



HAL
open science

Delta oscillations coordinate intra-cerebellar and cerebello-hippocampal network dynamics during sleep

A Torres-Herraez, T C Watson, L Rondi-Reig

► **To cite this version:**

A Torres-Herraez, T C Watson, L Rondi-Reig. Delta oscillations coordinate intra-cerebellar and cerebello-hippocampal network dynamics during sleep. *Journal of Neuroscience*, 2022, 42 (11), pp.2268-2281. 10.1523/JNEUROSCI.1479-21.2021. . hal-03368185

HAL Id: hal-03368185

<https://hal.science/hal-03368185v1>

Submitted on 6 Oct 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 **Delta oscillations coordinate intra-cerebellar and cerebello-hippocampal network**
2 **dynamics during sleep**

3 Torres-Herraez A¹, Watson TC*¹ and Rondi-Reig L*^{1§}

4 ¹Sorbonne Université, CNRS, INSERM, Institut de Biologie Paris Seine (IBPS), Neurosciences Paris Seine
5 (NPS), Cerebellum Navigation and Memory Team (CeZaMe), F-75005 Paris, France

6 ATH current address: Department of Psychiatry, Columbia University Medical Center, New York, NY
7 10032

8 TCW current address: Centre for Discovery Brain Sciences, University of Edinburgh, Edinburgh, United
9 Kingdom; Simons Initiative for the Developing Brain, University of Edinburgh, Edinburgh, United
10 Kingdom; Patrick Wild Centre for Autism Research, University of Edinburgh, Edinburgh, United
11 Kingdom

12 § Corresponding author: laure.rondi-reig@sorbonne-universite.fr
13 IBPS, Neurosciences Paris Seine, Sorbonne Université, Campus Jussieu, CeZaMe team, 9 Quai Saint
14 Bernard, 5e étage, Pièce 519, 75005 Paris, France

15 * These authors contributed equally to this work

16

17

18

19

20

21

22

23

24

25

26

27

28

29 **Abstract:**

30 During sleep, the widespread coordination of neuronal oscillations across both cortical and subcortical
31 brain regions is thought to support various physiological functions, including memory consolidation.
32 However, how sleep-related activity within the brain's largest sensorimotor structure, the cerebellum,
33 is multiplexed with well described sleep-related mechanisms in regions such as the hippocampus
34 remains unknown.

35 To address this gap in knowledge, we simultaneously recorded from the dorsal hippocampus and
36 three distinct regions of the cerebellum (Crus I, lobule VI and lobules II/III) during natural murine sleep.
37 We found that LFP oscillations are coordinated between the two structures in a sleep-stage specific
38 manner. Particularly during non-REM sleep, prominent delta frequency coherence was observed
39 between lobule VI and hippocampus. We additionally observed that non-REM associated hippocampal
40 sharp wave ripple activity can drive discrete LFP modulation in all the recorded cerebellar regions,
41 with the shortest latency effects observed in lobule VI.

42 We also describe discrete phasic sharp potentials, synchronized across cerebellar regions, which were
43 strongly phase locked to the peak of ongoing cerebellar delta oscillations and found in greatest
44 numbers during REM. These phasic sharp potentials recorded within the cerebellar cortex were found
45 to be phase-locked to the trough of the hippocampal theta oscillation, further suggesting cross-
46 structural coordination. During REM, cerebellar delta oscillation phase significantly modulated
47 hippocampal theta frequency, and this effect was greatest when phasic sharp potentials were most
48 abundant. Within all three cerebellar regions, prominent LFP oscillations were observed at both low
49 (delta, <4 Hz) and very high frequencies (~ 250 Hz) during non-REM and REM sleep. Intra-cerebellar
50 cross-frequency analysis revealed that delta frequency oscillations strongly modulate those in the very
51 high frequency range.

52 Together, these results reveal multiple candidate physiological mechanisms to support 'offline', bi-
53 directional interaction within distributed cerebello-hippocampal networks. In particular, we describe
54 a prominent cerebellar delta oscillation, which appears to act as a temporal coordinator of cerebellar
55 activity at both local (intra-cerebellar) and distributed (cerebello-hippocampal) network levels.

56

57

58

59

60 **Introduction**

61 Many important physiological processes are associated with sleep, including memory formation and
62 consolidation (Diekelmann and Born, 2010). In particular, sleep-related neurophysiological events in
63 the hippocampus, such as place cell reactivations and high frequency sharp wave ripples are vital to
64 spatial memory formation (e.g. de Lavilléon et al., 2015). Additionally, widespread slow wave
65 oscillations are thought to play a crucial role in the temporal coordination of discrete sleep-related
66 events, such as hippocampal ripples and thalamo-cortical spindles, across a large network of brain
67 regions (e.g. Nicola et al., 2019)

68 Recent studies have shown that during wakeful behaviour the cerebellum is crucial for hippocampal
69 place cell stability and efficient navigation (Rocheffort et al., 2011; Lefort et al., 2019; Burguière et al.,
70 2005, Babayan et al., 2017). Furthermore, the neuroanatomical connectivity required to support this
71 influence has been recently described and physiological correlates of cerebello-hippocampal
72 interaction identified 'online' during goal-directed navigation (Watson et al., 2019). So far, however,
73 nothing is known about possible 'offline' cerebello-hippocampal physiological interactions during
74 sleep.

75 To date, sleep research has primarily focused on state-dependent correlation in neocortical and
76 subcortical structures. However, early studies in epileptic patients implanted with intra-cerebellar
77 electrodes (Niedermeyer and Uematsu, 1974) and recent work using non-invasive techniques (Jahnke
78 et al., 2012; Kaufmann et al., 2006; Schabus et al., 2007) have described state-dependent modulation
79 of cerebellar activity during sleep in humans. During non-rapid eye movement (non-REM) sleep,
80 coordinated slow oscillations, recorded predominantly in cerebellar vermis and fastigial nucleus
81 (Niedermeyer and Uematsu, 1974; Schabus et al., 2007), are correlated with neocortical K-complexes
82 (Jahnke et al., 2012) and sleep spindles (Schabus et al., 2007). During REM sleep, an increase in blood-
83 oxygen-level-dependent signals has been observed in both the cerebellar vermis and hemispheres
84 (Braun, 1997).

85 Similarly, single-cell recording in animal models has revealed sleep-state related changes in both
86 Purkinje cell and deep cerebellar nuclei neuron firing. During non-REM, no clear neuronal firing rate
87 changes were observed either in cats (Hobson and McCarley, 1972; Marchesi and Strata, 1970;
88 McCarley and Hobson, 1972; Palmer, 1979) or monkeys (Mano, 1970). However, a reduced probability
89 for short interspike intervals was observed in Purkinje cell simple spike firing (McCarley and Hobson,
90 1972). Consistent with observations made in humans, during REM sleep a significant increase in the
91 firing rate of Purkinje cells was observed in the cerebellar cortex of cats (Hobson and McCarley, 1972;
92 Marchesi and Strata, 1970) and monkeys (Mano, 1970). The presence of large amplitude, phasic

93 events in the cerebellum of cats (Harley et al., 1974; Pellet and Harley, 1977) and rats (Marks et al.,
94 1980), mainly during REM sleep epochs, has also been attributed to the transmission of ponto-
95 geniculo-occipital waves (PGO waves; Farber et al., 1980; Velluti et al., 1985). Finally, recent studies
96 have highlighted cerebellar roles in the generation of sleep spindles in monkeys (Xu et al., 2020) and
97 sleep-wake transitions in mice (Zhang et al., 2020).

98 Thus, in addition to the multitude of studies highlighting the functional importance of sleep-state
99 dependent processes in the hippocampus (see Klinzing et al., 2019 for review) the aforementioned
100 evidence indicates clear cerebellar activity modulation during sleep (reviewed in Canto et al., 2017).
101 Nevertheless, our understanding of spatial and temporal organisation of cerebellar activity across
102 sleep states remains rudimentary. Furthermore, to the best of our knowledge, nothing is known about
103 the physiological links between cerebellum and hippocampus during sleep. We therefore
104 simultaneously recorded spontaneous local field potentials (LFPs) from the dorsal hippocampus,
105 vermal cerebellar lobules II/III (Lob II/III), VI (Lob VI) and hemispheric Crus I in freely behaving and
106 sleeping mice. Our analysis reveals that delta oscillations, along with associated phasic sharp
107 potentials (PSPs), coordinate both local cerebellar and distributed cerebello-hippocampal network
108 dynamics in a sleep-state dependent manner.

109

110 **Results**

111 **Spectral profiling of cerebellar and hippocampal activity across sleep states**

112 In line with previous studies (e.g. Montgomery et al., 2008), hippocampal LFP was dominated by
113 sustained, low amplitude theta oscillations (6 - 12 Hz) during wake and REM states, and high amplitude
114 slow oscillations in the delta range (< 4 Hz) during non-REM sleep (Figure 1 A-C).

115 Conversely, high amplitude low frequency oscillations (including < 4 Hz delta waves) were
116 characteristic of wake, REM and non-REM states in the cerebellum (Figure 1 A-C). However,
117 differences in delta oscillation power, as well as peak frequency, were observed both across cerebellar
118 subregions and wake/sleep states (Figure 1C, Supplemental Figure 1A-B). Similarly, a significant shift
119 in the peak delta frequency was observed during non-REM sleep, specifically in Lob VI (Supplemental
120 Figure 1B). In contrast, these differences were not observed during REM, when similar spectral profiles
121 were found across cerebellar regions (Figure 1C). Moreover, delta oscillations were highly coherent
122 between cerebellar recording sites (Figure 1B, Supplementary Figure 2), suggesting they may play a
123 role in intra-cerebellar coordination during REM sleep.

124 In addition to delta activity during wake, high-frequency oscillations (100-160 Hz) were also observed
125 in the cerebellar power spectra (Figure 1C). However, during both non-REM and REM states, power in
126 the high-frequency range was overshadowed by a prominent, narrowband ~240-280 Hz oscillation
127 (classified as very-high frequency oscillations, VHFOs; de Solages et al., 2008; Figure 1C; Supplemental
128 Figure 1C). Local variability within this frequency band was observed across cerebellar regions and
129 sleep states, with maximal values observed in Lob II/III during non-REM and REM sleep (Supplemental
130 Figure 1D). In contrast, Crus I VHFO power was particularly reduced in REM (Figure 1C, Supplemental
131 Figure 1D, paired t-tests: Crus I: n = 11, p = 0.0005; Lob II/III, n = 11, Crus I, n = 11; Lob VI, n = 15; Lob
132 II/III, n = 11 mice).

133 Overall, these data illustrate the presence of lobule and sleep-state dependent LFP dynamics across
134 anterior (Lob II/III), posterior (Lob VI) and hemispheric (Crus I) cerebellum and highlight the existence
135 of a prominent cerebellar delta oscillation.

136

137 Cerebello-hippocampal coherence across sleep states

138 Next, we sought to measure the level of functional coupling (measured as coherence; cf Watson et al.,
139 2019; Xu et al., 2020) between the cerebellum and hippocampus during wake/sleep states (Figure 1D,
140 E). During wake, coherence peaks were similarly observed across delta and theta frequencies in all
141 cerebello-hippocampal combinations (Figure 1D, left panel). Strikingly, as mice moved to non-REM
142 sleep, delta band coherence between hippocampus and Lob VI was significantly increased relative to
143 other recorded cerebellar regions (Figure 1D, Supplemental Figure 3) indicating region-specific
144 cerebello-hippocampal coupling during this sleep state. Furthermore, significant modulation of delta
145 and theta coherence across sleep states was present in HPC-Lob VI and HPC-Lob II/III recording
146 combinations, while remaining stable between HPC-Crus I (Figure 1D; Supplemental Figure 3). In
147 contrast, during REM sleep, coherence patterns were similar to wake, with the most prominent peaks
148 observed in the theta and low frequency range (< 1Hz; Figure 1D, right panel; Supplemental Figure 3).

149 In summary, by characterizing the spectral properties of cerebello-hippocampal network LFP during
150 wake and sleep we reveal that coherence between these regions is sleep-state dependent and
151 particularly prominent between hippocampus and Lob VI during the non-REM stage of sleep.

