Online supporting supplementary material for publication:

Sleep spindles in humans: insights from intracranial EEG and unit recordings

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Supplementary Table ST1. Recording details

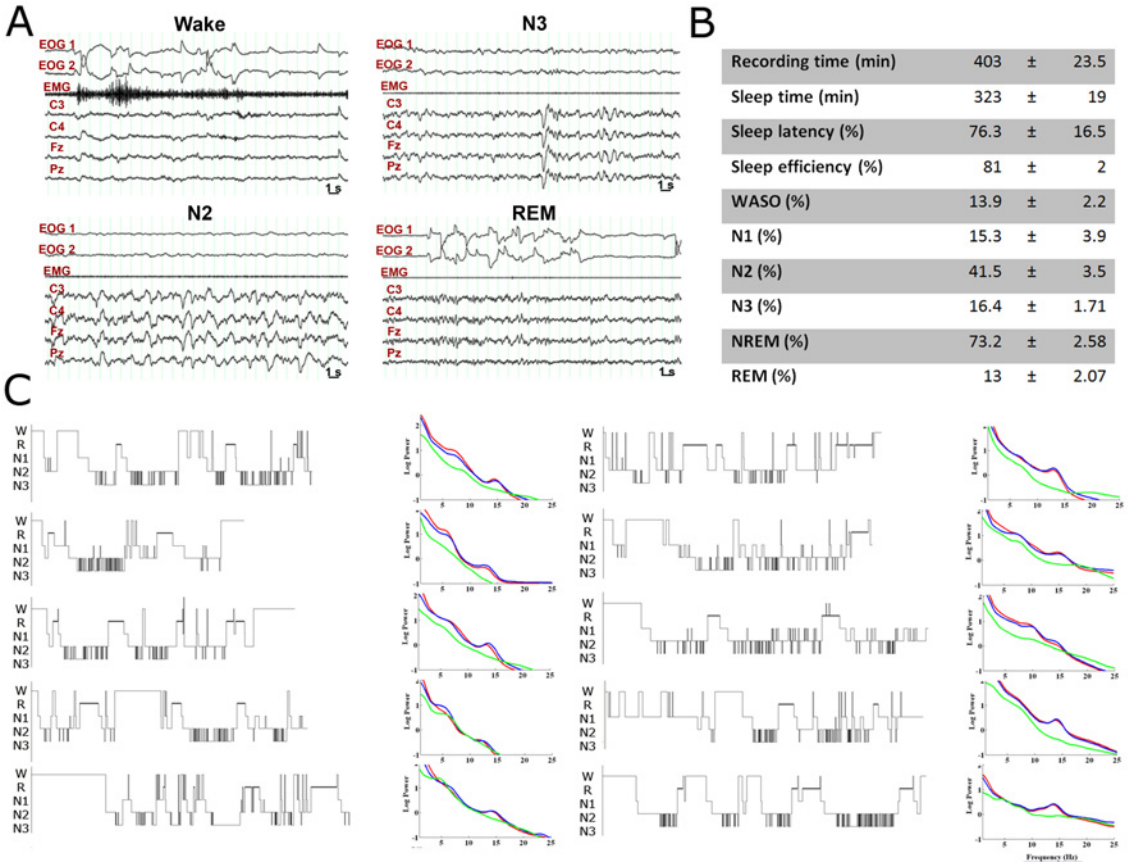
		Left Hemisphere													Right Hemisphere												Regions	Units
	Patient	H	A	EC	PH	TG	AC	MC	PC	OF	SM	P	TO	PT	H	A	EC	PH	TG	AC	MC	PC	OF	SM	P	TO	PT		
1	P396	5	4	2	8					1					2		2											7	24
2	P398				6		9								5		11	2										11	33
3	P399	14			7				1		12					13		15		14			12					11	88
4	P402	3	9	5											2	6	10			1			6					12	42
5	P404						9		6											10	11							9	36
6	P405	3	4		11					2					5	1		3				7						10	36
7	P406	6	8		13		3								8	8		6		4								11	56
8	P415																											12	NA
9	P416	3		1			3			10					16	8	7		12									12	60
10	P417				4							8			9			8						7				8	36
11	P422				8		1			11	8			2	5			6				7		10				9	58
12	P423	5		8						17					1		11											8	32
13	P424	8		10		12	13	13											12	17		5			11			9	99
	Regions	12	10	6	9	2	8	1	2	7	5	1	1	1	11	9	6	7	3	8	2	9	4	2	1	1	1	129	
	Units	47	25	26	57	12	38	13	7	31	20	8	NA	2	53	36	41	40	24	46	11	17	18	17	11	NA	NA		600

