron emission tomography (PET) studies have shown changes in regional  
262 cerebral blood flow in the thalamus related to sleep spindles (Hofle et al., 1997). These human  
263 neuroimaging findings are supported by a large body of animal studies, which at the cellular  
264 level, suggest that spindles reflect oscillatory activity in widespread thalamocortical circuits, and  
265 involve complex interactions between reticular, thalamocortical and pyramidal cells (Steriade,  
266 2005). Classically, spindle generation was shown to be maintained by synchronized firing in the  
267 reticular-thalamocortical-reticular circuit (Steriade, Nunez, & Amzica, 1993; von Krosigk et al.,  
268 1993). More recent evidence (Bonjean et al., 2011) however, suggests that corticothalamic

269 input initiates spindles by triggering spike bursts in the reticular nucleus and are terminated by  
270 desynchronization of thalamic and cortical neuronal firing. Thus, taken together, animal and  
271 recent human neuroimaging studies, including the current study, supports the involvement of  
272 thalamocortical circuitry in spindle generation.

273         The results of the current study identified a correlation between Reasoning, but not Short  
274 Term Memory or Verbal abilities with spindle-related brain activations in thalamocortical  
275 circuitry, especially the thalamus and the prefrontal cortex (PFC) region, which are thought to  
276 be implicated in modulation of cognitive performance (Blair, 2006; Ferguson & Gao, 2015;  
277 Mitchell & Chakraborty, 2013). Spindles and the thalamus have been shown to be related to  
278 human intellectual abilities (Fangmeier et al., 2006; Melrose et al., 2007). The thalamus,  
279 especially the mediodorsal thalamus has been reported to be related to the fluid intelligence  
280 (Van der Werf et al., 2003; Van Der Werf et al., 2000) particularly for the extrapolation  
281 component process of inductive reasoning (Jia et al., 2011; Liang et al., 2014) and other higher-  
282 level cognition (e.g., problem solving, working memory, goal direct seeking) (Karatekin et al.,  
283 2000; Mitchell & Chakraborty, 2013; Schiff et al., 2002; Shirvalkar et al., 2006). Lesions studies  
284 in both humans (De Witte et al., 2011; Kubat-Silman et al., 2002; Little et al., 2010) and non-  
285 human primates (for review, see Mitchell & Chakraborty 2013) have revealed that thalamic  
286 damage impairs various broadly defined aspects of cognitive performance, including  
287 discrimination, memory, learning, attention and other neuropsychological behaviors. Other  
288 neuroanatomical studies (Bohlken et al., 2014) found that only thalamic volume was  
289 significantly correlated with general intellectual functioning. In addition, at least one study  
290 identified structural and functional abnormalities in the thalamus in adults with reduced  
291 intellectual functioning who experienced prenatal exposure to alcohol (Clark et al., 2000). Thus,

292 suggesting that integrity and functioning of the neural circuitry involved in spindle generation  
293 support intellectual abilities, and in particular Reasoning abilities.

294 The prefrontal cortex has been defined as the projection area of the mediodorsal thalamus  
295 (Behrens et al., 2003), and the prefrontal-thalamic loop plays a critical role in various higher-  
296 order cognitive processes, especially executive function (for reviews see Baxter 2013;  
297 Ferguson & Gao 2015; Funahashi 2013; Mitchell & Chakraborty 2013; Watanabe & Funahashi  
298 2012). A large body of literature has identified the role of the prefrontal cortex area in fluid  
299 intelligence and Reasoning (Coricelli & Nagel, 2009; Duncan, 2000; Gray et al., 2003; Melrose  
300 et al., 2007; Sandman et al., 2014; Waltz et al., 1999). For example, patients with damage to  
301 the prefrontal cortex exhibited a selective and catastrophic deficit for both deductive and  
302 inductive reasoning tasks (Waltz et al., 1999). In addition, Gray et al., (2003) found that  
303 individuals with higher fluid intelligence have greater activations in the prefrontal cortex.  
304 Coricelli and Nagel (2009) have shown that reasoning abilities correlate with neural activity in  
305 the medial prefrontal cortex. Additionally, at least one neuroanatomical MRI study employing  
306 voxel-based morphometry has revealed a positive correlation between gray matter intensity in  
307 the medial prefrontal cortex and reasoning abilities assessed by Cattell's Culture Fair  
308 Intelligence Test, and also the WAIS-R (Gong et al., 2005). Taken together, these findings  
309 suggest that the thalamus and prefrontal cortex region supports Reasoning abilities.

### 310 **Spindle-related activation of the basal ganglia**

311 Consistent with previous results (Caporro et al., 2012; Tyvaert et al., 2008), the present  
312 study shows that the basal ganglia, including striatal areas (caudate and putamen) and the  
313 globus pallidus were recruited during spindle events. The basal ganglia are primarily known for  
314 playing a role in cognitive functions (for reviews see Burgaleta et al. 2014; Chakravarthy et al.  
315 2010; Leisman et al. 2014; Doyon et al. 2009) such as action selection, reward-based learning,

316 motor sequence learning, planning (Elsinger et al., 2006) and motor execution (Monchi et al.,  
317 2006). In addition, several studies have observed robust activations in the basal ganglia for  
318 reasoning-related tasks compared to other cognitive tasks, including the caudate nucleus,  
319 putamen and globus pallidus (Ferguson & Gao, 2015; Melrose et al., 2007; Rodriguez-Moreno  
320 & Hirsch, 2009). Taken together, these findings complement the results of the current study  
321 whereby activation of the putamen time-locked spindles was correlated with Reasoning abilities.  
322 The Reasoning subtests of the Cambridge Brain Sciences Trials, consists of tasks requiring  
323 planning (Shallice, 1982), spatial rotation (Silverman et al., 2000), and visuomotor ability  
324 (Folstein et al., 1975). Sandman et al., (2014) has reported that the morphometry of the  
325 putamen was associated with performance on reasoning-related subtests of the WAIS including  
326 block design, matrix reasoning and perceptual index in preadolescent children. These findings  
327 suggest that the function and structure of the basal ganglia are related to Reasoning abilities.  
328 The current study suggests that interindividual differences in spindle-related activation of these  
329 regions are related to Reasoning ability.

### 330 **Spindle-related activation of the cerebellum**

331 Similar to previous studies (Schabus et al., 2007), here, we also observed spindle-related  
332 activation of the cerebellum which was also correlated with Reasoning abilities. Many studies  
333 overlook cognition-related activity in the cerebellum, although this area is responsible for  
334 modulating thalamic activity through direct cerebello-thalamic projections, which may be related  
335 to spindle generation (Calzavara et al., 2005; Shouse & Serman, 1979). In addition, it has  
336 been suggested that the cerebellum supports cognitive functions (for reviews, see Gordon 2007;  
337 Rapoport et al. 2000; Stoodley 2012) such as response reassignment during a complex task  
338 (Bischoff-Grethe et al., 2002), decision making (Blackwood et al., 2004), associative learning  
339 (Logan & Grafton, 1995), adaptation (Krakauer & Mazzoni, 2011), and executive function

340 (Bellebaum & Daum, 2007; Tomasi et al., 2007). Importantly, the cerebellum is activated during  
341 the deductive reasoning processing (Goel et al., 2000; Goel & Dolan, 2004) supporting our  
342 finding that reasoning-related functions supported by the cerebellum is reflected during sleep,  
343 time-locked to spindles.

344 Unlike previous studies, we did not observe spindle-related activation of the medial  
345 temporal lobe (Andrade et al., 2011; Caporro et al., 2012; Laufs et al., 2007; Schabus et al.,  
346 2007; Tyvaert et al., 2008). In addition, Schabus et al., (2007) and Andrade et al. (2011)  
347 reported brain activation differences between fast spindles and slow spindles, particularly in  
348 hippocampal regions. However, here, we observed similar activation patterns for both spindle  
349 types and no significant differences between spindle types. However, we did find medial frontal  
350 activation for slow, but not fast spindle events. Despite having a large proportion of participants  
351 who slept for an adequate amount of NREM sleep, there may not have been an adequate  
352 number of each spindle type when categorized orthogonally for sufficient power, or perhaps not  
353 enough intersubject variability to detect any relationship to cognitive abilities. Moreover, sleep  
354 was recorded only from the first couple of hours of the night, where the relationship between  
355 Reasoning abilities and spindles has been found to be much less robust than the later part of  
356 the night (Fogel et al., 2007). This might also help explain that when separated into fast spindles  
357 and slow spindles, we did not observe significant relationship with Reasoning abilities in each  
358 spindle subtype. Lastly, due to the limited duration, and high intersubject variability of sleep in  
359 the scanner, we did not have sufficient SWS to test whether a different pattern of results was  
360 observed during SWS.