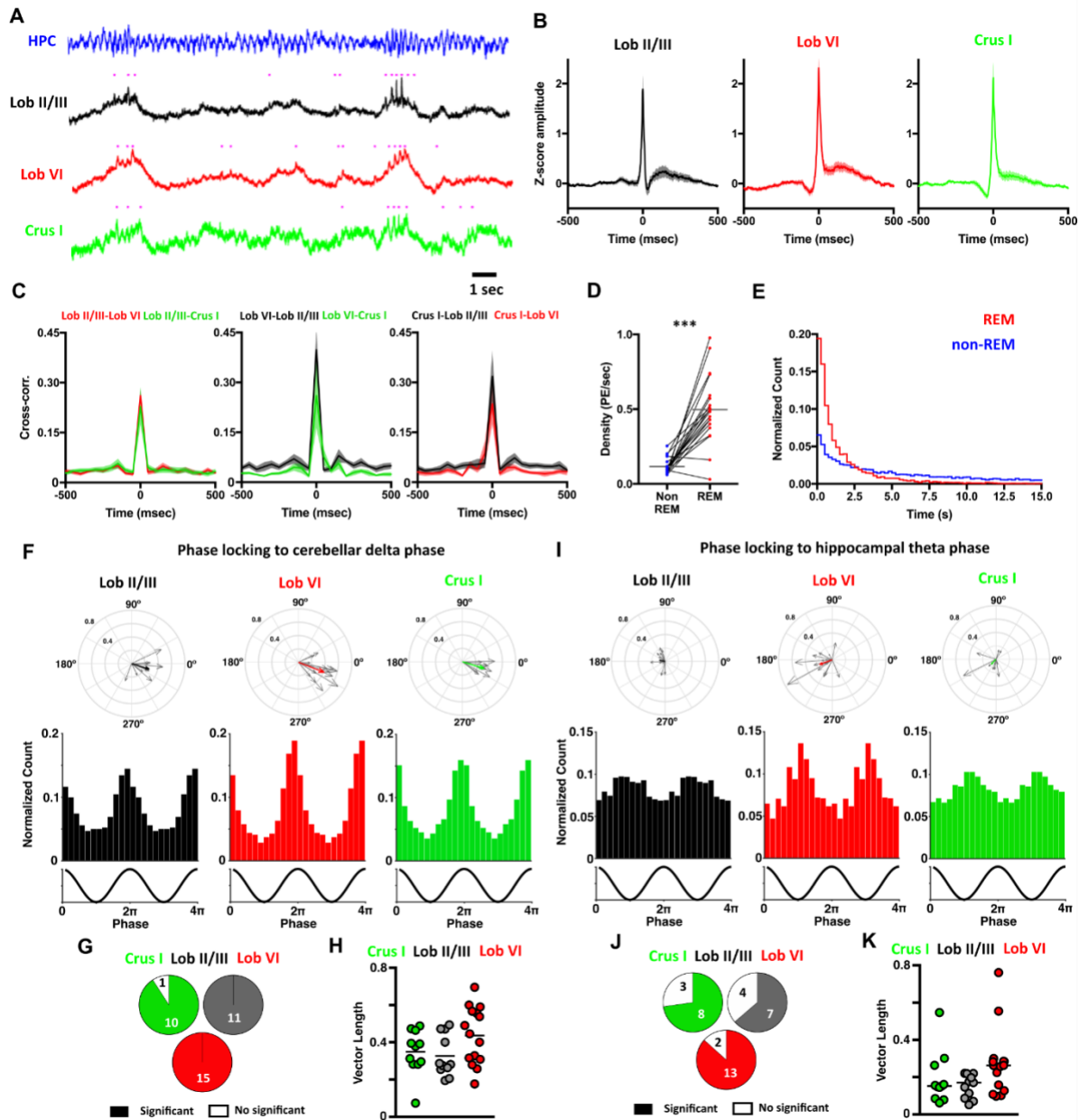
152

153

165 REM associated cerebellar phasic sharp potentials phase lock to both local cerebellar and distant
166 hippocampal oscillations, respectively.

167 In addition to the striking sleep-state related changes observed in ongoing cerebellar LFP oscillations,
168 we also noted prominent phasic sharp potential events (PSPs; large-amplitude voltage fluctuations of
169 129.5 ± 5.68 ms duration and 2.31 ± 0.15 z-score amplitude) across the three cerebellar recording sites
170 (Figure 2A-C). PSPs occurred in all three cerebellar regions at similar times (cross-correlation between
171 all pairs of cerebellar recorded PSPs revealed a peak at 0 latency; Figure 2A-C) and were found during
172 both REM and non-REM epochs; however, they occurred in greatest numbers during REM (PSP density
173 during non-REM = 0.12 ± 0.01 , PSP density during REM = 0.5 ± 0.05 , Wilcoxon test $P < 0.0001$; Figure
174 2A, D). Moreover, PSPs occurred in concentrated clusters during REM (inter-event interval < 1 s) but
175 were distributed more sparsely during non-REM (Figure 2E). We also observed that during REM
176 epochs, PSPs tended to occur at specific phases of the ongoing cerebellar delta waves in all three
177 cerebellar regions (Figure 2A). This observation was confirmed by computing the distribution of PSP
178 events relative to the phase of REM associated cerebellar delta waves (Figure 2F-H; PSPs occurred
179 most often near the peak of the cycle with a preferred angle of $350.6 \pm 2.248^\circ$ and with similar levels
180 across all three cerebellar regions, Figure 2G, H). Next, we investigated phase locking of PSPs recorded
181 in the cerebellum relative to hippocampal LFP theta phase during REM (Figure 2I), which revealed that
182 these events occur consistently near the trough of the theta cycle (preferred phase angle, $147.4 \pm$
183 15.93° ; Figure 2I) and at similar levels across cerebellar regions (Figure 2 J,K).

184



185

186 **Figure 2. Phasic potentials (PSPs) occur at preferred phases of cerebellar delta and hippocampal**
 187 **theta oscillations during REM.** **A**, We observed phasic potentials in the cerebellar LFP recordings
 188 during REM (indicated by purple dots), which occurred preferentially during up-phase of the delta
 189 oscillations. Moreover, hippocampal theta frequency was transiently accelerated during the up-phase
 190 of the cerebellar delta oscillations. **B**, PSPs were found in all cerebellar recording sites and all mice.
 191 Averaged waveforms across animals (Lob II/III n = 11; Lob VI n = 15; Crus I n = 11). **C**, Cross-
 192 correlograms between the PSPs detected at a given cerebellar region and those recorded in the others.
 193 All cross-correlograms show a peak with ≤ 50 ms lag suggesting that most of the PSPs co-occurred at
 194 the three cerebellar regions near simultaneously. **D**, PSPs were observed during non-REM and REM
 195 sleep, however, the density of these events was significantly higher during REM (non-REM density =
 196 0.1152 ± 0.012 PSPs/s; REM density = 0.4973 ± 0.050 PSPs/s; paired t-test, $P < 0.0001$). **E**, The
 197 distributions of the inter-event intervals (IEIs) were significantly different between non-REM and REM
 198 epochs (Two-sample Kolmogorov-Smirnov test, $P < 0.0001$). During REM, PSPs were preferentially

199 concentrated as clusters (IEIs < 1 s). **F**, PSPs recorded at all cerebellar regions were phase-locked to
200 the local delta oscillations during REM. In the top panels, the individual vectors of the phase locking
201 for each mouse (grey arrows) and the average vector across all mice (colour coded; resultant vector
202 angle: Crus I = 342.97 °, Lob II = 343.05 °, Lob VI = 338.67 °. Resultant vector length: Crus I = 0.34, Lob
203 II = 0.28, Lob VI = 0.41). In the bottom panels, the normalized count of PSPs recorded at the different
204 phases of delta oscillations in all mice for each cerebellar region (Lob II/III = 4004 PSPs/11 mice,
205 Rayleigh's test, $P < 0.001$; Lob VI = 3445 PSPs/15 mice, Rayleigh's test, $P < 0.001$; Crus I = 3398 PSPs/11
206 mice, Rayleigh's test, $P < 0.001$). **G**, Fraction of mice with significant phase locking (significant phase
207 locking was found in Crus I, 10/11 mice; Lob II/III, 11/11 mice; Lob VI 15/15 mice). **H**, The level of the
208 phase locking did not differ across cerebellar regions (1-way ANOVA, $P = 0.0932$). **I-K**, Same as for **F-H**
209 but here calculating phase locking of PSPs detected in the cerebellum to ongoing hippocampal theta
210 oscillations. **I**, Top row; Lob II/III Rayleigh's test, $P < 0.001$; Lob VI Rayleigh's test, $P < 0.001$; Crus I
211 Rayleigh's test, $P < 0.001$. **J**, Fraction of mice with significant phase locking of PSPS to hippocampal
212 theta (significant phase locking was found in Crus I, 8/11 mice; Lob II/III, 7/11 mice; Lob VI 13/15 mice).
213 **K**, The level of the phase locking to hippocampal theta did not differ across cerebellar regions (Kruskal-
214 Wallis Test of vector lengths, $P = 0.0717$).

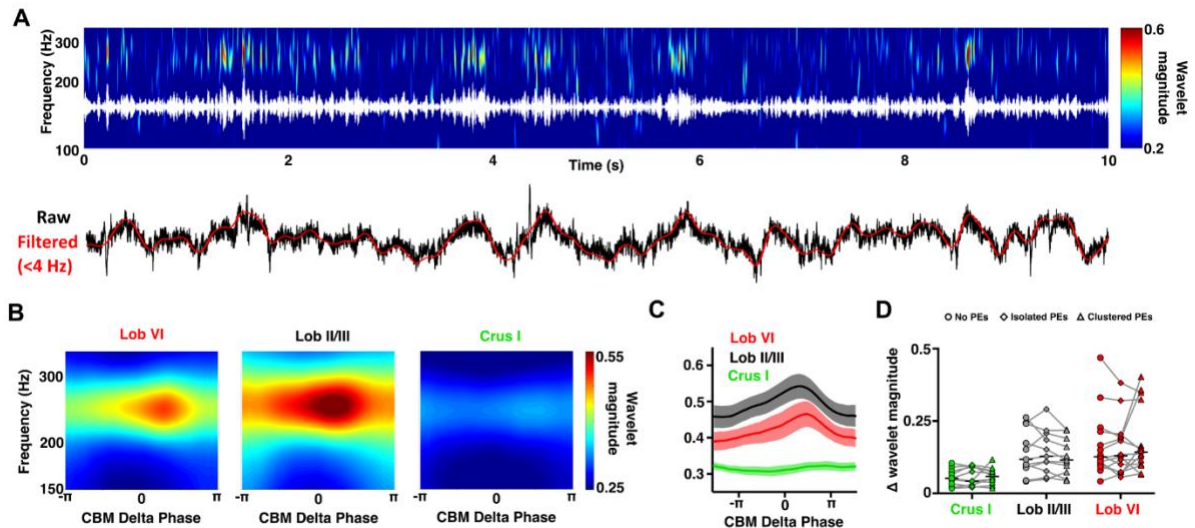
215

216 Intracerebellar cross-frequency modulation: cerebellar delta is a modulator of VHFOs during REM.

217 The most prominent, ongoing LFP oscillations observed in the cerebellum during REM sleep were
218 found in the delta (<4 Hz) and VHFO (~ 250Hz) frequency ranges, respectively (see Figure 1). Thus, to
219 investigate any relationship between these two oscillators, we conducted cross-frequency spectral
220 analysis (Figure 3). This revealed that during REM, the power of cerebellar VHFOs is significantly
221 modulated by the phase of those in the delta range (Figure 3B, C). Interestingly, this modulation was
222 significant only in vermal regions (Lob VI, II/III) and not in Crus I. This finding is consistent with the
223 reduced presence of VHFOs during REM in this cerebellar region compared to the others recorded
224 (Figure 1C, Supplemental Figure 1D), further indicating spatial heterogeneity in cerebellar processing
225 during sleep.

226 Since PSPs were highly abundant during REM and also phase locked to cerebellar delta, we
227 investigated whether they play a role in local cross-frequency modulation between delta phase and
228 VHFO power. By comparing modulation in delta cycles with no PSPs, those containing isolated PSPs
229 and those containing clusters of PSPs (Figure 3D), we found that PSP density did not significantly
230 influence the degree of cross-frequency modulation observed in any of the recorded cerebellar
231 regions (Figure 3D).