A full description of the brain structures and number of units identified in our recordings. Rows correspond to individual patients and columns correspond to different brain regions. Grey boxes mark implanted brain regions and numbers show detected units. For each brain region and subject we show the total of implantation sites (Regions) and units identified (Units). Abbreviations: LH, left hemisphere; RH, right hemisphere; H, hippocampus; A, amygdala; EC, entorhinal cortex; PH, parahippocampal gyrus; TG, temporal gyrus; AC, anterior cingulate; MC, middle cingulate; PC, posterior cingulate; OF, orbitofrontal and medial prefrontal cortex; SM, supplementary motor area; P, parietal cortex; TO, temporo-occipital, PT, posterior temporal cortex; FG, fusiform gyrus; IFG, inferior frontal gyrus.

Supplementary Table ST2. Patient information and details of sleep studies
Clinical information and sleep study details for all patients.

	Patient	Age	Gender	Handedness	Recording length (h)	Recording start time	Imaging: PET & MRI	Seizure onset	Resection / outcome
1	P396	27	M	R	7.0	11:00 PM	Metabolic and structural abnormalities left temporal	Left temporal	Left temporal, seizure free
2	P398	41	F	R	5.1	12:41 PM	Metabolic abnormalities bilateral temporal lobe, normal structural	Left temporal spreading to right entorhinal cortex	Left temporal, significant improvement
3	P399	43	F	R	6.3	11:45 PM	Normal metabolism, right frontal dysplasia	Right prefrontal cortex	Right prefrontal, seizure free
4	P402	25	F	R	6.6	11:30 PM	Mild metabolic abnormality right temporal, normal structural	Bilateral medial temporal lobe	No surgery
5	P404	25	M	L	10.9	6:29 PM	Normal metabolism, periventricular structural abnormalities	Left prefrontal	Left prefrontal, significant improvement
6	P405	38	F	R	6.6	10:29 PM	Mild metabolic abnormality bilateral temporal, possible dysplasia right temporal	Right medial temporal lobe spreading to parahippocampal gyrus	Right MTL, seizure free
7	P406	33	F	R	6.6	10:40 PM	Mild metabolic abnormality left temporal, structural abnormality right frontal lobe	Left medial temporal lobe	No surgery
8	P415	39	M	R	7.7	10:13 PM	Normal	Left medial temporal lobe	Left temporal, seizure free
9	P416	26	M	R	7.7	10:43 PM	Mild metabolic abnormality right temporal, mild structural abnormality left temporal	Bilateral medial temporal lobe and right inferior frontal gyrus	No surgery
10	P417	23	M	R	8.7	9:51 PM	Metabolic abnormality right parietal lobe, normal structural	Right parietal	Right parietal, seizure free
11	P422	19	F	R	7.9	10:01 PM	Normal	Bilateral multifocal	No surgery
12	P423	52	F	R	8.3	10:09 PM	Metabolic and structural abnormalities left temporal	Left medial temporal lobe	To be determined
13	P424	26	M	R	7.9	10:15 PM	Metabolic abnormalities right temporal, dysplasia left frontal	Left lateral temporal	Left lateral temporal to be resected