361 The clinical significance and applications of the relationship between spindles and  
362 cognitive abilities is yet to be realized. Deficient or dysfunctional spindle generation may be  
363 associated with compromised intellectual functioning. More specifically, it has been suggested

364 that deficient gating mechanisms of thalamocortical circuitry (Bixler,1968) may explain  
365 abnormal spindle production in children with mental disability (Gibbs & Gibbs, 1962; Shibagaki  
366 & Kiyono, 1983) . Moreover, the present study is an important first step which may lead to the  
367 development of novel interventions utilizing spindle-enhancing neuromodulatory techniques  
368 (e.g., neurofeedback, transcranial direct current stimulation, pharmacological) to improve  
369 daytime cognitive performance and explore the physiological mechanisms which support the  
370 function of sleep for memory and cognitive performance. Such an approach could target  
371 cognitive deficits, in cases where spindle production is abnormal such as in learning disabilities  
372 (Gibbs & Gibbs, 1962; Shibagaki & Kiyono, 1983), below normal cognitive functioning (Fogel &  
373 Smith, 2011) , normal, healthy aging (Carrier et al., 2001; Fogel et al., 2014; Fogel et al., 2017),  
374 developmental disorders (Limoges et al., 2005) and in schizophrenia (Wamsley et al., 2012).

375 Here, we investigated what neural substrates support cognitive strengths and  
376 weaknesses. There are considerable interindividual differences in sleep spindles, which are  
377 very trait-like(Gaillard & Blois, 1981; Silverstein & Michael Levy, 1976). While the neural  
378 circuitry and generating mechanisms of spindles are well-understood, the neurophysiological  
379 basis of the relationship between spindles and cognitive abilities remain to be fully elucidated.  
380 In summary, our results show for the first time the neuroanatomical functional correlates of the  
381 relationship between sleep spindles and intellectual abilities. In particular, our study found  
382 that the extent of the activation of the prefrontal cortex, basal ganglia, cerebellum and the  
383 thalamus time-locked to sleep spindles was correlated with interindividual differences in  
384 Reasoning, but not Verbal or STM abilities. Thus, spindles may serve as an electrophysiological  
385 marker of brain activations in regions which support the ability to employ reasoning to solve  
386 problems and apply logic in novel situations.

387

## 388 **METHODS**

### 389 **Participants**

390 A total of 35 healthy right-handed adults (20 female) between 20-35 years old ( $M = 25.6$ ,  
391  $SD = 3.6$ ), were recruited to participate in this study. All participants were non-shift workers and  
392 medication-free, had no history of head injury or seizures, had a normal body mass index ( $<25$ ),  
393 and did not consume excessive caffeine, nicotine or alcohol. To be included, interested  
394 participants had to score  $<10$  on the Beck Depression (Beck et al., 1974) and the Beck Anxiety  
395 (Beck et al., 1988) inventories and have no history or signs of sleep disorders indicated by the  
396 Sleep Disorders Questionnaire (Douglass et al., 1994). All participants were required to keep a  
397 regular sleep-wake cycle (bed-time between 22h00-24h00, wake-time between 07h00-09h00)  
398 and to abstain from taking daytime naps at least 7 days prior to and throughout participation in  
399 the study. Compliance with this schedule was assessed using both sleep diaries and wrist  
400 actigraphy (Actiwatch 2, Philips Respironics, Andover, MA, USA) worn on the non-dominant  
401 wrist. All participants met the MRI safety screening criteria. In addition, participants were given  
402 a letter of information, provided informed written consent before participation, and were  
403 financially compensated for their participation. This research was approved by the Western  
404 University Health Science research ethics board.

405 Sample sizes were determined a-priori based on previous studies, and power calculated,  
406 where possible using G\*Power for Mac version 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009;  
407 Faul, Erdfelder, Lang, & Buchner, 2007). Based on the most comparable simultaneous EEG-  
408 fMRI studies (Andrade et al., 2011; Caporro et al., 2012; Laufs et al., 2007; Schabus et al.,  
409 2007; Tyvaert et al., 2008), previous studies have employed sample sizes  $N < 15$ . A recent study  
410 by our group using the same cognitive tests as the current study (Fang et al., 2017) found  
411 robust associations between spindles and cognitive abilities in a sample size of  $N = 24$ ,

412 replicating previous findings in smaller samples (e.g.,  $N < 12$ : Fogel et al., 2007; Fogel & Smith,  
413 2006). Based on power calculation for correlation with  $p(2\text{-tailed}) = 0.05$  ( $b = 0.20$ , effect size =  
414 0.56) from (Fang et al., 2017), an  $N = 22$  was required. Thus,  $N = 29$  subjects included in this  
415 study was considered to provide adequate statistical power for the main effects of interest.

## 416 **Experimental procedure**

417 Each participant underwent a screening/orientation session one week prior to the  
418 experimental sleep session. All participants completed the CBS test battery online at least 3  
419 days prior to the experimental session. The experimental sleep session took place between  
420 21h00 and 23h00, during which time simultaneous EEG-fMRI was recorded while participants  
421 slept in the scanner. To be included in the analyses, participants were required to sleep for a  
422 period of at least 5 minutes of uninterrupted NREM sleep during the sleep session. This was  
423 considered to be the minimum amount of data necessary for EEG and fMRI data analysis  
424 purposes, and to ensure a minimum duration, quality and continuity of sleep. It should be noted  
425 that all subjects had at least 14.67 minutes of sleep, with at least 63 total bandwidth spindles  
426 (11-16 Hz) at Cz. Importantly, the average duration of NREM sleep was 39.29 minutes, with an  
427 average of 334.74 total bandwidth spindles (11-16 Hz) at Cz. Following the sleep session,  
428 participants were allowed to sleep in the nearby sleep laboratory for the remainder of the night.

429 Of the 35 participants who met the inclusion criteria, only 5 participants did not meet the  
430 5-minute consolidated NREM sleep criteria for the sleep session. As well, one participant did  
431 not complete the Cambridge Brain Sciences Trials test battery. In total, 29 participants (M age  
432 = 23.97, SD = 3.83, 17 female) were included in the final data analyses.

## 433 **Cognitive ability test**



434 The Cambridge Brain Sciences test battery (Hampshire et al., 2012) was used to assess  
435 participants' cognitive abilities. Cambridge Brain Sciences is a web-based battery of 12  
436 cognitive tests that assesses a broad range of cognitive abilities including reasoning, problem  
437 solving, planning, attention, and memory. A recent study, based on scores from a population-  
438 sized pool of 44,600 participants, revealed three factors that govern performance across the  
439 Cambridge Brain Sciences subtests. These factors have been described as "Reasoning",  
440 "Short Term Memory" and "Verbal" ability (Hampshire et al., 2012). The descriptive statistics of  
441 each subtest score are shown in **Table 1**.

## 442 **Polysomnographic Recording and Analysis**

443 **Recording Parameters.** EEG was recorded using a 64-channel magnetic resonance (MR)-  
444 compatible EEG cap which included one electrocardiogram (ECG) lead (Braincap MR, Easycap,  
445 Herrsching, Germany) and two MR-compatible 32-channel amplifiers (Brainamp MR plus, Brain  
446 Products GmbH, Gilching, Germany). EEG caps included scalp electrodes referenced to FCz.  
447 Two bipolar electrocardiogram (ECG) recordings were taken from V2-V5 and V3-V6 using an  
448 MR-compatible 16-channel bipolar amplifier (Brainamp ExG MR, Brain Products GmbH,  
449 Gilching, Germany). Using high-chloride abrasive electrode paste (Abralyt 2000 HiCL; Easycap,  
450 Herrsching, Germany), electrode-skin impedance was reduced to < 5 KOhm. To reduce  
451 movement-related EEG artifacts, participants' heads were immobilized in the MRI head-coil  
452 using foam cushions. EEG was digitized at 5000 samples per second with a 500-nV resolution.  
453 Data were analog filtered by a band-limiter low pass filter at 500 Hz and a high pass filter with  
454 a 10-sec time constant corresponding to a high pass frequency of 0.0159 Hz. Data were  
455 transferred via fiber optic cable to a personal computer where Brain Products Recorder  
456 Software, Version 1.x (Brain Products, Gilching, Germany) was synchronized to the scanner  
457 clock. EEG was monitored online with Brain Products RecView software using online artifact