232



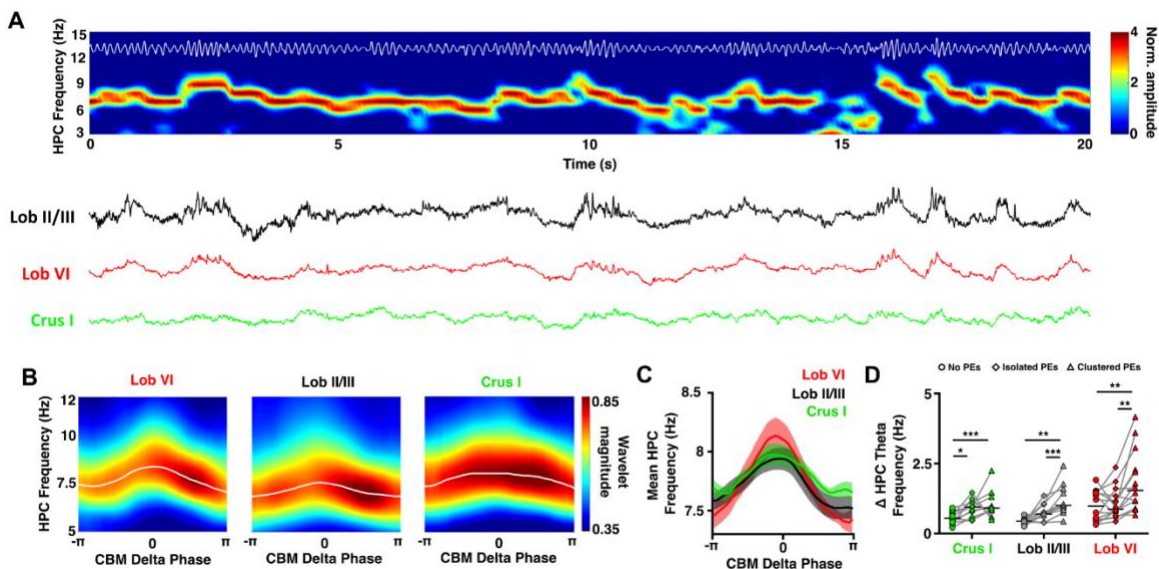
233
 234 **Figure 3. Modulation of VHFOs frequency oscillations by delta oscillations within the cerebellum**
 235 **during REM.** A, Representative spectrogram (top; with VHFO frequency filtered trace overlaid in
 236 white) and raw cerebellar LFP recordings (bottom; with delta frequency filtered oscillations overlaid
 237 in red) showing the modulation of VHFOs by cerebellar delta oscillations during a REM epoch. The
 238 cerebellar LFP is dominated by both delta oscillations and VHFOs, which fluctuate dynamically within
 239 the ~ 250 Hz and <4 Hz ranges, respectively. The fluctuations in cerebellar VHFO power appear
 240 temporally aligned to the prominent delta oscillations in the cerebellar LFP. B, Average spectrograms
 241 aligned to the phase of the cerebellar delta oscillations (<4 Hz) during REM sleep. The power of
 242 cerebellar VHFOs appears greatest following the peak of cerebellar delta (zero phase radians) in
 243 vermal lobules (VI, II/III) but not Crus I. C, Average cerebellar VHFO power aligned to cerebellar delta
 244 oscillation phase (RM 2-Way ANOVA Cerebellar Region \times Delta Phase: Delta Phase $P < 0.0001$,
 245 Cerebellar region $P = 0.0001$, Interaction $P = 0.0002$. Multiple comparisons of power across delta phase
 246 compared to trough value with FDR correction: Crus I: $p > 0.05$, Lob II: $p < 0.01$ from $-18.9^\circ - 78.5^\circ$ ($-$
 247 $0.105\pi - 0.44\pi$) Lob VI: $p < 0.01$ from $-3.72^\circ - 93.97^\circ$ ($-0.02\pi - 0.52\pi$). D, Effect of PSP abundance
 248 during the cerebellar delta oscillations on the modulation of VHFOs during REM. We compared the
 249 maximal change in cerebellar VHFO power during cerebellar delta oscillations in which no PSPs,
 250 isolated PSPs or clusters of PSPs were detected. No significant differences were observed for the three
 251 cerebellar regions (2-Way ANOVA Cerebellar Region \times Content of PSPs: Content of PSPs $P = 0.8449$,
 252 Cerebellar Region $P = 0.003$, Interaction $P = 0.2601$, Multiple comparisons across cerebellar region
 253 effect with FDR correction: Crus I \times Lob II, corrected $p = 0.0101$, Crus I \times Lob VI, corrected $p = 0.0009$,
 254 Lob II \times Lob VI, corrected $p = 0.1004$). In all mean plots, $n =$ Lob VI, $n = 15$ mice; Crus I, $n = 11$ mice; Lob
 255 II/III, $n = 11$ mice.

256

257 Cerebellar delta and phasic sharp potentials modulate hippocampal theta oscillations during REM

258 We next investigated if the prominent cerebellar delta oscillations and the high density of PSPs
 259 observed during REM was related to, or impacted upon, theta oscillations in the hippocampus, which
 260 are a well described physiological signature of REM sleep (Figure 4). During REM, hippocampal theta
 261 oscillations fluctuated within a frequency range of approximately 6-12 Hz and visual inspection of

262 spectra and raw LFP traces revealed that these theta frequency fluctuations appeared to be
 263 temporally aligned with cerebellar delta oscillation cycles/PSP events (Figure 4A). Therefore, we next
 264 calculated hippocampal LFP power spectra triggered from the peak of cerebellar delta wave cycles.
 265 This analysis revealed that hippocampal theta frequency increased during the ascending phase of the
 266 cerebellar delta oscillation when compared with the values at the trough ($-\pi$) (triggered from Crus I:
 267 maximal frequency of hippocampal theta = 7.97 ± 0.095 Hz at -18.74° (-0.1π); triggered from Lob II:
 268 maximal frequency of hippocampal theta = 7.94 ± 0.095 Hz at -3.72° (-0.02π); triggered from Lob VI:
 269 maximal frequency of hippocampal theta = 8.14 ± 0.154 Hz at -18.74° (-0.1π) Figure 4B,C).
 270 Given that PSP timing is locked to specific phases of both cerebellar delta and hippocampal theta
 271 oscillation cycles (Figure 2), we next investigated if the number of PSPs occurring during the cerebellar
 272 delta wave was associated with the level of hippocampal theta modulation. In contrast to intra-
 273 cerebellar delta phase modulation of VHFOs, by comparing cycles with no PSPs, those containing
 274 isolated PSPs and those containing clusters of PSPs (Figure 4D), we found that the acceleration of
 275 hippocampal theta was most prominent when clusters of cerebellar PSPs were present (PSP quantity
 276 x cerebellar < 4 Hz phase repeated measures two-way ANOVA, quantity of PSP effect, $F(1,4) = 43.94$,
 277 $p = 0.0027$; interaction effect $F(47,188) = 4.678$, p -value < 0.0001), suggesting that these phasic events
 278 are linked to the observed changes in hippocampal theta frequency.



279

280 **Figure 4. Modulation of hippocampal theta frequency by cerebellar delta oscillations during REM.**
 281 **A**, Representative spectrogram (top; with theta filtered trace overlaid in white) and raw cerebellar LFP
 282 recordings (bottom) showing the modulation of hippocampal theta frequency by cerebellar delta
 283 oscillations during a REM epoch. The hippocampal LFP is dominated by theta oscillations, which
 284 fluctuate dynamically within the 6-12 Hz range. These fluctuations in hippocampal theta frequency
 285 appear temporally aligned to the delta oscillations dominating cerebellar LFPs (examples of this are

286 indicated by black horizontal bars above spectrogram). **B**, Example hippocampal spectrograms aligned
287 to the phase of the cerebellar delta oscillations (<4 Hz) during REM sleep. The preferred hippocampal
288 theta frequency (white line, overlaid) shows an acceleration coincident with the peak of the cerebellar
289 delta oscillations (0 phase radians). **C**, Average preferred hippocampal theta frequency aligned to
290 cerebellar delta oscillation phase (Lob VI, n = 15; Crus I, n = 11; Lob II/III, n = 11). Significant
291 hippocampal theta frequency acceleration was found from the trough of delta to the peak of delta in
292 all cerebellar regions. However, no differences in hippocampal theta frequency modulation were
293 observed between the delta oscillations recorded across the three cerebellar locations (repeated
294 measurements Two-way ANOVA phase x cerebellar region, phase effect $p < 0.0001$, region effect $p =$
295 0.7953 , interaction effect $p = 0.0295$). **D**, Effect of PSP abundance during the cerebellar delta
296 oscillations on the modulation of preferred hippocampal theta frequency during REM. We compared
297 the maximal change in hippocampal theta frequency during cerebellar delta oscillations in which no
298 PSPs, isolated PSPs or clusters of PSPs were detected. Significant differences were observed for the
299 three cerebellar regions (Crus I, Friedman test with FDR correction, $p = 0.0011$; Lob II/III, Friedman test
300 with FDR correction, $p < 0.0001$; Lob VI, Friedman test with FDR correction, $p = 0.0015$) with a
301 significant increase in the hippocampal theta modulation during delta waves when clusters of PSPs
302 were detected compared with those with no PSPs or isolated PSPs.

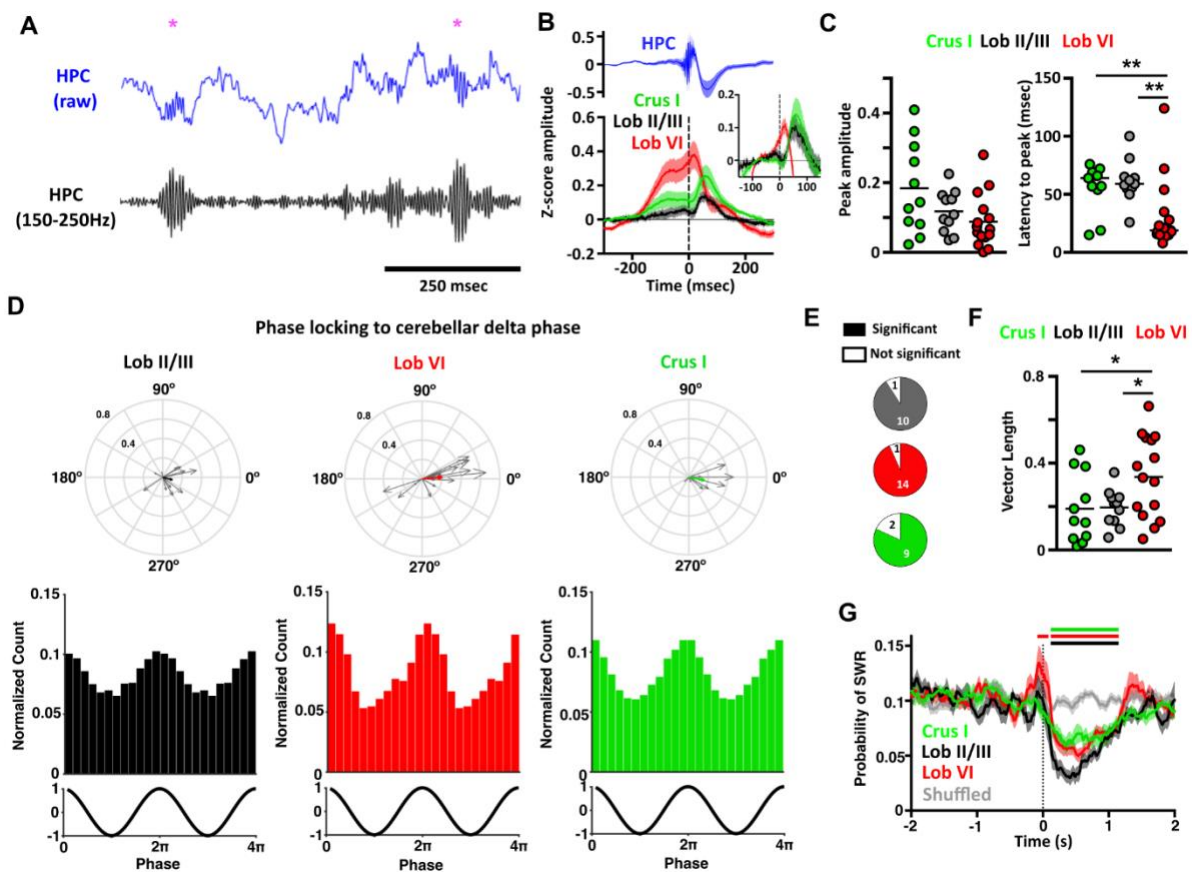
303

304 Hippocampal ripples drive LFP changes in the cerebellum

305 During REM, dominant hippocampal theta oscillations are coordinated with prominent cerebellar LFP
306 network activity (delta oscillations and PSPs). During non-REM sleep, however, hippocampal activity
307 is characterized by the presence of prominent sharp-wave ripples (SWRs). Therefore, we next asked if
308 cerebellar activity is coordinated or modulated by hippocampal SWRs during non-REM sleep. To
309 address this question, we first detected SWRs (Figure 5A) and computed the cerebellar LFP averaged
310 relative to SWR maximal amplitude (Figure 5B). Event related field potentials (ERPs) were clearly
311 observed in all the recorded cerebellar regions. The SWR triggered responses were characterized by a
312 prominent slow component that preceded the onset timing of SWR maximal amplitude followed by
313 an ERP (occurring after SWR ripple maximal amplitude; Figure 5B). In order to compare the amplitude
314 of the ERPs across cerebellar regions, we normalized them by subtracting the pre-SWR maximal
315 baseline levels (Figure 5B inset). The onset-to-peak amplitude in normalized ERPs did not differ across
316 cerebellar regions (Figure 5C, left panel). In contrast, latency to ERP peak was shortest in Lob VI (32
317 ± 7.89 ms) compared to Crus I and to Lob II/III (Figure 5C, right panel).