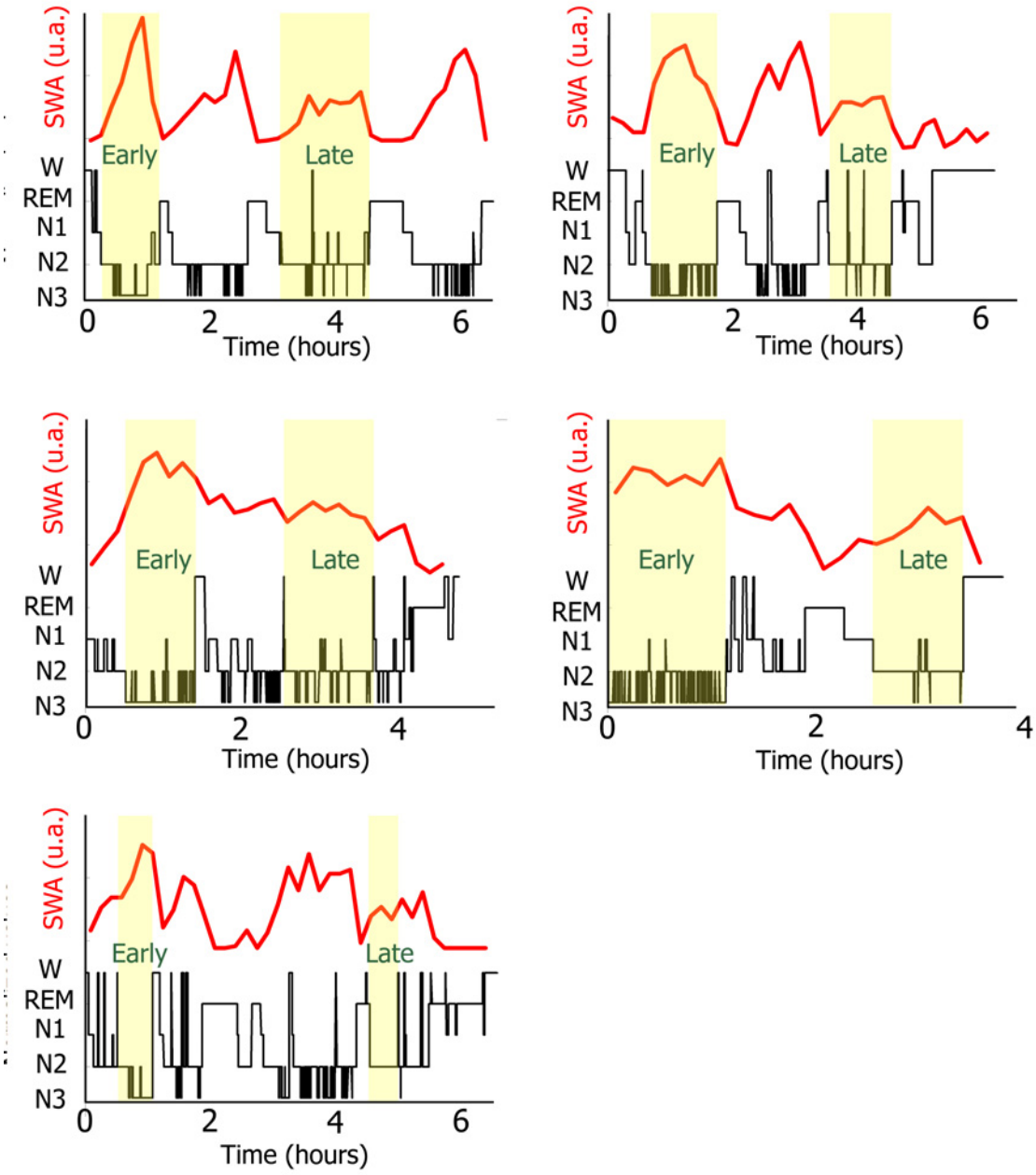
Supplementary Figure S1. Patient sleep resembles normal sleep in healthy individuals



Recording time (min)	403	±	23.5
Sleep time (min)	323	±	19
Sleep latency (%)	76.3	±	16.5
Sleep efficiency (%)	81	±	2
WASO (%)	13.9	±	2.2
N1 (%)	15.3	±	3.9
N2 (%)	41.5	±	3.5
N3 (%)	16.4	±	1.71
NREM (%)	73.2	±	2.58
REM (%)	13	±	2.07

