Figure 1. Urethane exerts dose dependent effects on brain activity

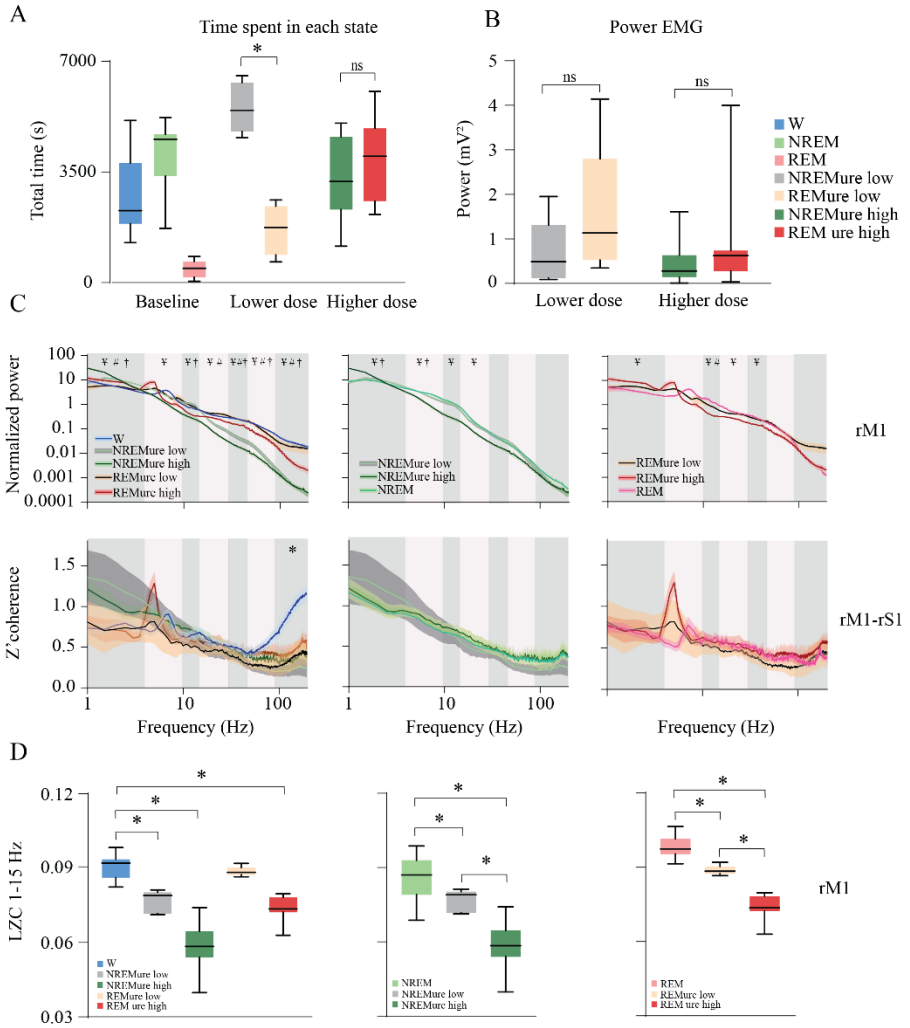


Figure 1. Effect of a subanesthetic dose of urethane on the electrocortical activity. (**A**) Total time spent in each behavioral state during baseline recordings (left), subanesthetic (lower) dose of urethane (middle) and urethane (higher dose) anesthesia (right). **(B)** Electromyography power during NREMure and REMure under subanesthetic (lower) dose of urethane (left) and urethane (higher dose) anesthesia (right); both states showed no significant (ns) differences. The boxes represent 25–75% range of the data, and the

whiskers represent the minimum and maximum values. **(C)** rM1 power spectral (top) and rM1-rS1 z'coherence (bottom) profiles. Left, Mean and SEM (shadow) normalized power spectral profiles/z'coherence of the rM1 during wakefulness (W), the states under a lower (subanesthetic) dose of urethane and the anesthetic dose of urethane (NREMure low and REMure low, and NREMure high and REMure high, respectively). Significant differences are indicated by symbols: ♯, W Vs. NREMure low; ¥, W Vs. NREMure high; †, W Vs. REMure high; *, differences among all conditions. Center, Mean and SEM (shadow) of normalized power spectral/z'coherence profiles of the right hemisphere during NREM sleep and its analogous under each dose of urethane. Significant differences are indicated by symbols: ¥, NREM Vs. NREMure high; † NREMure low Vs. NREMure high; *, indicates differences among all conditions. Right, Mean and SEM (shadow) normalized power/z'coherence spectral profiles of the right hemisphere during REM sleep and its analogous under each dose of urethane Significant differences are indicated by symbols: ♯, REM Vs. REMure low; ¥, REM Vs. REMure high; † REMure low Vs. REMure high; *, indicates differences among all conditions. **(D)** Lempel Ziv Complexity for frequencies between 1-15 Hz during W and the urethane states (Left), NREM sleep and NREMure under both doses of urethane (middle) and REM sleep and REMure under both doses of urethane (right) for rM1 cortex. *, indicates significant differences. M1, primary motor cortex; S1, primary somato-sensory cortex; W, wakefulness; r, right; δ, delta; θ, theta; σ, sigma; β, beta; lγ, low gamma or LG; hγ, high gamma or HG; HFO, high frequency oscillations.