318 We next asked whether the slow frequency component observed in the SWR-triggered responses
319 resulted from the timing of SWRs at the peak of cerebellar slow oscillation cycles. To probe this
320 question, we calculated phase locking of the detected hippocampal SWR relative to the phase of
321 cerebellar delta oscillations (<4 Hz, Figure 5D-F). We confirmed that hippocampal SWRs were phase
322 locked to the delta rhythm observed in all three recorded cerebellar regions but that the strength of

323 phase-locking was significantly greatest for Lob VI (Figure 5E, F). Given recent description of SWR
 324 propagation from hippocampus to neocortex (Nitzan et al., 2020), we also calculated SWR triggered
 325 spectral analysis of the cerebellar LFP (Supplemental Figure 4), which revealed no changes in the SWR
 326 frequency range (~150 Hz) and thus suggests hippocampal SWRs do not propagate directly or
 327 indirectly to the cerebellum. Finally, we investigated potential interplay between PSPs recorded in the
 328 cerebellum and hippocampal SWRs. To do so, we computed the probability of detecting a SWR
 329 following the detection of a PSP. We found a consistent decrease in SWR probability ~10 ms after the
 330 PSP peak in all cerebellar regions, which lasted for ~1 sec (compared with a shuffled dataset; Figure
 331 5G). This reduction in SWR occurrence immediately following the PSPs suggests that the latter have
 332 an impact on local hippocampal activity.



333

334 **Figure 5. Hippocampal sharp-waves ripples (SWR) trigger evoked activity in the cerebellum.**

335 **A**, Example of the raw (blue) and filtered (150-250 Hz, black) hippocampal LFP during non-REM sleep.
 336 SWR were identified (purple asterisks) at the maximal value in the filtered signal. **B**, Averaged SWR-
 337 triggered waveforms from the cerebellar recordings. Zero time represents the time of detected SWR
 338 peak in the filtered signal. Evoked field potentials were observed in all the cerebellar recordings. The
 339 averaged waveforms in Lob VI and Crus I revealed that the SWR occurred at the peak of cerebellar
 340 delta oscillations. Inset, shows the same data but baselined against values from -100 to -50 msec,
 341 eliminating the slow frequency component and allowing clearer visualization of the evoked potentials.

342 **C**, From the baseline normalised data, we quantified the ERP amplitude measured as the onset-to-
343 peak value and also the onset latency. No significant differences were observed for amplitude (Crus
344 I, mean amplitude = 0.184 +- 0.04; Lob II, mean amplitude = 0.118 +- 0.02; Lob VI, mean amplitude =
345 0.088 +- 0.02; Kruskal-Wallis test $P = 0.0968$); however, Lob VI ERPs occurred at significantly shorter
346 latencies compared to both Lob II/III and (Crus I: mean = 55.91 +- 6.14 ms; Lob II/III: mean = 61.45 +-
347 5.53 ms; Lob VI: mean = 32 +- 7.89 ms; Kruskal-Wallis test $P = 0.0053$; Multiple comparisons FDR
348 corrected: Lob VI vs Crus I $P = 0.0044$, Lob VI vs Lob II $P = 0.0044$, Crus I vs Lob II $P = 0.3034$). **D**, Significant
349 phase locking of SWRs to delta oscillations was found in all cerebellar regions during non-REM sleep.
350 In the upper panels, the normalized count of PSPs recorded at the different phases of delta oscillations
351 in all mice for each cerebellar region (Lob II/III = 14012 SWRs/11 mice, Rayleigh's test, $P < 0.001$; Lob
352 VI = 11915 SWRs/15 mice, Rayleigh's test, $P < 0.001$; Crus I = 15532 SWRs/11 mice, Rayleigh's test, $P <$
353 0.001). In the lower panels, the individual vectors of the phase locking for each mouse (grey arrows)
354 and the average vector across all mice (colour coded; resultant vector angle: Crus I = 348.27 °, Lob II =
355 345.4 °, Lob VI = 4.26 °. Resultant vector length: Crus I = 0.16, Lob II = 0.1, Lob VI = 0.21). **E**, Fraction of
356 mice with significant SWR-to-cerebellar delta phase locking (significant phase locking was found in
357 Crus I, 9/11 mice; Lob II/III, 10/11 mice; Lob VI 14/15 mice). **F**, The level of SWR phase locking was
358 higher with Lob VI compared to Crus I or Lob II/III (1-way ANOVA, $P = 0.0324$; multiple comparisons
359 FDR corrected, Lob VI-Crus I $P = 0.0149$, Lob VI-Lob II/III $P = 0.0149$, Crus I-Lob II/III $P = 0.3317$). **G**,
360 Probability of SWRS relative to PSP onset. The number of SWRs are reduced following PSP occurrence
361 (at time zero; cf. Tsunematsu et al., 2020; 2-way ANOVA, region vs time, time effect $P < 0.0001$, region
362 effect $P < 0.0001$, interaction effect $P < 0.0001$. Multiple comparisons between cerebellar regions and
363 shuffled data). For all mean plots, Crus 1, $n = 11$ mice; Lob II/III, $n = 11$ mice; Lob VI, $n = 15$ mice.

364

365 Discussion

366 Despite the extensive literature on sleep-related neurophysiological processes in the hippocampus
367 (for review, see Klinzing et al., 2019) and recent advances in understanding of sleep-related processes
368 in the cerebellum (Canto et al., 2017; Xu et al., 2020; Zhang et al., 2020), no report exists on potential
369 functional or physiological interplay between these regions during sleep. Therefore, to bridge this
370 knowledge gap, we investigated cerebello-hippocampal interactions as well as intrinsic cerebellar LFP
371 dynamics across sleep states in mice.

372 Intra-cerebellar LFP dynamics during sleep

373 We first profiled sleep-related activity within three distinct regions of the cerebellar cortex: Lob VI,
374 Lob II/III and Crus I. We found modulation of cerebellar LFP activity across sleep states, both locally,
375 in spatially segregated cerebellar lobules, and globally, in a coordinated manner across the cerebellar
376 cortex. Overall, during REM and non-REM sleep, prominent delta (< 4 Hz) and VHFOs (~ 250 Hz)
377 dominate the spectral profile in all three regions. The presence of VHFOs has been described
378 previously in vermal lobules V/VIa of anaesthetised and awake, head-fixed rats, and attributed to

379 activity in recurrent Purkinje cell collaterals (de Solages et al., 2008). In contrast, previous studies in
380 freely moving mice have predominantly described high frequency oscillations in the cerebellar cortex
381 (~150 Hz: Cheron et al., 2005, 2004; Servais et al., 2005), which is consistent with our observations
382 during wake. Thus, given the high presence of VHFOs in head-fixed or sleeping animals they may be
383 related to the absence of voluntary movements. Our findings additionally extend the work of de
384 Solages et al. (2008) by showing for the first time that VHFOs are concurrently present across multiple
385 cerebellar cortical regions, highly prevalent during sleep (above wake levels) and, furthermore, that
386 they are temporally coordinated by local cerebellar delta rhythms during REM sleep.

387 During non-REM sleep, our description of prominent delta oscillations in the cerebellar cortex is in
388 keeping with previous work showing that neocortical slow oscillations can entrain those in the
389 cerebellar cortex (Roš et al., 2009a; Rowland et al., 2010; Xu et al., 2020). In contrast, REM sleep is
390 traditionally associated with theta (~6-12 Hz) frequency, LFP oscillations. Our recordings from the
391 cerebellum revealed no discernible increase in theta power during REM. Surprisingly, however, we did
392 observe highly synchronous, large delta (< 4 Hz) oscillations in all three recorded cerebellar regions
393 during REM. This may be a local circuitry peculiarity; however, recent evidence rodent and human
394 studies suggest that localized delta oscillations should be considered an integral component of REM
395 sleep (Bernardi et al., 2019; Funk et al., 2016; Siclari and Tononi, 2017).

396 Cerebello-hippocampal coherence during sleep

397 Next, we sought evidence for putative functional coupling, as measured by LFP-LFP coherence,
398 between the hippocampus and cerebellum across sleep states. Of particular note, we found that
399 hippocampus-Lob VI coherence was significantly and dynamically modulated across sleep states.
400 Specifically, during non-REM, hippocampus-Lob VI delta coherence was significantly higher than
401 during wake/REM whilst during REM, hippocampus-Lob VI theta coherence was significantly higher
402 than during non-REM and, surprisingly, was also significantly modulated to above wake levels. The
403 comparatively heightened, frequency-specific, offline coupling between hippocampus and Lob VI
404 during non-REM illustrates the potential for both sleep stage and regionally specific interactions
405 between the two brain structures in addition to those we previously described during active
406 movement in the homecage (Watson et al., 2019). Indeed, this interaction may be supported by
407 previously described anatomical connections linking Lob VI and hippocampus via the medial septum
408 or the supramammillary nucleus (Watson et al., 2019).

409

410 Putative PGO waves provide a potential substrate for cerebello-hippocampal interactions during REM

411 In addition to the ongoing LFP oscillations observed in the cerebello-hippocampal network during
412 sleep, we also detected high amplitude PSPs in the cerebellar cortical recordings that were particularly
413 abundant during REM sleep. Previous studies have described similar phasic events in the cerebellum
414 and attributed them to propagation of PGO waves (Farber et al., 1980; Velluti et al., 1985). In keeping
415 with our observations, PGO waves are found to be highly concentrated in REM epochs across multiple
416 brain regions (Harlay et al., 1974; Marks et al., 1980; Pellet and Harley, 1977; Tsunematsu et al., 2020).
417 Furthermore, PGO-waves are known to phase-lock to hippocampal theta rhythms during REM and
418 modulate its frequency (increasing the preferred theta frequency; Karashima et al., 2007, 2002). We
419 confirmed that this was also the case with phase-locking of cerebellar PSPs to the hippocampal LFP
420 theta oscillation. Additionally, we also show that cerebellar PSPs are significantly phase-locked to the
421 cerebellar delta oscillation cycle and cross-frequency analysis revealed that cerebellar delta
422 modulation of hippocampal theta oscillations occurs preferentially when PSP content is high. Thus,
423 overall, the most parsimonious explanation is that the PSPs we recorded in the cerebellum are
424 propagated PGO waves. During REM, PGOs have been shown to play a crucial role in coordinating long
425 range network dynamics underlying sleep-dependent cognitive processes required for establishment
426 of fear memory (Datta, 2000; Datta et al., 1998; Datta and O'Malley, 2013). It is tempting to speculate
427 that the PSPs observed in the cerebellum may play a similar role by coordinating interactions with the
428 hippocampus and that this could subserve sleep-dependent memory formation of the explored
429 environment.

430 Sharp wave ripples link hippocampus and cerebellum during non-REM sleep

431 Sharp wave ripples (SWRs) are a prominent physiological feature of hippocampal activity during non-
432 REM sleep. SWRs are fast oscillations during which both CA3 and CA1 pyramidal cells fire
433 synchronously (Buzsáki, 1986; Csicsvari et al., 2000). Their occurrence is coordinated with cortical
434 spindles, which are themselves synchronized with cortical slow-delta oscillations (Siapas and Wilson,
435 1998) and this tripartite interaction is important for memory formation (Girardeau et al., 2009;
436 Latchoumane et al., 2017; Maingret et al., 2016). Consequently, we next examined the relationship
437 between hippocampal SWRs and cerebellar LFP oscillations. SWR-triggered cerebellar LFP waveform
438 averages in combination with phase-locking analysis revealed two main findings. Firstly, ERPs are
439 present in the cerebellar cortical LFP at short latency (particularly in Lob VI) following hippocampal
440 SWR onset. Previously, hippocampal SWRs have been shown to drive evoked LFP and single-unit
441 changes in the cingulate cortex of a similar latency to those triggered by direct hippocampal electrical
442 stimulation; as such SWR activity may be considered indicative of efferent flow from the hippocampal

443 formation (Wang and Ikemoto, 2016). Indeed, we found that SWRs triggered cerebellar ERPs with a
444 short onset latency of ~ 9.17 ms, which is in agreement with previous reports in anaesthetised rats
445 (Saint-Cyr and Woodward, 1980; Saint-Cyr and Woodward, 1980b) in which direct electrical
446 stimulation of the hippocampal fornix elicited both short latency mossy fibre (5-10 ms, routed via the
447 pontine nuclei) and longer latency, climbing fibre (10-20 ms, routed via the inferior olive) responses
448 within the cerebellar cortex. Also consistent with our results, topographical mapping of cerebellar
449 responses following direct hippocampal electrical stimulation revealed evoked activity mainly in the
450 Lob VI region of both cats (Newman and Reza, 1979) and rats (Saint-Cyr and Woodward, 1980b). Given
451 the short latency of evoked SWR ERPs, particularly in Lob VI, it seems likely that SWR mediated
452 hippocampal input to the cerebellum during non-REM sleep could be routed via the pontine nuclei.
453 This hypothesis is further strengthened by evidence of a direct hippocampal projection to the pons
454 (Schmahmann and Pandya, 1997).