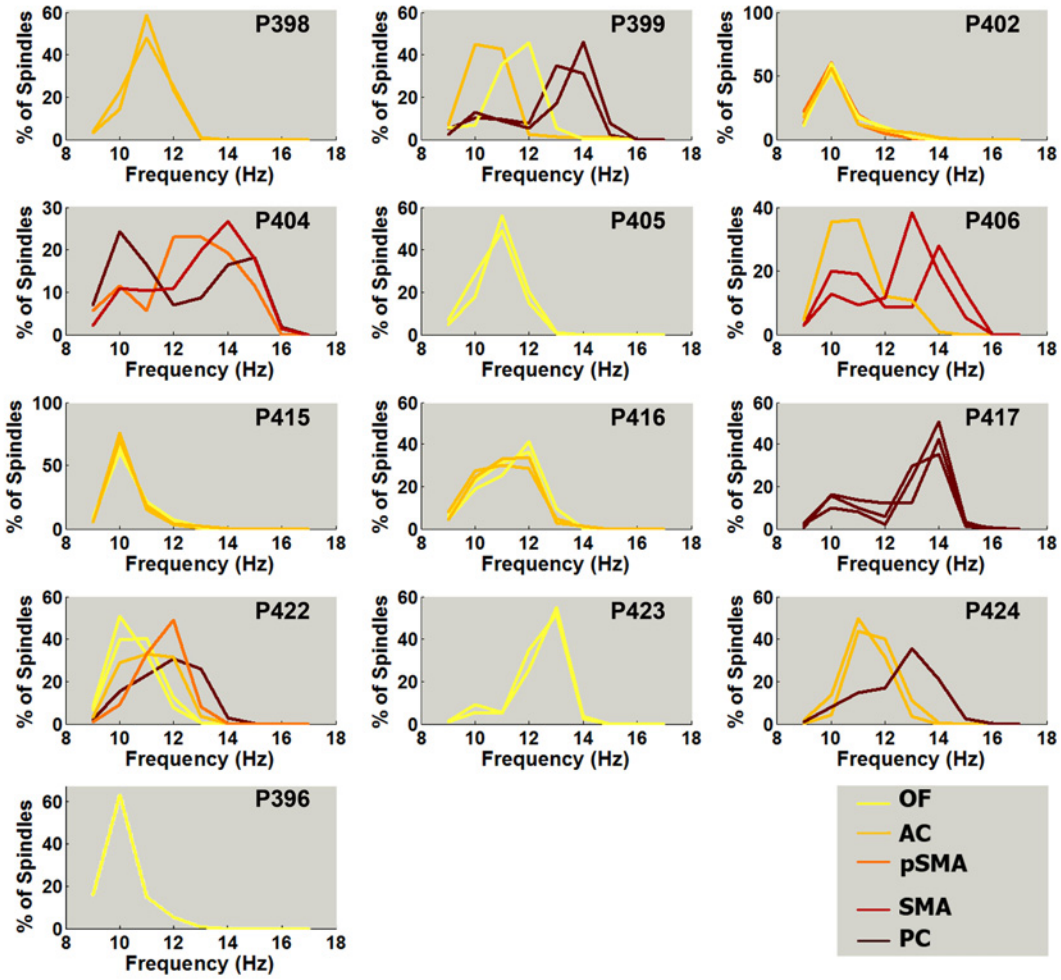
(A) Representative examples of 30s polysomnographic data used for sleep scoring in Wake stages, N2 , N3 and REM sleep in one individual. (B) Sleep measures for the entire night expressed as mean ± SEM (n=13). Sleep efficiency corresponds to total sleep time per time in bed. Sleep latency is to Stage 2. WASO refers to waking after sleep onset; SWS, slow-wave sleep (N2 + N3); NREM, non-rapid eye movement; REM, rapid eye movement. (C) Individual hypnograms (time course of sleep stages throughout sleep) and power spectra of scalp EEG in all derivations for all the 13 individuals. In hypnograms, rows (top to bottom) denote wake (W), REM sleep (R), N1, N2, and N3. Colors code in power spectra is: Blue, N2; Red, N3; Green, REM sleep. First five individuals (red asterisks) mark patients who showed the typical dissipation of SWA throughout sleep (see Figure S2).