458 correction. Sleep stages were scored in accordance with  
459 standard criteria (Iber et al., 2007) using the “VisEd Marks” toolbox (<https://github.com/jade>  
460 [sjardins/vised\\_marks](https://github.com/sjardins/vised_marks)) for eeglab (Delorme & Makeig, 2004). Automatic spindle detection was  
461 carried out using a previously published (Fogel et al., 2014; Fogel et al., 2015) and validated  
462 (Ray et al., 2015) method employing EEGlab-compatible (Delorme & Makeig, 2004) software  
463 ([github.com/stuartfogel/detect\\_spindles](https://github.com/stuartfogel/detect_spindles)) written for MATLAB R2014a (The MathWorks Inc.,  
464 Natick, MA). The detailed processing steps and procedures are reported elsewhere (Ray et al.,  
465 2015) and are thus presented only briefly here. The EEG data were initially downsampled to  
466 250 Hz. The detection was performed at Fz, Cz and Pz derivations. The spindle data were  
467 extracted from movement artifact-free, NREM stage 2 sleep epochs. The detection method  
468 (Ray et al., 2015) used a complex demodulation transformation of the EEG signal with a  
469 bandwidth of 5 Hz centered about a carrier frequency of 13.5 Hz (i.e., 11–16 Hz) (Iber et al.,  
470 2007). To utilize a fixed amplitude detection threshold, but still account for individual differences  
471 in spindles, each data point was transformed into a z-score using the mean and standard  
472 deviation derived from a 60-sec sliding window. Events (spindle onsets, peaks, and offsets)  
473 were then detected on the transformed signal with a z-score threshold of  $z = 2.33$ ,  
474 corresponding to the 99<sup>th</sup> percentile. The dependent variables of interest extracted from this  
475 method include spindle amplitude, spindle duration, and spindle density (number of spindles  
476 per minute of NREM sleep) for each participant and at each derivation (Fz, Cz and Pz). Spindles  
477 were categorized so that they were orthogonal (non-overlapping detections) at the scalp  
478 locations where they predominate topographically (Jobert et al., 1992; Werth et al., 1997;  
479 Zeitlhofer et al., 1997) as slow spindles (11–13.5 Hz) at Fz, total bandwidth spindles (11-16 Hz)  
480 at Cz, and fast spindles (13.5–16 Hz) at Pz (**Table 2**). Despite having no minimum detection

481 criteria, the detection method employed here did not detect spindles lower than 0.2 sec, as  
482 found in a previous validation study (Ray et al., 2015).

### 483 **MRI Imaging Acquisition and Analysis**

484 **Recording Parameters.** Brain images were acquired using a 3.0T TIM TRIO magnetic  
485 resonance imaging system (Siemens, Erlangen, Germany) and a 64-channel head coil. In all  
486 participants, a structural T1-weighted MRI image was acquired using a 3D MPRAGE sequence  
487 (TR = 2300 ms, TE = 2.98 ms, TI = 900 ms, FA = 9°, 176 slices, FoV = 256×256 mm<sup>2</sup>, matrix  
488 size = 256×256×176, voxel size = 1×1×1 mm<sup>3</sup>). Multislice T2\*-weighted fMRI images were  
489 acquired during the sleep session with a gradient echo-planar sequence using axial slice  
490 orientation (TR = 2160 ms, TE = 30 ms, FA = 90°, 40 transverse slices, 3 mm slice thickness,  
491 10% inter-slice gap, FoV = 220×220 mm<sup>2</sup>, matrix size = 64×64×40, voxel size = 3.44×3.44×3  
492 mm<sup>3</sup>). Importantly, the sequence parameters were chosen so that the gradient artifact would  
493 be time stable, and the lowest harmonic of the gradient artifact (18.52 Hz) would occur outside  
494 the spindle band (11-16 Hz). This was achieved by setting the MR scan repetition time to 2160  
495 ms, such that it matched a common multiple of the EEG sample time (0.2 ms), the product of  
496 the scanner clock precision (0.1 μs) and the number of slices (40 slices) used (Mulert & Lemieux,  
497 2009) .

### 498 **Image Preprocessing**

499 Functional images were preprocessed and analyzed using SPM8  
500 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>; Welcome Department of Imaging  
501 Neuroscience, London, UK) implemented in MATLAB (ver. 8.5 R2015a) for Windows (Microsoft,  
502 Inc. Redmond, WA). Functional scans of each session were realigned using rigid body  
503 transformations, iteratively optimized to minimize the residual sum of squares between the first

504 and each subsequent image separately for each session. A mean realigned image was then  
505 created from the resulting images. The structural T1-image was coregistered to this mean  
506 functional image using a rigid body transformation optimized to maximize the normalized mutual  
507 information between the two images. Coregistration parameters were then applied to the  
508 realigned blood-oxygen-level dependent (BOLD) time series. The coregistered structural  
509 images were segmented into grey matter, white matter and cerebrospinal fluid. An average  
510 subject-based template was created using DARTEL in SPM8. All functional and anatomical  
511 images were spatially normalized using the resulting template, which was generated from the  
512 structural scans. Finally, spatial smoothing was applied on all functional images (Gaussian  
513 kernel, 8 mm full-width at half-maximum (FWHM)).

#### 514 **Sleep sessions**

515 For data acquired during the simultaneous EEG-fMRI sleep recordings, within-session  
516 series of consecutive fMRI volumes sleep stage scored as NREM stage 2 sleep according to  
517 standard criteria (Iber et al., 2007) by an expert, registered polysomnographic technologist were  
518 selected from the complete fMRI time series of sleep session. To be included in the fMRI  
519 analysis, the EEG had to be visibly movement artifact-free and be a segment of uninterrupted  
520 sleep longer in duration than 55 volumes (i.e., ~120 seconds or longer; corresponding to the  
521 minimum amount of sleep that was needed to perform the automated spindle detection),  
522 resulting in the inclusion of 36% of the total recorded data (i.e., 11,466 of 31,852 MRI volumes  
523 during NREM stage 2 sleep). Each time series corresponding to NREM stage 2 sleep that met  
524 these criteria, were entered into the general linear model (GLM) as a separate session so that  
525 no gaps existed in the design matrix. For each participant, brain responses were estimated in  
526 an event-related design using a fixed-effects GLM including responses time-locked to spindle  
527 events (11-16 Hz) detected at Cz, slow spindles (11-13.5 Hz) detected at Fz, and fast spindle

528 events (13.5-16 Hz) detected at Pz. Consistent with similar previous studies (Andrade et al.,  
529 2011; Bergmann et al., 2011; Dang-Vu et al., 2008; Schabus et al., 2007), the vectors, including  
530 spindle events, were convolved with the canonical hemodynamic response function (HRF), as  
531 well as with its temporal and dispersion derivatives. Nuisance variables in the model included:  
532 the movement parameters estimated during realignment (translations in x, y, and z directions  
533 and rotations around x, y, and z axes), the squared value of the movement parameter, the first  
534 derivative of each movement parameter, and the square of the first derivative of each  
535 movement parameter, as well as, to the mean white matter intensity and the mean cerebral  
536 spinal fluid intensity for each participant. Slow wave activity is a defining characteristic of NREM  
537 sleep (Iber et al., 2007), but is related to spindle generation (Mölle et al., 2011; Siapas & Wilson,  
538 1998). This activity was accounted for by including spectral power ( $\mu V^2$ ) in the delta band (0.5-  
539 4 Hz) for each TR window (2160 ms) as a variable of no interest, convolved with the  
540 hemodynamic response function. Slow drifts were removed from the time series using a high  
541 pass filter with a cut-off period of 128 seconds. Serial correlations in the fMRI signal were  
542 estimated using an autoregressive (order 1) plus white noise model and a restricted maximum  
543 likelihood (ReML) algorithm. These analyses generated statistical parametric t maps [(SPM(T))].  
544 The resulting contrast images were then smoothed (FWHM 6 mm Gaussian Kernel) and  
545 entered into a second-level analysis.

546 The resulting group-level analysis consisted of one sample t-tests for each contrast of  
547 interest (i.e., all spindle events, fast spindle events, and slow spindle events). To investigate  
548 the relationship between the magnitude of the spindle-dependent activation and the cognitive  
549 abilities assessed by the CBS Trials, cognitive test scores for each subtest (i.e., Reasoning,  
550 Verbal, and Short Term Memory) were entered as covariates of interest in the described GLM.  
551 These activation maps constituted maps of the t-statistic [SPM(t)] testing for the main effect for

552 each contrast of interest. Statistical inferences were performed at a threshold of  $p < 0.05$ , family  
553 wise error (FWE) corrected at the cluster level.

#### 554 **Overlap between spindle-related maps and reasoning-spindle correlation maps**

555 To illustrate the overlap of activations between the spindle-related activation maps and  
556 reasoning-spindle correlation maps, the conjunction was taken as the minimum t-statistic using  
557 the conjunction hypothesis (Friston et al., 2005; Nichols et al., 2005) over: (1) a t-map testing  
558 for the main effect of the spindle events during the sleep session, and (2) a t-map testing for  
559 the main effect of the correlation between the Reasoning ability and spindle events. These two  
560 statistical maps were thresholded at  $p < 0.05$ , FWE corrected at the cluster level.