455 Our second main finding was that SWRs are significantly phase locked to the up-state of cerebellar
456 delta oscillations in striking similarity to the well described locking of SWRs to neocortical delta, which
457 is thought to facilitate transfer of memory information from subcortical to cortical loci (Maingret et
458 al., 2016). As cerebellar Purkinje cells are known to toggle between depolarizing 'up-states' and
459 hyperpolarizing 'down-states' (see Engbers et al., 2013 for review) it may be considered that, during
460 non-REM sleep, cerebellar delta oscillations may facilitate the transfer of hippocampal information via
461 phase-locking of SWRs to periods of high Purkinje cell excitability thus favouring plasticity mechanisms
462 associated with memory formation. Consistent with our finding that hippocampus - Lob VI delta
463 coherence during non-REM sleep is higher compared to other cerebellar regions, SWRs were
464 significantly more phase locked to Lob VI delta compared to Crus I or Lob II/III, further supporting the
465 potential for regionally and sleep stage specific hippocampal-cerebellar interactions. Another
466 physiological explanation of SWR links to cerebellar delta oscillations may be provided by the fact that
467 SWRs are known to nest to the upstate of neocortical slow-delta oscillations. In turn, these neocortical
468 oscillations have been shown to entrain cerebellar activity in both anaesthetised rats (Roš et al.,
469 2009b; Rowland et al., 2010; Schwarz, 2010) and naturally sleeping monkeys (Xu et al., 2020). Thus,
470 SWR phase-locking to cerebellar delta oscillations may be mediated via upstream SWR-to-neocortical
471 delta nesting.

472 Taken together, the SWR-triggered evoked LFP activity recorded in the cerebellar cortex and their
473 coordination with cerebellar delta oscillations illustrate the existence of robust physiological links and
474 candidate mechanisms that could subservise hippocampal-cerebellar (particularly Lob VI) interactions
475 during non-REM sleep.

476 In summary, our findings illustrate the presence of multiple physiological events in the cerebello-
477 hippocampal network during sleep (Supplemental Figure 5), centred around prominent delta
478 oscillations. In particular, we have highlighted lobule specific hippocampus-to-cerebellum directed
479 interaction during non-REM sleep mediated via SWR and delta oscillations. During REM, we identified
480 prominent cerebellar delta oscillations and associated PSPs, which modulate both local cerebellar
481 VHFO and distant hippocampal theta oscillations. Thus, it appears that delta oscillations play a key
482 role in temporal coordination both within and between these regions. Similar sleep-stage specific,
483 transient physiological events have been shown to be important for memory formation across other
484 brain circuits, and by analogy it may be hypothesised that the events described in the hippocampal-
485 cerebellar network serve a similar role in affording the two regions the ability to preferentially interact
486 during windows of enhanced synaptic plasticity.

487 As the cerebellum is thought to compute forward models that predict sensory consequences of actions
488 adapted to a particular context, we speculate that the aforementioned mechanisms may allow offline
489 updating and refinement of such models across the cerebello-hippocampal network during sleep.
490 These refinements may be important during online navigation behaviours in which animals must
491 predict the spatial consequences of their movements.

492

493

494

495 **Material and Methods:**

496 Mice

497 20 adult male C57BL6-J mice were used for this study (Janvier, France). Mice were housed individually
498 under a 12 hr light/12 hr dark cycle (light cycle beginning at 8 am) and received food and water *ad*
499 *libitum*. All behavioural experiments were performed in accordance with the official European
500 guidelines for the care and use of laboratory animals (86/609/EEC) and in accordance with the Policies
501 of the French Committee of Ethics (Decrees n° 87-848 and n° 2001-424). The animal housing facility
502 of the laboratory where experiments were made is fully accredited by the French Direction of
503 Veterinary Services (B-75-05-24, 18 May 2010). The protocol was approved by the Committee on the
504 Ethics of Animal Experiments (APAFIS#4315-2016042708195884v1). Data obtained from the mice
505 used in this study have been published in Watson et al., (2019).

506 Surgery

507 Surgical and implant procedures have been already described in Watson et al., (2019). Briefly, surgical
508 implantation was performed under constant isoflurane anaesthesia (1.5 %) combined with oxygen (1.5
509 L/min). Animals were placed in a stereotaxic frame device (David Kopf Instruments, USA) and an
510 incision was performed in order to expose the scalp. Coordinates for implantation were calculated
511 from bregma following the references given in Franklin and Paxinos, 2007. We targeted bilateral
512 hippocampi (AP -2.2 mm, ML \pm 2.0 mm, DV 1.0 mm), cerebellar lobules II/III (AP -5.52 mm, ML 0 mm,
513 DV 1.8 mm), cerebellar lobule VI (AP -6.72 mm, ML 0 mm, DV 0.1 mm) and left cerebellar Crus I (AP -
514 6.24 mm, ML 2.5 mm, DV 0.1 mm). Small craniotomies were performed over the target regions using
515 a drill and the dura was carefully removed with a needle. Two wires of 140 μ m diameter teflon coated
516 stainless-steel (A-M system, USA) were twisted together to create bipolar LFP recording electrodes
517 (interpolar distance \sim 0.5 mm) and were implanted in the brain. Pairs of flexible stainless-steel wires
518 were also sutured to the neck muscles to obtain EMG recordings (Cooner wire, USA). 14 mice were
519 also implanted with bipolar stimulation electrodes (same as the LFP electrodes but with interpolar
520 distance of \sim 140 μ m) in the left medial forebrain bundle (AP -1.4 mm, ML 1.2 mm, DV 4.8 mm) to
521 serve as a reward signal in a set of experiments already published (Watson et al., 2019). All electrodes
522 were attached to an electrode interface board (EIB-18, Neuralynx, USA) and the assembly was fixed
523 to the skull using a combination of UV activated cement (SpeedCem, Henry Shein, UK), SuperBond
524 (SunMedical, Japan) and dental cement (Simplex Rapid, Kemdent, UK). Four miniature screws (Antrin,
525 USA) were also attached to the skull for additional support and to serve as recording ground. Animals
526 were given a minimum of 5 days post-surgery recovery time before experiments commenced.

527 Electrophysiological recordings

528 The EMG and LFP recordings were obtained via a unity-gain headstage preamplifier (HS-18, Neuralynx,
529 USA) and a Digital Lynx SX system and Cheetah software (Neuralynx, USA). Signals were bandpass-
530 filtered between 0.1 and 600 Hz and sampled at 1 kHz. Mouse position was tracked at 30 Hz using
531 video tracker software and infra-red LEDs attached to the headstage (Neuralynx, USA).

532 Histology

533 After completion of the experiments, mice were deeply anaesthetized with ketamine/xylazine
534 solution (150 mg/Kg) and electrolytic lesions were created by passing a positive current through the
535 electrodes (30 μ A, 10 s). The animals were then perfused transcardially with saline (0.9 %) followed
536 by paraformaldehyde (4%). Once perfused, the electrode assembly was carefully removed, the brain
537 extracted and post-fixed in paraformaldehyde (4%) for 24 hr and then embedded in agarose (3%). 50
538 μ m sagittal and coronal sections for the cerebellum and the hippocampus, respectively, were made
539 using a vibratome. The sections were mounted on gelatinized slides and stained with cresyl violet. The
540 electrolytic lesions were then identified in order to reconstruct the recording locations using standard
541 maps with reference to a stereotaxic atlas (Franklin and Paxinos, 2007). The anatomical location of the
542 electrodes used in this study were verified in Watson et al., (2019).

543 Behaviour and sleep scoring

544 The animals were recorded during the day (between 10 am and 6 pm) in their home-cages (30 cm x
545 10 cm x 10 cm), with the lid removed and the lights off for periods up to 4 hr. Recordings were made
546 prior to training in a linear track task (described in Watson et al., 2019). The homecage environment
547 was familiar to the mice as they had been housed in it since completion of implantation surgery.
548 Animals exhibited different behavioural states that were scored off-line and included in four
549 categories: active wakefulness, resting, non-REM sleep and REM sleep. The scoring was semi-
550 automatically performed using multi-parameter thresholds based upon instantaneous speed, neck
551 EMG (rectified, smoothed with 1 s window and z-scored) and theta/delta ratio in the hippocampal LFP
552 (z-scored and calculated in 100 ms bins). Thus, epochs of more than 4 s with instantaneous speed
553 above 3 cm/s were considered as active wakefulness, periods of less than 30 s where the speed stayed
554 below 3 cm/s and were surrounded by active wakefulness epochs were considered as rest. Similarly,
555 when the EMG recording was optimal, a manually selected threshold was also used to discriminate
556 between rest and sleep epochs. We finally used manual thresholding of the theta/delta ratio to
557 separate non-REM and REM sleep epochs. Only epochs of more than four seconds were selected for
558 further analysis.

559 Data preprocessing

560 All the data processing was performed using custom-made MATLAB scripts (Mathworks, USA). Raw
561 signals were pre-processed by applying a notch filter to remove electrical line noise (filter centred to
562 50 Hz). Voltages were z-scored to reduce overall differences in amplitude in the signal recorded from
563 different electrodes.

564 Offline detection of ripples, slow oscillations and phasic events

565 Discrete sharp-waves ripples (SWRs) were detected using criteria employed elsewhere (Maingret et
566 al., 2016). The raw signal was then filtered using a second order zero-phase bandpass filter between
567 150-250 Hz, squared, smoothed (using 8 ms running average) and z-scored. The SWRs were defined
568 as events in which the transformed signal remained above 2 z-scores for 30 to 100 ms with a peak
569 above 5 z-scores.

570 Slow oscillations in the cerebellum were divided into individual cycles which were identified as follows:
571 first the raw signal was filtered using a second order zero-phase bandpass filter between 0-1-4Hz. The
572 instantaneous phase was obtained by applying a Hilbert transform to the filtered signal. Each cycle
573 was defined by the epoch between two negative peaks on the cosine of the instantaneous phase. Only
574 cycles which lasted more than 1 s and presented peak amplitudes higher than 4 z-scores and trough
575 amplitudes no lower than 2 z-scores were further analysed.

576 For the detection of PSPs (putative p-waves) in the cerebellum, we first filtered the signal using a
577 second order zero-phase bandpass filter between 5-80 Hz, squared it, and then calculated the z-score
578 across all obtained sleep epochs. A double threshold strategy was then applied, first to the
579 transformed signal so that epochs separated by at least 75 ms with values above 1 z-score and a peak
580 in the filtered data above 4 z-scores were considered as events.

581 Spectral analysis

582 All the spectral analyses were performed employing freely available signal processing toolboxes. For
583 computing the overall spectral power and spectral coherence across sleep-states, a multi-taper
584 Fourier transform (Chronux toolbox) was computed with 4 s sliding windows in 1 s steps and using 4
585 tapers. The mean power spectrum and coherence was obtained for each behavioural state by
586 averaging the spectrogram and coherogram from the identified epochs. To reduce the impact of the
587 different data durations for each state, we split the epochs to match with the minimal data duration
588 and then we averaged them. For computing the triggered spectrogram and coherograms we used the

589 continuous wavelet transform and wavelet coherence (wavelet toolbox, MATLAB). We used analytic
590 Morse wavelets with 8 octaves and 48 voices per octave.

591 Phase locking of phasic events and slow-wave triggered power spectra and coherograms

592 Cerebellar and hippocampal signals were filtered using a second order zero-phase bandpass filter
593 between 0.1 - 4 Hz and 6 - 12 Hz, respectively. The instantaneous phase of the cerebellar infra-slow
594 oscillations and the hippocampal theta oscillations were obtained by applying a Hilbert transform to
595 the filtered signals. The phase locking of the detected cerebellar phasic events to these rhythms was
596 tested using circular statistics (Matlab) and significance was determined as Raleigh test p-value < 0.05.