Supplementary Figure S2. Homeostatic decline of SWA throughout sleep



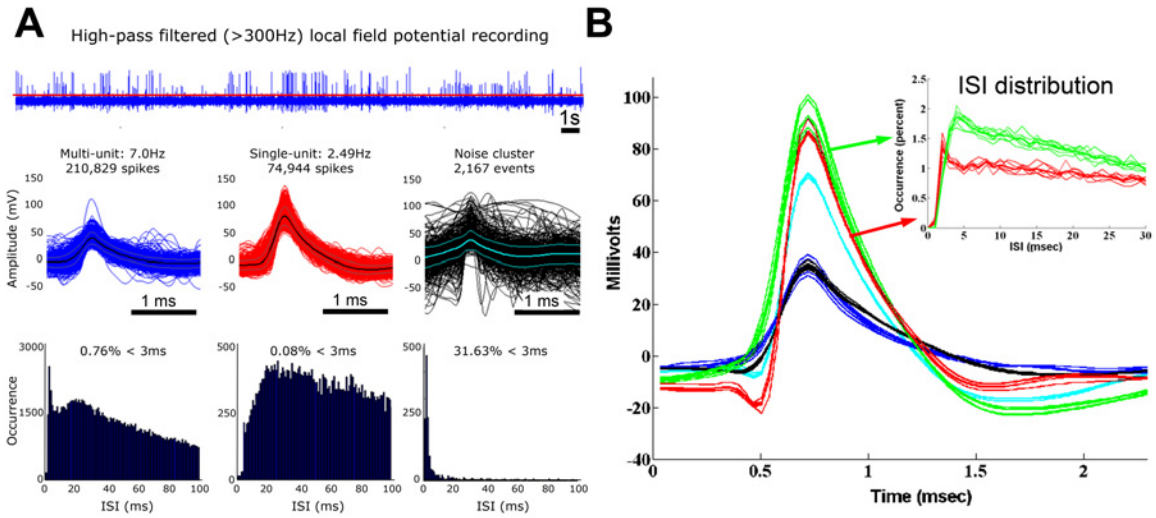
Individual hypnograms (black) and time-courses of SWA (red) in five individuals who showed a clear homeostatic decline of SWA throughout sleep. Sleep stages: W, wake; REM, rapid eye movement sleep; N1, N2 and N3: non-rapid eye movement sleep stages 1,2 and 3. Yellow highlights denote intervals of 'early' and 'late' sleep used for analysis presented in Figure 7.

Supplementary Figure S3. Spindle frequencies across all individuals and electrodes.