561 Finally, to confirm that activations time-locked to spindles and correlated with Reasoning  
562 abilities were not simply an epiphenomenon of NREM sleep, we generated the same number  
563 of random events as sleep spindles in each segment of NREM sleep for all participants during  
564 the sleep session. These random onsets did not overlap with any spindle events. We conducted  
565 the exact same GLM as for actual spindle onsets, with the only difference being that the  
566 randomly generated onsets were included in the model, as opposed to the spindle onsets.

567

568

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574 **REFERENCE**

- 575 Alhola, P., & Polo-Kantola, P. (2007). Sleep deprivation: Impact on cognitive performance.  
576 *Neuropsychiatric Disease and Treatment*, 3(5), 553–567.  
577 <https://doi.org/10.1016/j.smrv.2012.06.007>
- 578 Andrade, K. C., Spoormaker, V. I., Dresler, M., Wehrle, R., Holsboer, F., Samann, P. G., &  
579 Czisch, M. (2011). Sleep Spindles and Hippocampal Functional Connectivity in Human  
580 NREM Sleep. *Journal of Neuroscience*, 31(28), 10331–10339.  
581 <https://doi.org/10.1523/JNEUROSCI.5660-10.2011>
- 582 Baxter, M. G. (2013). Mediodorsal thalamus and cognition in non-human primates. *Frontiers*  
583 *in Systems Neuroscience*, 7(August), 38. <https://doi.org/10.3389/fnsys.2013.00038>
- 584 Beck, A. T., Rial, W. Y., & Rickels, K. (1974). Short form of depression inventory: cross-  
585 validation. *Psychol Rep*, 34(3), 1184–1186.
- 586 Beck, A. T., Steer, R. A., & Carbin, M. G. (1988). Psychometric properties of the Beck  
587 Depression Inventory: Twenty-five years of evaluation. *Clinical Psychology Review*, 8(1),  
588 77–100. [https://doi.org/10.1016/0272-7358\(88\)90050-5](https://doi.org/10.1016/0272-7358(88)90050-5)
- 589 Behrens, T. E., Johansen-Berg, H., Woolrich, M. W., Smith, S. M., Wheeler-Kingshott, C. A.,  
590 Boulby, P. A., Barker, G.J., Sillery, E.L., Sheehan, K., Ciccarelli, O., Thompson, A.J.,  
591 Brady J.M., & Matthews, P. M. (2003). Non-invasive mapping of connections between  
592 human thalamus and cortex using diffusion imaging. *Nature Neuroscience*, 6(7), 750–7.  
593 <https://doi.org/10.1038/nn1075>
- 594 Bellebaum, C., & Daum, I. (2007). Cerebellar involvement in executive control. *Cerebellum*  
595 *(London, England)*, 6(3), 184–192. <https://doi.org/10.1080/14734220601169707>
- 596 Bergmann, T. O., Mölle, M., Diedrichs, J., Born, J., & Siebner, H. R. (2011). Sleep spindle-  
597 related reactivation of category-specific cortical regions after learning face-scene  
598 associations. *Neuroimage*, 59(3), 2733–2742. Journal Article.  
599 <https://doi.org/10.1016/j.neuroimage.2011.10.036>
- 600 Bischoff-Grethe, A., Ivry, R. B., & Grafton, S. T. (2002). Cerebellar involvement in response  
601 reassignment rather than attention. *The Journal of Neuroscience : The Official Journal of*  
602 *the Society for Neuroscience*, 22(2), 546–553. <https://doi.org/22/2/546> [pii]
- 603 Bixler EO, R. J. (1968). Spindle activity during sleep in cultural-familial mild retardates.  
604 *Psychophysiology*, 5, 212.
- 605 Blackwood, N., Ffytche, D., Simmons, A., Bentall, R., Murray, R., & Howard, R. (2004). The  
606 cerebellum and decision making under uncertainty. *Cognitive Brain Research*, 20(1), 46–  
607 53. <https://doi.org/10.1016/j.cogbrainres.2003.12.009>
- 608 Blair, C. (2006). How similar are fluid cognition and general intelligence? A developmental  
609 neuroscience perspective on fluid cognition as an aspect of human cognitive ability. *The*  
610 *Behavioral and Brain Sciences*, 29(2006), 109-125-160.  
611 <https://doi.org/10.1017/S0140525X06009034>
- 612 Bódizs, R., Kis, T., Lázár, A. S., Havrán, L., Rigó, P., Clemens, Z., & Halász, P. (2005).  
613 Prediction of general mental ability based on neural oscillation measures of sleep.  
614 *Journal of Sleep Research*, 14(3), 285–292. <https://doi.org/10.1111/j.1365->

- 615 2869.2005.00472.x
- 616 Bódizs, R., Lázár, A. S., & Rigó, P. (2008). Correlation of visuospatial memory ability with  
617 right parietal EEG spindling during sleep. *Acta Physiologica Hungarica*, *95*(3), 297–306.  
618 <https://doi.org/10.1556/APhysiol.95.2008.3.5>
- 619 Bohlken, M. M., Brouwer, R. M., Mandl, R. C. W., van Haren, N. E. M., Brans, R. G. H., van  
620 Baal, G. C. M., de Geus, E.J.C., Boomsma, D.I., Kahn, R.S., & Hulshoff Pol, H. E.  
621 (2014). Genes contributing to subcortical volumes and intellectual ability implicate the  
622 thalamus. *Human Brain Mapping*, *35*(6), 2632–2642. <https://doi.org/10.1002/hbm.22356>
- 623 Bonjean, M., Baker, T., Lemieux, M., Timofeev, I., Sejnowski, T., & Bazhenov, M. (2011).  
624 Corticothalamic feedback controls sleep spindle duration in vivo. *J Neurosci*, *31*(25),  
625 9124–9134. <https://doi.org/10.1523/JNEUROSCI.0077-11.2011>
- 626 Bugg, J. M., Zook, N. A., DeLosh, E. L., Davalos, D. B., & Davis, H. P. (2006). Age  
627 differences in fluid intelligence: contributions of general slowing and frontal decline. *Brain*  
628 *and Cognition*, *62*(1), 9–16. <https://doi.org/10.1016/j.bandc.2006.02.006>
- 629 Burgaleta, M., Macdonald, P. A., Martínez, K., Román, F. J., Álvarez-Linera, J., González, A.  
630 R., ... Colom, R. (2014). Subcortical regional morphology correlates with fluid and spatial  
631 intelligence. *Human Brain Mapping*, *35*(5), 1957–1968.  
632 <https://doi.org/10.1002/hbm.22305>
- 633 Calzavara, R., Zappala, A., Rozzi, S., Matelli, M., & Luppino, G. (2005). Neurochemical  
634 characterization of the cerebellar-recipient motor thalamic territory in the macaque  
635 monkey. *European Journal of Neuroscience*, *21*(7), 1869–1894. Retrieved from  
636 <http://cat.inist.fr/?aModele=afficheN&cpsidt=16745682>
- 637 Caporro, M., Haneef, Z., Yeh, H. J., Lenartowicz, A., Buttinelli, C., Parvizi, J., & Stern, J. M.  
638 (2012). Functional MRI of sleep spindles and K-complexes. *Clinical Neurophysiology*,  
639 *123*(2), 303–309. <https://doi.org/10.1016/j.clinph.2011.06.018>
- 640 Carrier, J., Land, S., Buysse, D. J., Kupfer, D. J., & Monk, T. H. (2001). The effects of age  
641 and gender on sleep EEG power spectral density in the middle years of life (ages 20-60  
642 years old). *Psychophysiology*, *38*(2), 232–242.
- 643 Chakravarthy, V. S., Joseph, D., & Bapi, R. S. (2010). What do the basal ganglia do? A  
644 modeling perspective. *Biological Cybernetics*, *103*(3), 237–253.  
645 <https://doi.org/10.1007/s00422-010-0401-y>
- 646 Christoph Mulert, L. L., & Christoph Mulert, L. L. (2010). *EEG-fMRI: Physiological Basis,*  
647 *Technique and Applications* (illustrate). Springer.
- 648 Clark, C. M., Li, D., Conry, J., Conry, R., & Looock, C. (2000). Structural and functional brain  
649 integrity of fetal alcohol syndrome in nonretarded cases. *Pediatrics*, *105*(5), 1096–1099.  
650 <https://doi.org/10.1542/peds.105.5.1096>
- 651 Coricelli, G., & Nagel, R. (2009). Neural correlates of depth of strategic reasoning in medial  
652 prefrontal cortex. *Proceedings of the National Academy of Sciences of the United States*  
653 *of America*, *106*(23), 9163–9168. <https://doi.org/10.1073/pnas.0807721106>
- 654 Dang-Vu, T. T., Schabus, M., Desseilles, M., Albouy, G., Boly, M., Darsaud, A., Gais, S.,  
655 Rauchs, G., Sterpenich, V., Vandewalle, G., Carrier, J., Moonen, G., Balteau, E.,