597 To compute the cerebellar slow-wave triggered spectrogram and coherogram, for each cerebellar
598 slow-wave, the obtained time-frequency series was matched with the corresponding instantaneous
599 phase of the cerebellar delta oscillations (0.1-4 Hz) and then averaged by phase bins of 7.35 °.

600 Cross-correlation between PSPs and SWRs

601 The timing of the SWRs was calculated relative to the time of the peak of the detected PSPs. After
602 binning at 25 ms resolution, the probability density function (count normalized by the total number
603 of elements multiplied by the bin width) was obtained and smoothed (using a 250 ms running
604 average). Statistical significance of the obtained cross-correlation was performed by artificially
605 generating PSP trains of similar density as observed in the actual data, drawn at random from a Poisson
606 distribution, and recomputing the probability density function.

607 Statistical analysis

608 Statistical analyses were conducted using MATLAB Statistical Toolbox and Prism (Graphpad, USA).
609 Normality was assessed using a Shapiro-Wilk test. Parametric and non-parametric tests were then
610 used accordingly. Paired analyses were employed when possible.

611

612 **Author Contributions**

613 Arturo Torres-Herraez, Software, Formal analysis, Validation, Investigation, Visualization,
614 Methodology, Writing- original draft; Thomas Charles Watson, Conceptualization, Supervision, Formal
615 analysis, Validation, Visualization, Investigation, Methodology, Writing- original draft, review and
616 editing; Laure Rondi-Reig, Conceptualization, Resources, Supervision, Funding acquisition,
617 Methodology, Writing- critical revision, review and editing, Project administration.

618

619 **Competing interest**

620 The authors declare that no competing interests exist.

621

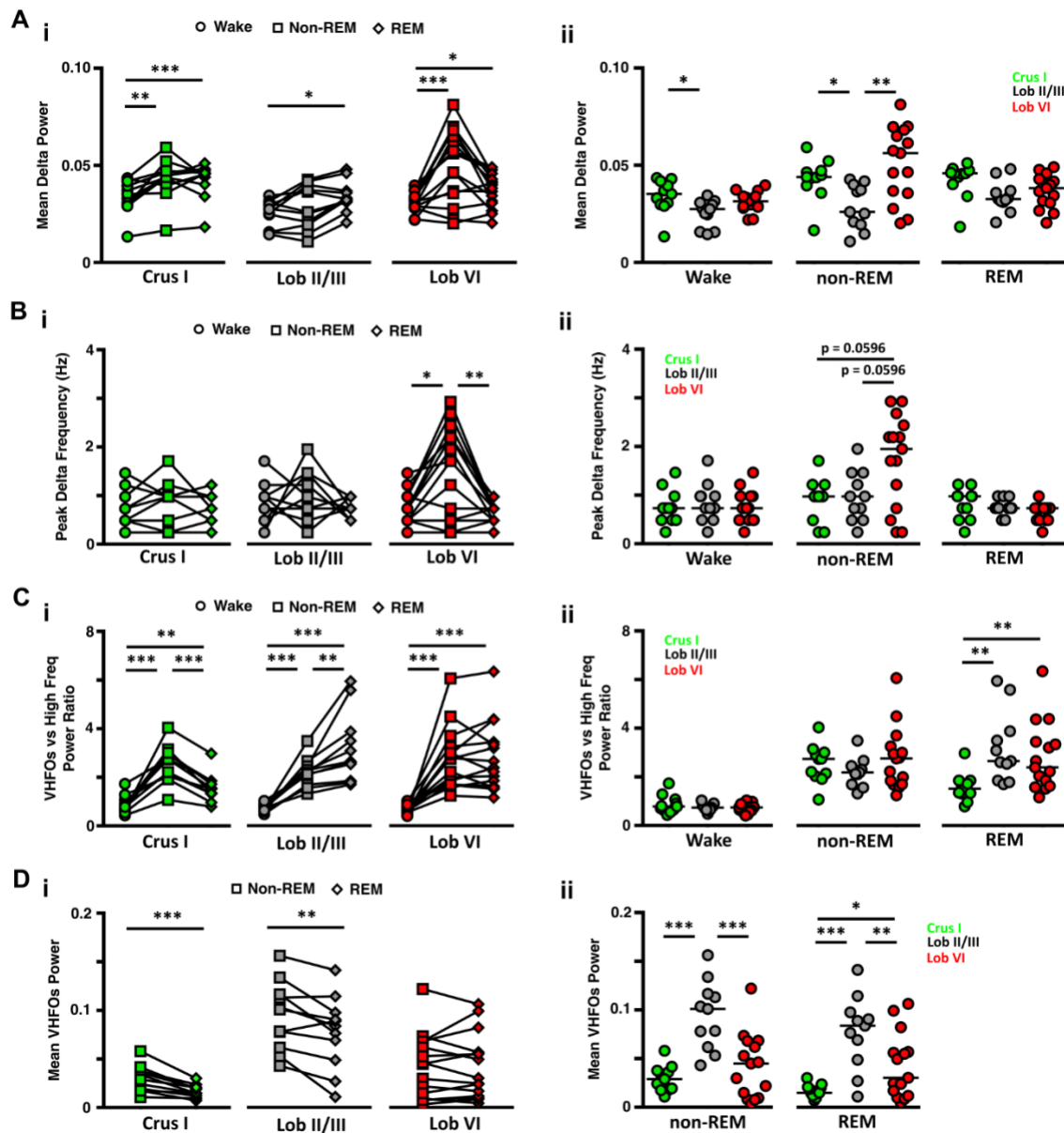
622 **Acknowledgments**

623 This work was supported by the Fondation pour la Recherche Médicale DEQ20160334907-France, the
624 National Agency for Research ANR-17-CE16-0019-SynPredict, CNRS, Inserm and Sorbonne University
625 (LRR). We thank all members of the CEZAME team for helpful discussions of the experiments and
626 manuscript. We gratefully acknowledge the IBPS animal facility staff for their support.

627

628

629 **Supplementary Figures**



630

631 **Supplemental Figure 1. LFP power in delta (0.1-4 Hz) and VHFO (240-280 Hz) frequency bands**

632 **during wake and sleep. A, i,** The power of delta oscillations varied between wake and the different

633 sleep states within the three cerebellar regions (Crus I, n = 11, Friedman test, p = 0.0004, multiple

634 comparisons with FDR correction: awake vs non-REM, p = 0.0015, awake vs REM, p = 0.0007, non-REM

635 vs REM, p = 0.2344; Lob II/III, n = 11, Friedman test, p = 0.0273, multiple comparisons with FDR

636 correction: awake vs non-REM, p = 0.3657, awake vs REM, p = 0.0221, non-REM vs REM, p = 0.0578;

637 Lob VI, n = 15, Friedman test, p = 0.0023, multiple comparisons with FDR correction: awake vs non-

638 REM, p = 0.0011, awake vs REM, p = 0.0468, non-REM vs REM, p = 0.1009). **ii,** Similarly, differences

639 between cerebellar regions were observed both during wake (Kruskal-Wallis test, p = 0.0133, multiple

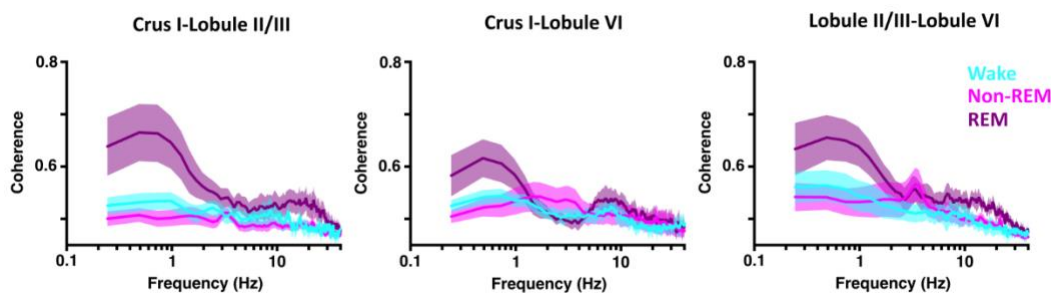
640 comparisons with FDR correction: Crus I vs Lob II/III, p = 0.0075, Crus I vs Lob VI, p = 0.1473, Lob II/III

641 vs Lob VI, p = 0.0633) and non-REM sleep (Kruskal-Wallis test, p = 0.0040, multiple comparisons with

642 FDR correction: Crus I vs Lob II/III, p = 0.0117, Crus I vs Lob VI, p = 0.1466, Lob II/III vs Lob VI, p =

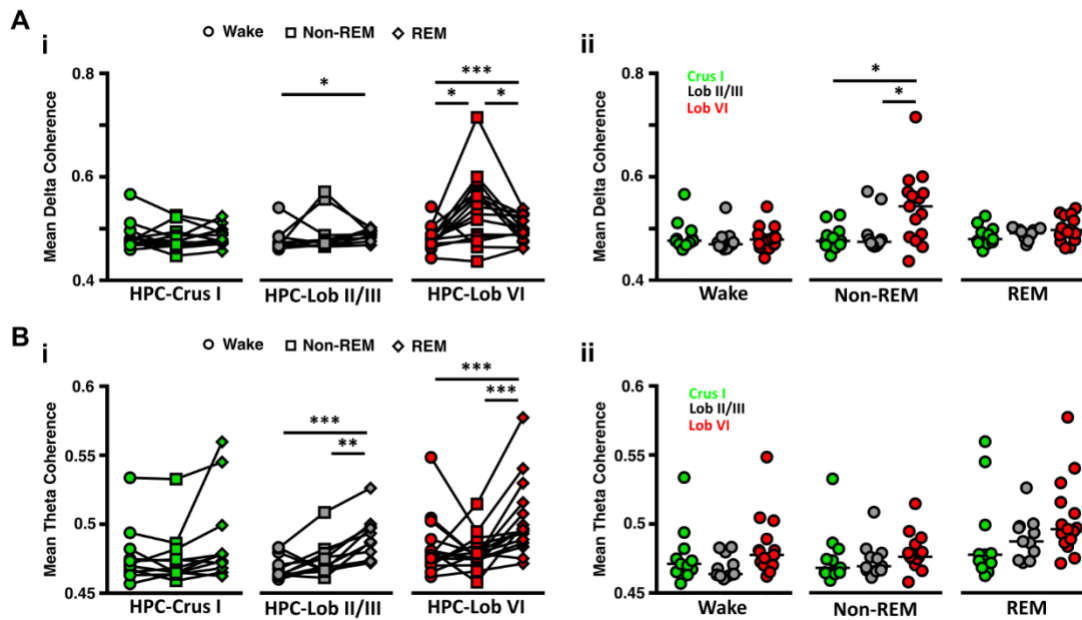
643 0.0012), but not during REM (Kruskal-Wallis test, $p = 0.0540$). **B, i**, The peak delta band frequency
644 differed across sleep states only in Lob VI (Crus I, Friedman test, $p = 0.1322$; Lob II/III, Friedman test,
645 $p = 0.2233$; Lob VI, Friedman test, $p = 0.009$, multiple comparisons with FDR correction: awake vs non-
646 REM, $p = 0.0107$, awake vs REM, $p = 0.1955$, non-REM vs REM, $p = 0.0039$). **ii**, Differences in the peak
647 peak delta frequency band across cerebellar regions were also restricted to non-REM epochs (wake, Kruskal
648 Wallis test, $p = 0.7732$, non-REM, Kruskal Wallis test, $p = 0.0364$, multiple comparisons with FDR
649 correction: Crus I vs Lob II/III, $p = 0.9095$, Crus I vs Lob VI, $p = 0.0596$, Lob II/III vs Lob VI, $p = 0.0596$).
650 **C, i**, During wake, the power of VHFOs was lower compared to high frequency oscillations in all regions,
651 as indicated by the mean values below 1. In contrast, during sleep, across all recorded cerebellar
652 regions, the ratio of VFHO to high frequency oscillation power increased significantly compared to
653 wake (shifted to values >1), and also differed between sleep states (Crus I, repeated measures ANOVA,
654 $p < 0.0001$, multiple comparisons with FDR correction: awake vs non-REM, $p < 0.0001$, awake vs REM,
655 $p = 0.0046$, non-REM vs REM, $p < 0.0001$; Lob II/III, repeated measures ANOVA, $p = 0.0002$, multiple
656 comparisons with FDR correction: wake vs non-REM, $p < 0.0001$, wake vs REM, $p = 0.0003$, non-REM
657 vs REM, $p = 0.0071$; Lob VI, repeated measures ANOVA, $p < 0.0001$, multiple comparisons with FDR
658 correction: wake vs non-REM, $p < 0.0001$, wake vs REM, $p < 0.0001$, non-REM vs REM, $p = 0.7226$). **ii**,
659 Significant differences across cerebellar regions were restricted to REM epochs when Crus I shown
660 significantly smaller ratios than the other two regions (wake, one-way ANOVA, $p = 0.2252$, non-REM,
661 one-way ANOVA, $p = 0.3705$, REM, one-way ANOVA, $p = 0.0098$, multiple comparisons with FDR
662 correction, Crus I vs Lob II/III, $p = 0.0042$, Crus I vs Lob VI, $p = 0.0083$, Lob II/III vs Lob VI, $p = 0.1538$).
663 **D, i**, VHFO power was significantly reduced during REM sleep compared with non-REM in Crus I (Paired
664 t-test, $p = 0.0005$) and Lob II/III (Paired t-test, $p = 0.0067$) but remained unchanged in Lob VI (Paired
665 t-test, $p = 0.9137$). **ii**, VHFOs power was significantly higher in Lob II during both non-REM (one-way
666 ANOVA, $p < 0.0001$, multiple comparisons with FDR correction, Crus I vs Lob II/III, $p < 0.0001$, Crus I vs
667 Lob VI, $p = 0.1020$, Lob II/III vs Lob VI, $p < 0.0001$) and REM sleep (one-way ANOVA, $p = 0.0002$, multiple
668 comparisons with FDR correction, Crus I vs Lob II/III, $p = 0.0001$, Crus I vs Lob VI, $p = 0.0393$, Lob II/III
669 vs Lob VI, $p = 0.0092$).