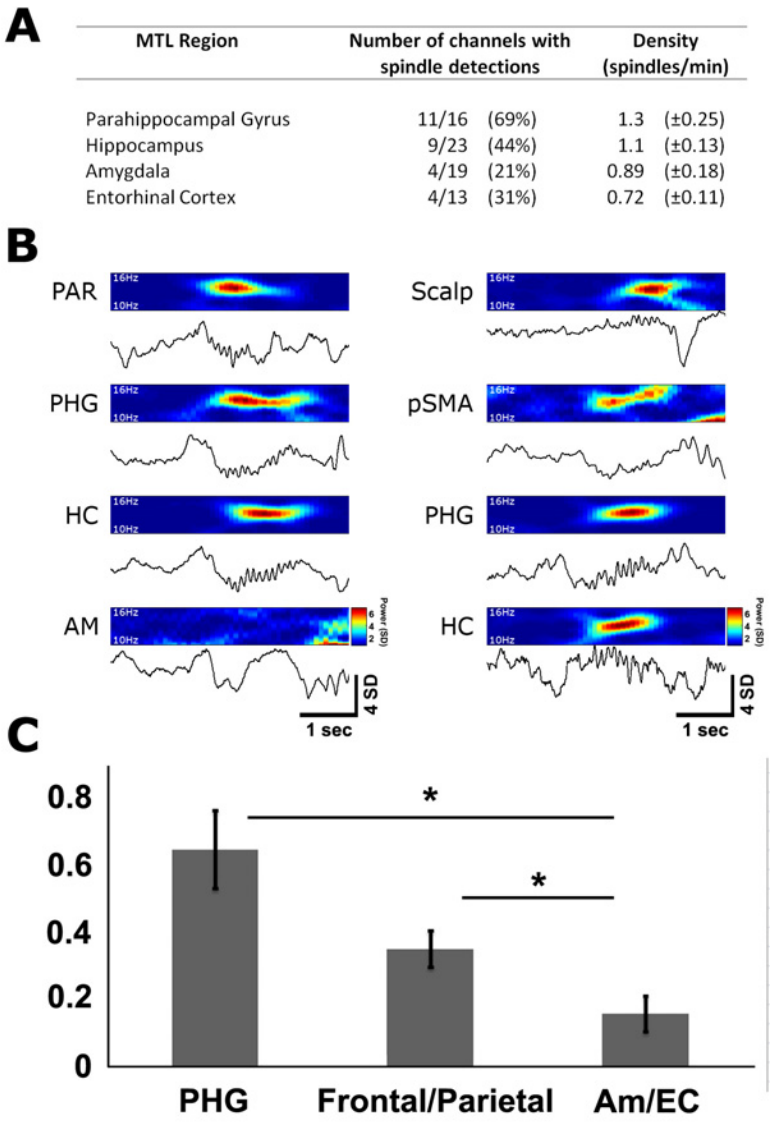
Spindle frequency distributions in each individual and depth electrode separately. Note that in every individual, fast centroparietal spindles differ from slow frontal spindles despite individual variability in the exact spindle frequencies. While frontal spindles consist of one group of slow events, centroparietal spindles often have a bimodal distribution with most spindles being fast and some being slow.

Supplementary Figure S4. Unit identification and stability throughout sleep recordings



(A) An illustration of unit identification scheme. Top row depicts the high-pass filtered LFP along with the threshold for spike identification set at 5 SDs above the noise level (red line). Middle row shows action potential waveforms for three detected clusters. Bottom row shows the distribution of inter-spike-intervals (ISIs). Based on the consistency of waveforms and the occurrence of ISIs within the expected refractory period (<3ms), we categorized clusters as a multi-unit cluster (blue), a single-unit cluster (red), and a noise cluster (black).
(B) Waveforms and ISI distributions are consistent and separable throughout sleep. Mean action potential waveforms for 5 distinct units recorded in the same individual. Each color denotes a different unit and each trace denotes the mean waveform in separate 1h intervals throughout sleep. Note that waveforms were consistent and separable between different units throughout sleep, confirming the stability of our unit recordings throughout long (~7h) recordings. Inset depicts ISI distributions in separate 1h intervals for two units.

Supplementary Figure S5. Spindles the in hippocampus and medial temporal lobe



(A) Spindle occurrence across MTL structures. Columns (left to right) show the region, the number of channels with spindle detections (over the total number of electrodes in that region), and the mean density of spindles per minute (±SEM across electrodes, n=13 individuals). Note that parahippocampal gyrus and hippocampus show higher spindle occurrence and density compared with entorhinal cortex and amygdala. (B) Two examples in two different individuals of spindles occurring concurrently in the MTL and other locations. Abbreviations, AM, Amygdala; PAR, parietal cortex; PHG, parahippocampal gyrus; HC, hippocampus. Note that in left example a spindle occurs concomitantly in hippocampus, parahippocampal gyrus, and parietal cortex but not in amygdala. (C) Probability of hippocampal spindles to co-occur with spindles in other brain regions. Note that hippocampal spindles co-occur often with spindles in parahippocampal gyrus, frontal and parietal spindles, but significantly less with amygdala and entorhinal cortex, supporting their difference from interictal epileptiform events.