- 656 Degueldre, C., Luxen, A., Phillips, C., & Maquet, P. (2008). Spontaneous neural activity  
657 during human slow wave sleep. *Proceedings of the National Academy of Science U S A*,  
658 *105*(39), 15160.
- 659 De Gennaro, L., Ferrara, M., Vecchio, F., Curcio, G., & Bertini, M. (2005). An  
660 electroencephalographic fingerprint of human sleep. *NeuroImage*, *26*(1), 114–122.  
661 <https://doi.org/10.1016/j.neuroimage.2005.01.020>
- 662 De Witte, L., Brouns, R., Kavadias, D., Engelborghs, S., De Deyn, P. P., & Mariën, P. (2011).  
663 Cognitive, affective and behavioural disturbances following vascular thalamic lesions: A  
664 review. *Cortex*, *47*(3), 273–319. <https://doi.org/10.1016/j.cortex.2010.09.002>
- 665 Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-  
666 trial EEG dynamics including independent component analysis. *Journal of Neuroscience*  
667 *Methods*, *134*(1), 9–21. <https://doi.org/10.1016/j.jneumeth.2003.10.009>
- 668 Diekelmann, S. (2014). Sleep for cognitive enhancement. *Front. Syst. Neurosci.*, *8*(April).  
669 <https://doi.org/10.3389/fnsys.2014.00046>
- 670 Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews*  
671 *Neuroscience*, *11*(2), 114–126. <https://doi.org/10.1038/nrn2762>
- 672 Douglass, A. B., Bornstein, R., Nino-Murcia, G., Keenan, S., Miles, L., Zarcone Jr, V. P.,  
673 Guilleminault, C., & Dement, W. C. (1994). The Sleep Disorders Questionnaire. I:  
674 Creation and multivariate structure of SDQ. *Sleep*, *17*(2), 160.
- 675 Doyon, J., Bellec, P., Amsel, R., Penhune, V., Monchi, O., Carrier, J., Lehericy, S., & Benali,  
676 H. (2009). Contributions of the basal ganglia and functionally related brain structures to  
677 motor learning. *Behavioural Brain Research*, *199*(1), 61–75.  
678 <https://doi.org/10.1016/j.bbr.2008.11.012>
- 679 Duncan, J. (2000). A Neural Basis for General Intelligence. *Science*, *289*(5478), 457–460.  
680 <https://doi.org/10.1126/science.289.5478.457>
- 681 Elsinger, C. L., Harrington, D. L., & Rao, S. M. (2006). From preparation to online control:  
682 reappraisal of neural circuitry mediating internally generated and externally guided  
683 actions. *NeuroImage*, *31*(3), 1177–87. <https://doi.org/10.1016/j.neuroimage.2006.01.041>
- 684 Fang, Z., Sergeeva, V., Ray, L. B., Viczko, J., Owen, A. M., & Fogel, S. M. (2017). Sleep  
685 Spindles and Intellectual Ability : Epiphenomenon or Directly Related ? *Journal of*  
686 *Cognitive Neuroscience*, *29*, 167–182. <https://doi.org/10.1162/jocn>
- 687 Fangmeier, T., Knauff, M., Ruff, C. C., & Sloutsky, V. (2006). fMRI Evidence for a Three-  
688 Stage Model of Deductive Reasoning, 320–334.
- 689 Faul, F., Erdfelder, E., Buchner, A., & Lang, A.G. (2009). Statistical power analyses using  
690 G\*Power 3.1: tests for correlation and regression analyses. *Behavior Research Methods*,  
691 *41*(4), 1149–60. <https://doi.org/10.3758/BRM.41.4.1149>
- 692 Faul, F., Erdfelder, E., Lang, A.G., & Buchner, A. (2007). GPOWER: A general power  
693 analysis program. *Behavior Research Methods*, *39*(2), 175–191.  
694 <https://doi.org/10.3758/BF03193146>
- 695 Ferguson, B. R., & Gao, W.J. (2015). Development of thalamocortical connections between

- 696 the mediodorsal thalamus and the prefrontal cortex and its implication in cognition.  
697 *Frontiers in Human Neuroscience*, 8, 1027. <https://doi.org/10.3389/fnhum.2014.01027>
- 698 Fogel, S. M., Albouy, G., Vien, C., Popovicci, R., King, B. R., Hoge, R. D., Jbabdi, S., Habib,  
699 B., Karni, A., Maquet, P., & Doyon, J. (2014). fMRI and sleep correlates of the age-  
700 related impairment in motor memory consolidation. *Hum Brain Mapp*, 35(8), 3625–3645.  
701 <https://doi.org/10.1002/hbm.22426>
- 702 Fogel, S. M., Ray, L. B., Binnie, L., & Owen, A. M. (2015). How to become an expert: A new  
703 perspective on the role of sleep in the mastery of procedural skills. *Neurobiology of*  
704 *Learning and Memory*, 125, 236–248. <https://doi.org/10.1016/j.nlm.2015.10.004>
- 705 Fogel, S. M., & Smith, C. T. (2011). The function of the sleep spindle: A physiological index of  
706 intelligence and a mechanism for sleep-dependent memory consolidation. *Neuroscience*  
707 *and Biobehavioral Reviews*, 35(5), 1154–1165.  
708 <https://doi.org/10.1016/j.neubiorev.2010.12.003>
- 709 Fogel, S., Nader, R. S., Cote, K. A., & Smith, C. (2007). Sleep spindles and learning potential.  
710 *Behavioral Neuroscience*, 121(1), 1–10. <https://doi.org/10.1037/0735-7044.121.1.1>
- 711 Fogel, S., & Smith, C. T. (2006). Learning-dependent changes in sleep spindles and Stage 2  
712 sleep. *Journal of Sleep Research*, 15(3), 250–255. <https://doi.org/10.1111/j.1365-2869.2006.00522.x>
- 714 Fogel, S., Vien, C., Karni, A., Benali, H., Carrier, J., & Doyon, J. (2017). Sleep spindles: a  
715 physiological marker of age-related changes in gray matter in brain regions supporting  
716 motor skill memory consolidation. *Neurobiology of Aging*, 49, 154–164.  
717 <https://doi.org/10.1016/j.neurobiolaging.2016.10.009>
- 718 Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-mental state”: a practical  
719 method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric*  
720 *Research*, 12(3), 189–198. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)
- 721 Friston, K., Penny, W., & Glaser, D. E. (2005). Conjunction revisited. *Neuroimage*, 25(3),  
722 661–667. Journal Article. <https://doi.org/10.1016/j.neuroimage.2005.01.013>
- 723 Funahashi, S. (2013). Thalamic mediodorsal nucleus and its participation in spatial working  
724 memory processes: comparison with the prefrontal cortex. *Frontiers in Systems*  
725 *Neuroscience*, 7(JUL), 36. <https://doi.org/10.3389/fnsys.2013.00036>
- 726 Gaillard, J. M., & Blois, R. (1981). Spindle density in sleep of normal subjects. *Sleep*, 4(4),  
727 385–91. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7313391>
- 728 Gibbs, E. L., & Gibbs, F. A. (1962). Extreme spindles: correlation of electroencephalographic  
729 sleep pattern with mental retardation. *Science*, 138, 1106–1107.
- 730 Goel, N., Rao, H., Durmer, J. S., & Dinges, D. F. (2009). Neurocognitive consequences of  
731 sleep deprivation. *Seminars in Neurology*, 29(4), 320–39. <https://doi.org/10.1055/s-0029-1237117>
- 733 Goel, V., Buchel, C., Frith, C., & Dolan, R. J. (2000). Dissociation of mechanisms underlying  
734 syllogistic reasoning. *NeuroImage*, 12(5), 504–14.  
735 <https://doi.org/10.1006/nimg.2000.0636>