670



672

672 **Supplemental Figure 2. Intra-cerebellar delta coherence is highest during REM sleep.** Delta band ($<$
673 4Hz) coherence was elevated during REM sleep compared with both awake and non-REM in all
674 combinations of cerebellar recordings (Crus I-Lob II/III, $n = 8$; Crus I-Lob VI, $n = 7$; Lob II/III-Lob VI, $n =$
675 7).

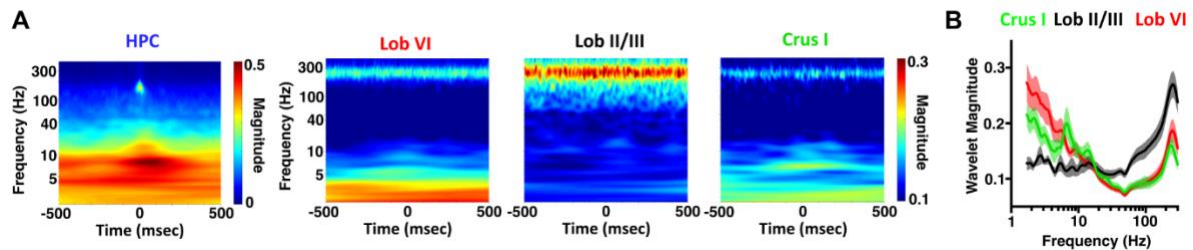


676

677 **Supplemental Figure 3. Cerebello-hippocampal coherence in the delta (<4 Hz) and theta (6-12 Hz)**
 678 **frequency ranges is modulated across sleep-states. A, i,** Significant modulation across sleep states in
 679 delta coherence was found between hippocampus and Lob II/III ($n = 11$, Friedman test, $p = 0.0273$,
 680 multiple comparisons with FDR correction: wake vs non-REM $p = 0.3657$, wake vs REM $p = 0.0221$,
 681 non-REM vs REM $p = 0.0578$), and particularly between the hippocampus and Lob VI ($n = 15$, Friedman
 682 test, $p = 0.0006$, multiple comparisons with FDR correction: wake vs non-REM $p = 0.0001$, wake vs
 683 REM $p = 0.0149$, non-REM vs REM $p = 0.0351$). Hippocampus-Crus I delta coherence remained
 684 unchanged ($n = 11$, Friedman test, $p = 0.8438$). **ii,** Significant differences in delta coherence between
 685 the cerebello-hippocampal combinations were restricted to non-REM epochs, with HPC-Lob VI levels
 686 being significantly higher than other combinations (wake, Kruskal-Wallis test, $p = 0.4283$; non-REM,
 687 Kruskal-Wallis test, $p = 0.0225$, multiple comparisons with FDR correction: HPC-Crus I vs HPC-Lob II/III,
 688 $p = 0.3225$, HPC-Crus I vs HPC-Lob VI, $p = 0.0122$, HPC-Lob II/III vs HPC-Lob VI, $p = 0.0122$; REM, Kruskal-
 689 Wallis test, $p = 0.2826$). **B, i,** Similarly, theta coherence was significantly increased during REM sleep
 690 between HPC-Lob II/III ($n = 11$, Friedman test, $p = 0.0002$, multiple comparisons with FDR correction:
 691 wake vs non-REM $p = 0.1378$, wake vs REM $p = 0.0003$, non-REM vs REM $p = 0.0029$) and HPC-Lob VI
 692 ($n = 15$, Friedman test, $p = 0.0007$, multiple comparisons with FDR correction: wake vs non-REM $p =$
 693 0.2503 , wake vs REM $p = 0.001$, non-REM vs REM $p = 0.0005$), but remained stable across sleep states
 694 between the HPC-Crus I ($n = 11$, Friedman test, $p = 0.1632$). **ii,** In contrast, no differences across
 695 cerebello-hippocampal combinations were found during any of the states analysed (wake, Kruskal-
 696 Wallis test, $p = 0.0677$; non-REM, Kruskal-Wallis test, $p = 0.1994$; REM, Kruskal-Wallis test, $p = 0.0979$).

697

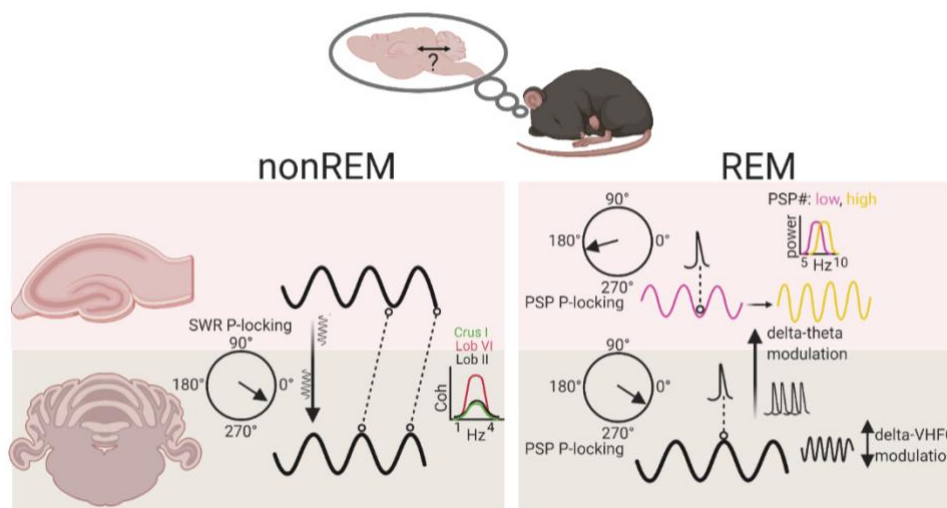
698



699

700 **Supplemental Figure 4. SWR triggered spectral analysis.** **A**, Averaged power spectra triggered by
 701 detected hippocampal SWR events (time zero). Nitzan et al., (2020) have recently shown that SWRs
 702 can propagate to the cortex. Here we observe discrete SWR activity in the hippocampal spectrogram
 703 (~150Hz) that is not present in the cerebellum. **B**, Mean cerebellar power spectra calculated during the
 704 the 500ms following ripple detection.

705



706

707 **Supplemental Figure 5. Summary diagram of main findings illustrating sleep-stage specific**
 708 **physiological events and interactions within the cerebello-hippocampal network.** During nonREM,
 709 coherence within the delta frequency range is highest between hippocampus and lobule VI compared
 710 to other cerebellar lobules. In addition, hippocampal sharp wave ripples (SWR) are phase locked to
 711 the cerebellar delta oscillation (black line) and drive modulation of cerebellar LFP activity. During REM,
 712 PSPs are significantly phase locked to both the trough of hippocampal theta (purple line) and the peak
 713 of cerebellar delta oscillations (black line). Within the cerebellum, delta oscillations can modulate
 714 activity within the VHFO range during REM. Additionally, cerebellar delta oscillations and associated
 715 PSPs modulate the frequency of hippocampal theta rhythms (from ~ 7.5 Hz (low, purple line) to 8 Hz
 716 (high, yellow line)). Abbreviations: SWR, sharp wave ripple; P-locking, phase locking; PSP, phasic sharp
 717 potential; VHFO, very high frequency oscillation. Created with BioRender.com.

718

719

720

721 **References:**

- 722 Babayan BM, Watilliaux A, Viejo G, Paradis A-L, Girard B, Rondi-Reig L. 2017. A hippocampo-
723 cerebellar centred network for the learning and execution of sequence-based navigation.
724 *Sci Rep* 7:17812. doi:10.1038/s41598-017-18004-7
- 725 Bernardi G, Betta M, Ricciardi E, Pietrini P, Tononi G, Siclari F. 2019. Regional delta waves in
726 human rapid eye movement sleep. *J Neurosci* 39:2686–2697.
727 doi:10.1523/JNEUROSCI.2298-18.2019
- 728 Braun A. 1997. Regional cerebral blood flow throughout the sleep-wake cycle. An H₂(15)O PET
729 study. *Brain* 120:1173–1197. doi:10.1093/brain/120.7.1173
- 730 Burguière E, Arleo A, Hojjati M reza, Elgersma Y, Zeeuw CI De, Berthoz A, Rondi-Reig L. 2005.
731 Spatial navigation impairment in mice lacking cerebellar LTD: a motor adaptation deficit?
732 *Nat Neurosci* 8:1292–1294. doi:10.1038/nn1532
- 733 Buzsáki G. 1986. Hippocampal sharp waves: Their origin and significance. *Brain Res* 398:242–252.
734 doi:10.1016/0006-8993(86)91483-6
- 735 Canto CB, Onuki Y, Bruinsma B, van der Werf YD, De Zeeuw CI. 2017. The Sleeping Cerebellum.
736 *Trends Neurosci*. doi:10.1016/j.tins.2017.03.001
- 737 Cheron G, Gall D, Servais L, Dan B, Maex R, Schiffmann SN. 2004. Inactivation of Calcium-Binding
738 Protein Genes Induces 160 Hz Oscillations in the Cerebellar Cortex of Alert Mice. *J Neurosci*
739 24:434–441. doi:10.1523/JNEUROSCI.3197-03.2004
- 740 Cheron G, Servais L, Wagstaff J, Dan B. 2005. Fast cerebellar oscillation associated with ataxia in
741 a mouse model of angelman syndrome. *Neuroscience* 130:631–637.
742 doi:10.1016/j.neuroscience.2004.09.013
- 743 Csicsvari J, Hirase H, Mamiya A, Buzsáki G. 2000. Ensemble patterns of hippocampal CA3-CA1
744 neurons during sharp wave-associated population events. *Neuron* 28:585–594.
745 doi:10.1016/S0896-6273(00)00135-5
- 746 Datta S. 2000. Avoidance task training potentiates phasic pontine-wave density in the rat: A
747 mechanism for sleep-dependent plasticity. *J Neurosci* 20:8607–8613.
748 doi:10.1523/jneurosci.20-22-08607.2000
- 749 Datta S, O'Malley MW. 2013. Fear extinction memory consolidation requires potentiation of
750 pontine-wave activity during REM sleep. *J Neurosci* 33:4561–4569.
751 doi:10.1523/JNEUROSCI.5525-12.2013

- 752 Datta S, Siwek DF, Patterson EH, Cipolloni PB. 1998. Localization of pontine PGO wave generation
753 sites and their anatomical projections in the rat. *Synapse* 30:409–423.
754 doi:10.1002/(sici)1098-2396(199812)30:4<409::aid-syn8>3.0.co;2-%23
- 755 de Lavilléon G, Lacroix MM, Rondi-Reig L, Benchenane K. 2015. Explicit memory creation during
756 sleep demonstrates a causal role of place cells in navigation. *Nat Neurosci* 18:493–495.
757 doi:10.1038/nn.3970
- 758 de Solages C, Szapiro G, Brunel N, Hakim V, Isope P, Buisseret P, Rousseau C, Barbour B, Léna C.
759 2008. High-Frequency Organization and Synchrony of Activity in the Purkinje Cell Layer of
760 the Cerebellum. *Neuron* 58:775–788. doi:10.1016/j.neuron.2008.05.008
- 761 De Zeeuw CI, Hoebeek FE, Schonewille M. 2008. Causes and consequences of oscillations in the
762 cerebellar cortex. *Neuron* 58:655–8. doi:10.1016/j.neuron.2008.05.019
- 763 Diekelmann S, Born J. 2010. The memory function of sleep. *Nat Rev Neurosci*.
764 doi:10.1038/nrn2762
- 765 Engbers JDT, Fernandez FR, Turner RW. 2013. Bistability in Purkinje neurons: Ups and downs in
766 cerebellar research. *Neural Networks* 47:18–31. doi:10.1016/j.neunet.2012.09.006
- 767 Farber J, Marks GA, Roffwarg HP. 1980. Rapid eye movement sleep PGO-type waves are present
768 in the dorsal pons of the albino rat. *Science (80-)* 209:615–617.
769 doi:10.1126/science.6994229
- 770 Franklin K, Paxinos G. 2007. The mouse brain in stereotaxic coordinates, 3rd ed. Elsevier.
- 771 Funk CM, Honjoh S, Rodriguez A V., Cirelli C, Tononi G. 2016. Local slow waves in superficial layers
772 of primary cortical areas during REM sleep. *Curr Biol* 26:396–403.
773 doi:10.1016/j.cub.2015.11.062
- 774 Girardeau G, Benchenane K, Wiener SI, Buzsáki G, Zugaro MB. 2009. Selective suppression of
775 hippocampal ripples impairs spatial memory. *Nat Neurosci* 12:1222–1223.
776 doi:10.1038/nn.2384
- 777 Harlay F, Pellet J, Tardy MF, Dubrocard S. 1974. Activité unitaire corticocérébelleuse et
778 mouvements oculaires: Modifications associées aux saccades du sommeil et de la veille.
779 *Physiol Behav* 12:939–949. doi:10.1016/0031-9384(74)90141-3
- 780 Hobson JA, McCarley RW. 1972. Spontaneous discharge rates of cat cerebellar purkinje cells in
781 sleep and waking. *Electroencephalogr Clin Neurophysiol* 33:457–469. doi:10.1016/0013-
782 4694(72)90210-6

- 783 Jahnke K, von Wegner F, Morzelewski A, Borisov S, Maischein M, Steinmetz H, Laufs H. 2012. To
784 wake or not to wake? The two-sided nature of the human K-complex. *Neuroimage*
785 59:1631–1638. doi:10.1016/j.neuroimage.2011.09.013
- 786 Karashima A, Katayama N, Nakao M. 2007. Phase-locking of spontaneous and tone-elicited
787 pontine waves to hippocampal theta waves during REM sleep in rats. *Brain Res* 1182:73–
788 81. doi:10.1016/j.brainres.2007.08.060
- 789 Karashima A, Nakamura K, Sato N, Nakao M, Katayama N, Yamamoto M. 2002. Phase-locking of
790 spontaneous and elicited ponto-geniculo-occipital waves is associated with acceleration of
791 hippocampal theta waves during rapid eye movement sleep in cats. *Brain Res* 958:347–358.
792 doi:10.1016/S0006-8993(02)03673-9
- 793 Kaufmann C, Wehrle R, Wetter TC, Holsboer F, Auer DP, Pollmächer T, Czisch M. 2006. Brain
794 activation and hypothalamic functional connectivity during human non-rapid eye
795 movement sleep: An EEG/fMRI study. *Brain* 129:655–667. doi:10.1093/brain/awh686
- 796 Klinzing JG, Niethard N, Born J. 2019. Mechanisms of systems memory consolidation during
797 sleep. *Nat Neurosci*. doi:10.1038/s41593-019-0467-3
- 798 Latchoumane CF V., Ngo HV V., Born J, Shin HS. 2017. Thalamic Spindles Promote Memory
799 Formation during Sleep through Triple Phase-Locking of Cortical, Thalamic, and
800 Hippocampal Rhythms. *Neuron* 95:424-435.e6. doi:10.1016/j.neuron.2017.06.025
- 801 Lefort JM, Vincent J, Tallot L, Jarlier F, De Zeeuw CI, Rondi-Reig L, Rochefort C. 2019. Impaired
802 cerebellar Purkinje cell potentiation generates unstable spatial map orientation and
803 inaccurate navigation. *Nat Commun* 10:1–13. doi:10.1038/s41467-019-09958-5
- 804 Maingret N, Girardeau G, Todorova R, Goutierre M, Zugaro M. 2016. Hippocampo-cortical
805 coupling mediates memory consolidation during sleep. *Nat Neurosci* 19:959–964.
806 doi:10.1038/nn.4304
- 807 Mano NI. 1970. Changes of simple and complex spike activity of cerebellar purkinje cells with
808 sleep and waking. *Science (80-)* 170:1325–1327. doi:10.1126/science.170.3964.1325
- 809 Marchesi GF, Strata P. 1970. Climbing fibers of cat cerebellum: modulation of activity during
810 sleep. *Brain Res* 17:145–148. doi:10.1016/0006-8993(70)90317-3
- 811 Marks GA, Farber J, Rubinstein M, Roffwarg HP. 1980. Demonstration of ponto-geniculo-occipital
812 waves in the albino rat. *Exp Neurol* 69:648–666. doi:10.1016/0014-4886(80)90058-8

- 813 McCarley RW, Hobson JA. 1972. Simple spike firing patterns of cat cerebellar purkinje cells in
814 sleep and waking. *Electroencephalogr Clin Neurophysiol* 33:471–483. doi:10.1016/0013-
815 4694(72)90211-8
- 816 Montgomery SM, Sirota A, Buzsáki G. 2008. Theta and gamma coordination of hippocampal
817 networks during waking and rapid eye movement sleep. *J Neurosci* 28:6731–6741.
818 doi:10.1523/JNEUROSCI.1227-08.2008
- 819 Newman PP, Reza H. 1979. Functional relationships between the hippocampus and the
820 cerebellum: an electrophysiological study of the cat. *J Physiol* 287:405–26.
- 821 Nicola, Geva-Sagiv M, Nir Y. 2019. Local Sleep Oscillations: Implications for Memory
822 Consolidation. *Front Neurosci | www.frontiersin.org* 1:813. doi:10.3389/fnins.2019.00813
- 823 Niedermeyer E, Uematsu S. 1974. Electroencephalographic recordings from deep cerebellar
824 structures in patients with uncontrolled epileptic seizures. *Electroencephalogr Clin*
825 *Neurophysiol* 37:355–365. doi:10.1016/0013-4694(74)90111-4
- 826 Nitzan N, McKenzie S, Beed P, English DF, Oldani S, Tukker JJ, Buzsáki G, Schmitz D. 2020.
827 Propagation of hippocampal ripples to the neocortex by way of a subiculum-retrosplenial
828 pathway. *Nat Commun* 11:1–17. doi:10.1038/s41467-020-15787-8
- 829 Palmer C. 1979. Interpositus and fastigial unit activity during sleep and waking in the cat.
830 *Electroencephalogr Clin Neurophysiol* 46:357–370. doi:10.1016/0013-4694(79)90137-8
- 831 Pellet J, Harley F. 1977. Relations between unit activity of the vermis and the phasic waves of the
832 electrocerebellogram during sleep in the chronic cat. - PsycNET. *Arch Ital Biol* 115:108–13.
- 833 Proville RD, Spolidoro M, Guyon N, Dugué GP, Selimi F, Isope P, Popa D, Léna C. 2014. Cerebellum
834 involvement in cortical sensorimotor circuits for the control of voluntary movements. *Nat*
835 *Neurosci* 17:1233–1239. doi:10.1038/nn.3773
- 836 Rochefort C, Arabo A, Andre M, Poucet B, Save E, Rondi-Reig L. 2011. Cerebellum Shapes
837 Hippocampal Spatial Code. *Science (80-)* 334:385–389. doi:10.1126/science.1207403
- 838 Rochefort C, Lefort J, Rondi-Reig L. 2013. The cerebellum: a new key structure in the navigation
839 system. *Front Neural Circuits* 7:35. doi:10.3389/fncir.2013.00035
- 840 Roš H, Sachdev RNS, Yu Y, Šestan N, McCormick DA. 2009a. Neocortical Networks Entrain
841 Neuronal Circuits in Cerebellar Cortex. *J Neurosci* 29.

- 842 Roš H, Sachdev RNS, Yu Y, Šestan N, McCormick DA. 2009b. Neocortical networks entrain
843 neuronal circuits in cerebellar cortex. *J Neurosci* 29:10309–10320.
844 doi:10.1523/JNEUROSCI.2327-09.2009
- 845 Rowland NC, Goldberg JA, Jaeger D. 2010. Cortico-cerebellar coherence and causal connectivity
846 during slow-wave activity. *Neuroscience* 166:698–711.
847 doi:10.1016/j.neuroscience.2009.12.048
- 848 Saint-Cyr J A, Woodward DJ. 1980. A topographic analysis of limbic and somatic inputs to the
849 cerebellar cortex in the rat. *Exp Brain Res* 40:13–22.
- 850 Saint-Cyr J.A., Woodward DJ. 1980b. Activation of mossy and climbing fiber pathways to the
851 cerebellar cortex by stimulation of the fornix in the rat. *Exp Brain Res* 40:1–12.
852 doi:10.1007/BF00236657
- 853 Schabus M, Dang-Vu TT, Albouy G, Balteau E, Boly M, Carrier J, Darsaud A, Degueldre C, Desseilles
854 M, Gais S, Phillips C, Rauchs G, Schnakers C, Sterpenich V, Vandewalle G, Luxen A, Maquet
855 P. 2007. Hemodynamic cerebral correlates of sleep spindles during human non-rapid eye
856 movement sleep. *Proc Natl Acad Sci U S A* 104:13164–13169.
857 doi:10.1073/pnas.0703084104
- 858 Schmahmann JD, Pandya DN. 1997. Anatomic organization of the basilar pontine projections
859 from prefrontal cortices in rhesus monkey. *J Neurosci* 17:438–458.
860 doi:10.1523/jneurosci.17-01-00438.1997
- 861 Schwarz C. 2010. The fate of spontaneous synchronous rhythms on the cerebrocerebellar loop.
862 *Cerebellum* 9:77–87. doi:10.1007/s12311-009-0143-3
- 863 Servais L, Bearzatto B, Schwaller B, Dumont M, De Saedeleer C, Dan B, Barski JJ, Schiffmann SN,
864 Cheron G. 2005. Mono- and dual-frequency fast cerebellar oscillation in mice lacking
865 parvalbumin and/or calbindin D-28k. *Eur J Neurosci* 22:861–870. doi:10.1111/j.1460-
866 9568.2005.04275.x
- 867 Siclari F, Tononi G. 2017. Local aspects of sleep and wakefulness. *Curr Opin Neurobiol.*
868 doi:10.1016/j.conb.2017.05.008
- 869 Tsunematsu T, Patel AA, Onken A, Sakata S. 2020. State-dependent brainstem ensemble
870 dynamics and their interactions with hippocampus across sleep states. *Elife* 9.
871 doi:10.7554/eLife.52244

- 872 Velluti R, Yamuy J, Hadjez J, Monti JM. 1985. Spontaneous cerebellar nuclei PGO-like waves in
873 natural paradoxical sleep and under reserpine. *Electroencephalogr Clin Neurophysiol*
874 60:243–248. doi:10.1016/0013-4694(85)90038-0
- 875 Wang D V., Ikemoto S. 2016. Coordinated interaction between hippocampal sharp-wave ripples
876 and anterior cingulate unit activity. *J Neurosci* 36:10663–10672.
877 doi:10.1523/JNEUROSCI.1042-16.2016
- 878 Watson TC, Obiang P, Torres-Herraez A, Watilliaux A, Coulon P, Rochefort C, Rondi-Reig L. 2019.
879 Anatomical and physiological foundations of cerebello-hippocampal interaction. *Elife* 8.
880 doi:10.7554/eLife.41896.001
- 881 Xu W, De Carvalho F, Clarke AK, Jackson A. 2020. Communication from the cerebellum to the
882 neocortex during sleep spindles. *Prog Neurobiol*. doi:10.1016/j.pneurobio.2020.101940
- 883 Zhang L Bin, Zhang J, Sun MJ, Chen H, Yan J, Luo FL, Yao ZX, Wu YM, Hu B. 2020. Neuronal Activity
884 in the Cerebellum During the Sleep-Wakefulness Transition in Mice. *Neurosci Bull* 36:919–
885 931. doi:10.1007/s12264-020-00511-9
- 886