- 736 Goel, V., & Dolan, R. J. (2004). Differential involvement of left prefrontal cortex in inductive  
737 and deductive reasoning. *Cognition*, 93(3).  
738 <https://doi.org/10.1016/j.cognition.2004.03.001>
- 739 Gong, Q. Y., Sluming, V., Mayes, A., Keller, S., Barrick, T., Cezayirli, E., & Roberts, N.  
740 (2005). Voxel-based morphometry and stereology provide convergent evidence of the  
741 importance of medial prefrontal cortex for fluid intelligence in healthy adults. *NeuroImage*,  
742 25(4), 1175–1186. <https://doi.org/10.1016/j.neuroimage.2004.12.044>
- 743 Gordon, N. (2007). The cerebellum and cognition. *European Journal of Paediatric Neurology*,  
744 11(4), 232–234. <https://doi.org/10.1016/j.ejpn.2007.02.003>
- 745 Gray, J. R., Chabris, C. F., & Braver, T. S. (2003). Neural mechanisms of general fluid.  
746 *Nature Neuroscience*, 6(3), 316–322. <https://doi.org/10.1038/nn1014>
- 747 Hampshire, A., Highfield, R. R., Parkin, B. L., & Owen, A. M. (2012). Fractionating human  
748 intelligence. *Neuron*, 76(6), 1225–1237. <https://doi.org/10.1016/j.neuron.2012.06.022>
- 749 Harrison, Y., & Horne, J. A. (2000). The impact of sleep deprivation on decision making: a  
750 review. *Journal of Experimental Psychology. Applied*, 6(3), 236–49.
- 751 Hofle, N., Paus, T., Reutens, D., Fiset, P., Gotman, J., Evans, A. C., & Jones, B. E. (1997).  
752 Regional Cerebral Blood Flow Changes as a Function of Delta and Spindle Activity  
753 during Slow Wave Sleep in Humans. *J. Neurosci.*, 17(12), 4800–4808.
- 754 Iber, C., Ancoli-Israel, S., Chesson, A. L., & Quan, S. F. (2007). *The AASM manual for the*  
755 *scoring of sleep and associated events: rules, terminology and technical specifications.*  
756 *American Academy of Sleep Medicine, Westchester, IL.* American Academy of Sleep  
757 Medicine Westchester, IL.
- 758 Jia, X., Liang, P., Lu, J., Yang, Y., Zhong, N., & Li, K. (2011). Common and dissociable neural  
759 correlates associated with component processes of inductive reasoning. *NeuroImage*,  
760 56(4), 2292–2299. <https://doi.org/10.1016/j.neuroimage.2011.03.020>
- 761 Jobert, M., Poiseau, E., Jahrig, P., Schulz, H., & Kubicki, S. (1992). Topographical analysis of  
762 sleep spindle activity. *Neuropsychobiology*, 26(4), 210–217. <https://doi.org/118923>
- 763 Karatekin, C., Lazareff, J. A., & Asarnow, R. F. (2000). Relevance of the cerebellar  
764 hemispheres for executive functions. *Pediatric Neurology*, 22(2), 106–112.  
765 [https://doi.org/10.1016/S0887-8994\(99\)00128-9](https://doi.org/10.1016/S0887-8994(99)00128-9)
- 766 Krakauer, J. W., & Mazzoni, P. (2011). Human sensorimotor learning: Adaptation, skill, and  
767 beyond. *Current Opinion in Neurobiology*, 21(4), 636–644.  
768 <https://doi.org/10.1016/j.conb.2011.06.012>
- 769 Kroger, J. K. (2002). Recruitment of Anterior Dorsolateral Prefrontal Cortex in Human  
770 Reasoning: a Parametric Study of Relational Complexity. *Cerebral Cortex*, 12(5), 477–  
771 485. <https://doi.org/10.1093/cercor/12.5.477>
- 772 Kubat-Silman, A. K., Dagenbach, D., & Absher, J. R. (2002). Patterns of impaired verbal,  
773 spatial, and object working memory after thalamic lesions. *Brain and Cognition*, 50(2),  
774 178–193. [https://doi.org/10.1016/S0278-2626\(02\)00502-X](https://doi.org/10.1016/S0278-2626(02)00502-X)
- 775 Laufs, H., Walker, M. C., & Lund, T. E. (2007). “Brain activation and hypothalamic functional

- 776 connectivity during human non-rapid eye movement sleep: an EEG/fMRI study"--its  
777 limitations and an alternative approach. *Brain : A Journal of Neurology*, 130(Pt 7), e75;  
778 author reply e76. <https://doi.org/10.1093/brain/awm084>
- 779 Leisman, G., Braun-Benjamin, O., & Melillo, R. (2014). Cognitive-motor interactions of the  
780 basal ganglia in development. *Frontiers in Systems Neuroscience*, 8(February), 16.  
781 <https://doi.org/10.3389/fnsys.2014.00016>
- 782 Liang, P., Jia, X., Taatgen, N. A., Zhong, N., & Li, K. (2014). Different strategies in solving  
783 series completion inductive reasoning problems: An fMRI and computational study.  
784 *International Journal of Psychophysiology*, 93(2), 253–260.  
785 <https://doi.org/10.1016/j.ijpsycho.2014.05.006>
- 786 Limoges, E., Mottron, L., Bolduc, C., Berthiaume, C., & Godbout, R. (2005). Atypical sleep  
787 architecture and the autism phenotype. *Brain*, 128(5), 1049–1061.  
788 <https://doi.org/10.1093/brain/awh425>
- 789 Little, D. M., Kraus, M. F., Joseph, J., Geary, E. K., Susmaras, T., Zhou, X. J., Pliskin, N., &  
790 Gorelick, P. B. (2010). Thalamic integrity underlies executive dysfunction in traumatic  
791 brain injury. *Neurology*, 74(7), 558–564. <https://doi.org/10.1212/WNL.0b013e3181cff5d5>
- 792 Logan, C. G., & Grafton, S. T. (1995). Functional anatomy of human eyeblink conditioning  
793 determined with regional cerebral glucose metabolism and positron-emission  
794 tomography. *PNAS: Proceedings of the National Academy of Sciences of the United  
795 States of America*, 92(16), 7500–7504. <https://doi.org/10.1073/pnas.92.16.7500>
- 796 Melrose, R. J., Poulin, R. M., & Stern, C. E. (2007). An fMRI investigation of the role of the  
797 basal ganglia in reasoning. *Brain Research*, 2, 146–158.  
798 <https://doi.org/10.1016/j.brainres.2007.01.060>
- 799 Mitchell, A. S., & Chakraborty, S. (2013). What does the mediodorsal thalamus do? *Frontiers  
800 in Systems Neuroscience*, 7(August), 37. <https://doi.org/10.3389/fnsys.2013.00037>
- 801 Mölle, M., Bergmann, T. O., Marshall, L., & Born, J. (2011). Fast and Slow Spindles during  
802 the Sleep Slow Oscillation: Disparate Coalescence and Engagement in Memory  
803 Processing. *Sleep*, 34, 1411–1421. <https://doi.org/10.5665/sleep.1290>
- 804 Monchi, O., Petrides, M., Strafella, A. P., Worsley, K., & Doyon, J. (2006). Functional role of  
805 the basal ganglia in the planning and execution of actions. *Ann Neurol*, 59(2), 257–264.  
806 <https://doi.org/10.1002/ana.20742>
- 807 Nader, R. S., & Smith, C. (2001). The relationship between stage 2 sleep spindles and  
808 intelligence. *Sleep*, 24, A160.
- 809 Nader, R. S., & Smith, C. (2003). A role for Stage 2 sleep in memory processing. *Sleep and  
810 Brain Plasticity*, 1(9), 87–99.
- 811 Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J. B. (2005). Valid conjunction  
812 inference with the minimum statistic. *Neuroimage*, 25(3), 653–660. Journal Article.  
813 <https://doi.org/10.1016/j.neuroimage.2004.12.005>
- 814 O'Doherty, J. P. (2004). Reward representations and reward-related learning in the human  
815 brain: Insights from neuroimaging. *Current Opinion in Neurobiology*, 14(6), 769–776.  
816 <https://doi.org/10.1016/j.conb.2004.10.016>

- 817 Rapoport, M., Reekum, R. Van, & Mayberg, H. (2000). The Role of the Cerebellum in  
818 Cognition and Behavior: A Selective Review. *Journal Of Neuropsychiatry*, 193–198.  
819 <https://doi.org/10.1176/appi.neuropsych.12.2.193>
- 820 Raven, J. C., Court, J. H. and Raven, J. (1976). *Manual for Raven's Progressive Matrices*.
- 821 Ray, L. B., Sockeel, S., Soon, M., Bore, A., Myhr, A., Stojanoski, B., Cusack, R., Owen, A.M.,  
822 Doyon, J., & Fogel, S. (2015). Expert and crowd-sourced validation of an individualized  
823 sleep spindle detection method employing complex demodulation and individualized  
824 normalization. *Frontiers in Human Neuroscience*, 9(9), 507.  
825 <https://doi.org/10.3389/fnhum.2015.00507>
- 826 Rechtschaffen, A.Kales, A. (1968). *Manual of Standardized Terminology, Techniques and*  
827 *Scoring System for Sleep Stages of Human Subjects*. UCLA Brain Information  
828 Service/Brain Research Institute, Los Angeles, 1968.
- 829 Rodriguez-Moreno, D., & Hirsch, J. (2009). The dynamics of deductive reasoning: An fMRI  
830 investigation. *Neuropsychologia*, 47(4), 949–961.  
831 <https://doi.org/10.1016/j.neuropsychologia.2008.08.030>
- 832 Sandman, C. A., Head, K., Muftuler, L. T., Su, L., Buss, C., & Poggi, E. (2014). NeuroImage  
833 Shape of the basal ganglia in preadolescent children is associated with cognitive  
834 performance. *NeuroImage*, 99, 93–102.  
835 <https://doi.org/10.1016/j.neuroimage.2014.05.020>
- 836 Schabus, M., Dang-Vu, T. T., Albouy, G., Balteau, E., Boly, M., Carrier, J., Darsaud, A.,  
837 Degueldre, C., Desseilles, M., Gais, S., Phillips, C., Rauchs, G., Schnakers, C.,  
838 Sterpenich, V., Vandewalle, G., Luxen, A., & Maquet, P. (2007). Hemodynamic cerebral  
839 correlates of sleep spindles during human non-rapid eye movement sleep. *Proceedings*  
840 *of the National Academy of Sciences of the United States of America*, 104(32), 13164–  
841 13169. <https://doi.org/10.1073/pnas.0703084104>
- 842 Schabus, M., Hödlmoser, K., Gruber, G., Sauter, C., Anderer, P., Klösch, G., Parapatics, S.,  
843 Saletu, B., Klimesch, W., & Zeitlhofer, J. (2006). Sleep spindle-related activity in the  
844 human EEG and its relation to general cognitive and learning abilities. *European Journal*  
845 *of Neuroscience*, 23(7), 1738–1746. <https://doi.org/10.1111/j.1460-9568.2006.04694.x>
- 846 Schiff, N. D., Plum, F., & Rezai, A. R. (2002). Developing prosthetics to treat cognitive  
847 disabilities resulting from acquired brain injuries. *Neurological Research*, 24(February),  
848 116–124. <https://doi.org/10.1179/016164102101199576>
- 849 Shallice, T. (1982). Specific Impairments of Planning. *Philosophical Transactions of the Royal*  
850 *Society B: Biological Sciences*, 298(1089), 199–209.  
851 <https://doi.org/10.1098/rstb.1982.0082>
- 852 Shibagaki, M., & Kiyono, S. (1983). Duration of spindle bursts during nocturnal sleep in  
853 mentally retarded children. *Electroencephalography and Clinical Neurophysiology*, 55(6),  
854 645–651. [http://doi.org/10.1016/0013-4694\(83\)90274-2](http://doi.org/10.1016/0013-4694(83)90274-2)
- 855 Shibagaki, M., Kiyono, S., & Watanabe, K. (1982). Spindle evolution in normal and mentally  
856 retarded children: a review. *Sleep*, 5(1), 47–57.
- 857 Shirvalkar, P., Seth, M., Schiff, N. D., & Herrera, D. G. (2006). Cognitive enhancement with

- 858 central thalamic electrical stimulation. *Proceedings of the National Academy of Sciences*  
859 *of the United States of America*, 103(45), 17007–17012.  
860 <https://doi.org/10.1073/pnas.0604811103>
- 861 Shouse, M. N., & Sterman, M. B. (1979). Changes in seizure susceptibility, sleep time and  
862 sleep spindles following thalamic and cerebellar lesions. *Electroencephalography and*  
863 *Clinical Neurophysiology*, 46(1), 1–12. [https://doi.org/10.1016/0013-4694\(79\)90044-0](https://doi.org/10.1016/0013-4694(79)90044-0)
- 864 Siapas, A. G., & Wilson, M. A. (1998). Coordinated interactions between hippocampal ripples  
865 and cortical spindles during slow-wave sleep. *Neuron*, 21(5), 1123–1128.  
866 [https://doi.org/10.1016/S0896-6273\(00\)80629-7](https://doi.org/10.1016/S0896-6273(00)80629-7)
- 867 Silverman, I., Choi, J., Mackewn, A., Fisher, M., Moro, J., & Olshansky, E. (2000). Evolved  
868 mechanisms underlying wayfinding. *Evolution and Human Behavior*, 21(3), 201–213.  
869 [https://doi.org/10.1016/S1090-5138\(00\)00036-2](https://doi.org/10.1016/S1090-5138(00)00036-2)
- 870 Silverstein, L. D., & Michael Levy, C. (1976). The stability of the sigma sleep spindle.  
871 *Electroencephalography and Clinical Neurophysiology*, 40(6), 666–670.  
872 [https://doi.org/10.1016/0013-4694\(76\)90142-5](https://doi.org/10.1016/0013-4694(76)90142-5)
- 873 Steriade, M. (2005). Sleep, epilepsy and thalamic reticular inhibitory neurons. *Trends*  
874 *Neurosci*, 28(6), 317–324. <https://doi.org/10.1016/j.tins.2005.03.007>
- 875 Steriade, M., Contreras, D., Curro Dossi, R., & Nunez, A. (1993). The slow (< 1 Hz) oscillation  
876 in reticular thalamic and thalamocortical neurons: scenario of sleep rhythm generation in  
877 interacting thalamic and neocortical networks. *Journal of Neuroscience*, 13(8), 3284.
- 878 Steriade, M., McCormick, D. A., & Sejnowski, T. J. (1993). Thalamocortical oscillations in the  
879 sleeping and aroused brain. *Science (New York, N.Y.)*, 262(5134), 679–85.  
880 <https://doi.org/10.1126/science.8235588>
- 881 Steriade, M., Nunez, A., & Amzica, F. (1993). A novel slow (< 1 Hz) oscillation of neocortical  
882 neurons in vivo: depolarizing and hyperpolarizing components. *Journal of Neuroscience*,  
883 13(8), 3252.
- 884 Stoodley, C. J. (2012). The cerebellum and cognition: Evidence from functional imaging  
885 studies. *Cerebellum*, 11(2), 352–365. <https://doi.org/10.1007/s12311-011-0260-7>
- 886 Tomasi, D., Chang, L., Caparelli, E. C., & Ernst, T. (2007). Different activation patterns for  
887 working memory load and visual attention load. *Brain Research*, 1132(1), 158–165.  
888 <https://doi.org/10.1016/j.brainres.2006.11.030>
- 889 Tyvaert, L., Levan, P., Grova, C., Dubeau, F., & Gotman, J. (2008). Clinical Neurophysiology  
890 Effects of fluctuating physiological rhythms during prolonged EEG-fMRI studies. *Clinical*  
891 *Neurophysiology*, 119(12), 2762–2774. <https://doi.org/10.1016/j.clinph.2008.07.284>
- 892 Ujma, P. P., Bódizs, R., Gombos, F., Stintzing, J., Konrad, B. N., Genzel, L., Steiger, A., &  
893 Dresler, M. (2015). Nap sleep spindle correlates of intelligence. *Scientific Reports*, 5,  
894 17159. <https://doi.org/10.1038/srep17159>
- 895 Ujma, P. P., Konrad, B. N., Genzel, L., Bleifuss, A., Simor, P., Pótári, A., Körmendi, J.,  
896 Gombos, F., Steiger, A., Bódizs, R., & Dresler, M. (2014). Sleep spindles and  
897 intelligence: evidence for a sexual dimorphism. *J Neurosci*, 34(49), 16358–16368.  
898 <https://doi.org/10.1523/JNEUROSCI.1857-14.2014>

- 899 Van der Werf, Y. D., Jolles, J., Witter, M. P., & Uylings, H. B. M. (2003). Contributions of  
900 thalamic nuclei to declarative memory functioning. *Cortex; a Journal Devoted to the*  
901 *Study of the Nervous System and Behavior*, 39(4–5), 1047–62.  
902 [https://doi.org/10.1016/S0010-9452\(08\)70877-3](https://doi.org/10.1016/S0010-9452(08)70877-3)
- 903 Van Der Werf, Y. D., Witter, M. P., Uylings, H. B. M., & Jolles, J. (2000). Neuropsychology of  
904 infarctions in the thalamus: A review. *Neuropsychologia*, 38(5), 613–627.  
905 [https://doi.org/10.1016/S0028-3932\(99\)00104-9](https://doi.org/10.1016/S0028-3932(99)00104-9)
- 906 von Krosigk, M., Bal, T., & McCormick, D. A. (1993). Cellular mechanisms of a synchronized  
907 oscillation in the thalamus. *Science*, 261(5119), 361–364.
- 908 Waltz, J. A., Knowlton, B. J., Holyoak, K. J., Boone, K. B., Mishkin, F. S., de Menezes Santos,  
909 M., Thomas, C.R., & Miller, B. L. (1999). A System for Relational Reasoning in Human  
910 Prefrontal Cortex. *Psychological Science*, 10(August 2015), 119–125.  
911 <https://doi.org/10.1111/1467-9280.00118>
- 912 Wamsley, E. J., Tucker, M. A., Shinn, A. K., Ono, K. E., McKinley, S. K., Ely, A. V, ...  
913 Manoach, D. S. (2012). Reduced sleep spindles and spindle coherence in schizophrenia:  
914 mechanisms of impaired memory consolidation? *Biological Psychiatry*, 71(2), 154–61.  
915 <https://doi.org/10.1016/j.biopsych.2011.08.008>
- 916 Watanabe, Y., & Funahashi, S. (2012). Thalamic mediodorsal nucleus and working memory.  
917 *Neuroscience and Biobehavioral Reviews*, 36(1), 134–142.  
918 <https://doi.org/10.1016/j.neubiorev.2011.05.003>
- 919 Wechsler, D. (1997). *Wechsler Adult Intelligence Scale—III*. The Psychological Corporation.  
920 San Antonio, TX.
- 921 Werth, E., Achermann, P., Dijk, D. J., & Borbely, A. A. (1997). Spindle frequency activity in  
922 the sleep EEG: individual differences and topographic distribution.  
923 *Electroencephalography and Clinical Neurophysiology*, 103(5), 535–542.  
924 <https://doi.org/S0013469497000709> [pii]
- 925 Zeitlhofer, J., Gruber, G., Anderer, P., Asenbaum, S., Schimicek, P., & Saletu, B. (1997).  
926 Topographic distribution of sleep spindles in young healthy subjects. *Journal of Sleep*  
927 *Research*, 6(3), 149–155.

928

929

930

931

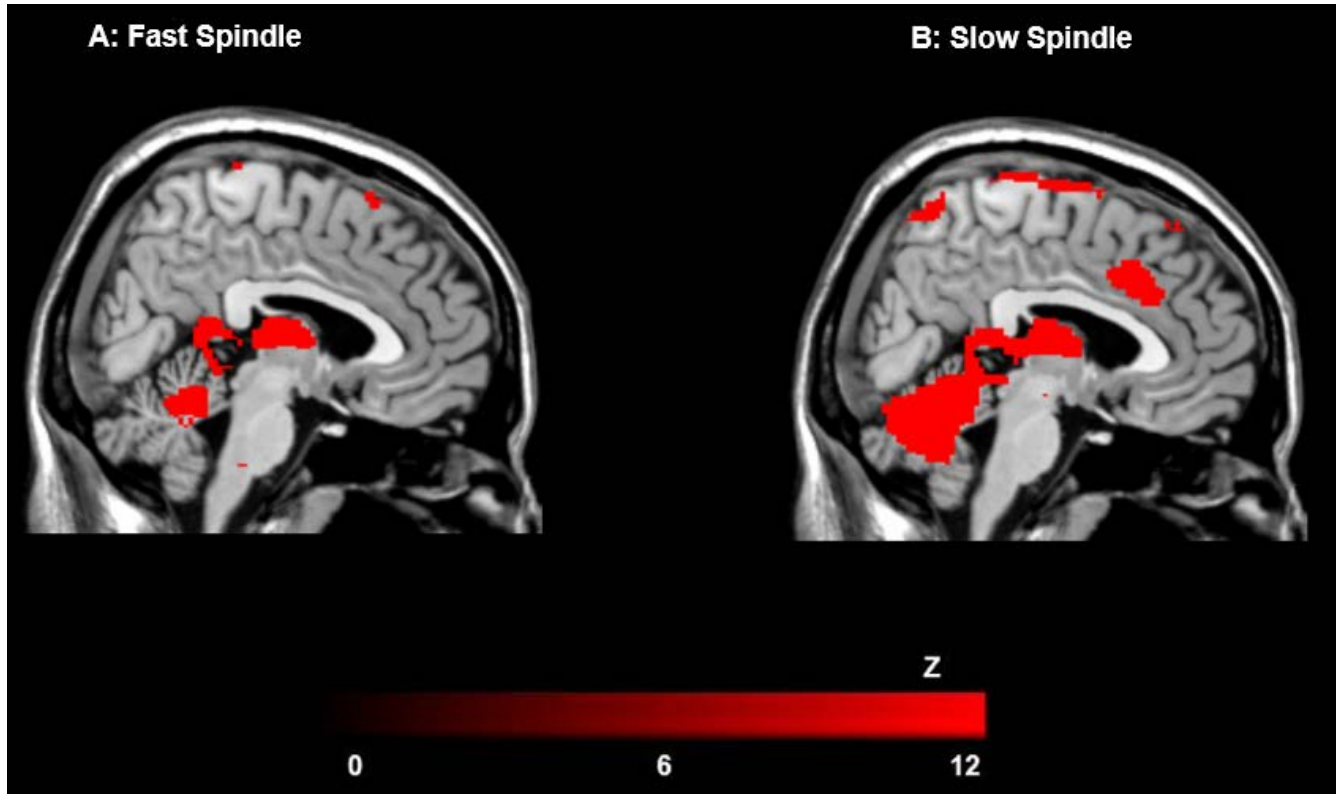
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935 **SUPPLEMENTARY FIGURES**

936 **Figure S1. Cerebral activation of fast and slow spindles.** Activations time-locked to fast spindles (13.5-16 Hz)  
937 at Pz (**A**) and slow spindles (11-13.5 Hz) at Fz (**B**) were similar in all brain areas, but visibly to a greater extent in  
938 fast spindles (with the exception of medial frontal activation in slow but not fast spindles). However, there were no  
939 significant difference between fast spindles vs. slow spindle-related activations.



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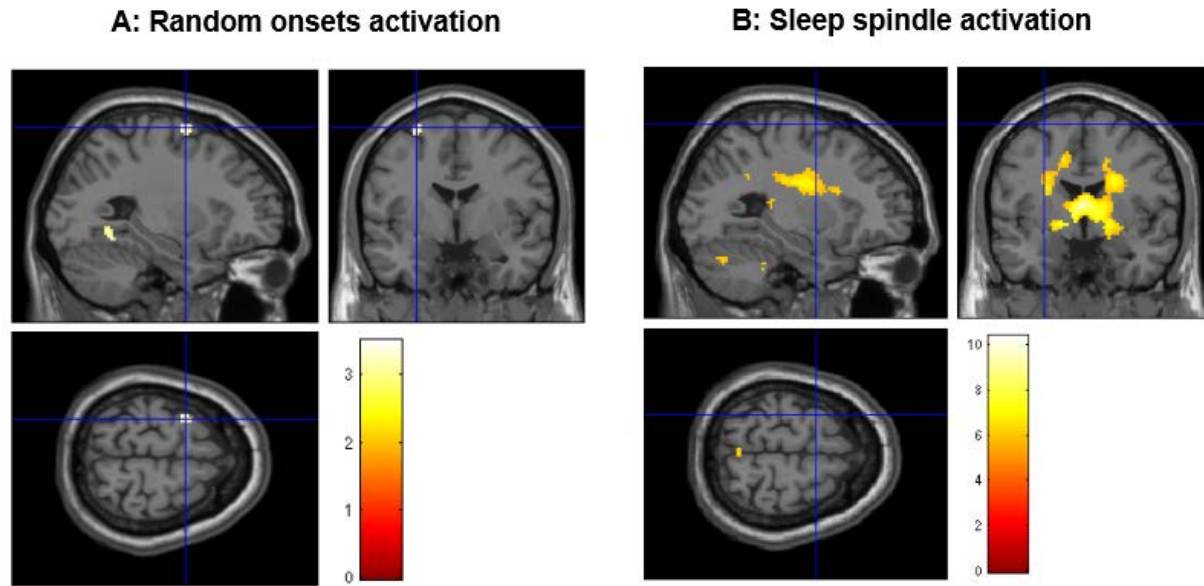
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948 **Figure S2. Cerebral activations time-locked to random onsets in NREM stage sleep.** The results revealed a  
949 small single cluster at left frontal lobe which did not survive FWE correction (peak coordinate: -28, -2, 68;  
950 uncorrected  $p < 0.005$ ) (A), and did not overlap with activations time-locked to spindles (B).