Table 1. Normalized Power, statistical analyses

A. One-way ANOVA results W Vs. Anesthetized States												
	rOB			**rM1**			**rS1**			**rV2**		
Frequency	**df**	**F**	**p**	**df**	**F**	**P**	**df**	**F**	**p**	**df**	**F**	**P**
Delta	2,7	19.24	0.001*	2,8	45.87	<0.001*	2,8	54.90	<0.001*	2,7	23.04	0.001*
Theta	2,7	13.77	0.005*	2,8	12.26	0.004*	2,8	18.19	0.002*	2,7	9.28	0.009*
Sigma	2,7	3.717	0.053	2,8	21.00	<0.001*	2,8	56.86	<0.001*	2,7	19.10	0.001*
Beta	2,7	19.12	0.001*	2,8	45.45	<0.001*	2,8	57.61	<0.001*	2,7	19.64	0.001*
LG	2,7	31.49	0.001*	2,8	90.21	<0.001*	2,8	66.21	<0.001*	2,7	12.25	0.008*
HG	2,7	24.63	0.001*	2,8	115.2	<0.001*	2,8	74.13	<0.001*	2,7	26.20	0.001*
HFO	2,7	29.84	0.001*	2,8	45.34	<0.001*	2,8	30.43	0.001*	2,7	20.43	0.002*
B. Adjusted p values. W Vs. Anesthetized States												
	rOB			**rM1**			**rS1**			**rV2**		
Frequency	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**
Delta	0.0070*	0.9570	0.0084*	0.0021*	0.0791	0.0048*	0.0021*	0.0905	0.0021*	0.0021*	0.9288	0.0048*
Theta	0.0198*	0.1191	0.0198*	0.0021*	0.4682	0.0228*	0.0021*	0.0905	0.0088*	0.0107*	0.9288	0.0706
Sigma	N/A	N/A	N/A	0.0027*	0.0220*	0.1244	0.0021*	0.0030*	0.0287*	0.0040*	0.1934	0.0706
Beta	0.0243*	0.3870	0.0088*	0.0021*	0.1244	0.0021*	0.0021*	0.0448*	0.0024*	0.0040*	0.9288	0.0060*
LG	0.0064*	0.5882	0.0018*	0.0021*	0.0098*	0.0021*	0.0021*	0.0287*	0.0024*	0.0040*	0.6448	0.0229*
HG	0.0064*	0.0548	0.0109*	0.0021*	0.0021*	0.0022*	0.0021*	0.0021*	0.0021*	0.0040*	0.1494	0.0104*
HFO	0.0078*	0.0143*	0.0034*	0.0021*	0.0022*	0.0021*	0.0030*	0.0088*	0.0088*	0.0098*	0.0706	0.0706
C. Paired student t test with adjusted p values. NREMure Vs. NREM												
	rOB			**rM1**			**rS1**			**rV2**		
Frequency	**df**	**t**	**p**	**df**	**t**	**p**	**Df**	**t**	**p**	**df**	**t**	**p**
Delta	8	8.566	<0.001*	8	7.273	<0.001*	8	6.491	0.001*	7	6.341	0.002*
Theta	8	7.602	<0.001*	8	9.500	<0.001*	8	6.983	0.001*	7	4.789	0.007*
Sigma	8	8.737	<0.001*	8	5.669	0.002*	8	5.895	0.002*	7	7.230	0.001*
Beta	8	4.604	0.010*	8	4.281	0.011*	8	4.686	0.006*	7	5.430	0.005*
LG	8	2.980	0.041*	8	3.287	0.033*	8	4.574	0.006*	7	1.503	0.007*
HG	8	3.622	0.025*	8	3.197	0.033*	8	3.806	0.010*	7	0.403	0.8977
HFO	8	2.909	0.041*	8	3.169	0.033*	8	3.340	0.010*	7	0.138	0.8977
D. Paired student T test with adjusted p values. REMure Vs. REM												
	rOB			**rM1**			**rS1**			**rV2**		
Frequency	**Df**	**t**	**p**	**df**	**t**	**P**	**Df**	**t**	**p**	**df**	**t**	**p**
Delta	8	3.722	0.029*	8	6.110	0.001*	8	5.581	0.002*	7	4.621	0.014*
Theta	8	0.688	0.513	8	1.171	0.475	8	3.404	0.018*	7	4.349	0.017*

Sigma	8	4.333	0.017*	8	7.396	0.001*	8	8.399	0.001*	7	10.12	0.001*
Beta	8	5.900	0.004*	8	13.63	0.001*	8	5.038	0.005*	7	0.235	0.958
LG	8	6.415	0.003*	8	6.380	0.001*	8	4.255	0.008*	7	0.440	0.824
HG	8	2.808	0.077	8	5.528	0.002*	8	4.831	0.005*	7	0.794	0.958
HFO	8	2.681	0.077	8	0.923	0.475	8	1.361	0.210*	7	0.307	0.770

A. One way ANOVA analysis results. B. Adjusted p values after Holm-Šídák post-hoc. We analyzed only frequency bands for which ANOVA was significant. The ones not analyzed are represented by “N/A”. C. Statistical results from two-tailed paired Student t test comparing NREMure with NREM sleep (Holm-Šídák correction for multiple comparisons). D. Statistical results from two-tailed paired Student t test comparing REMure with REM sleep (Holm-Šídák correction for multiple comparisons). Data are plotted in Figure 2A and differences between basal and anesthetized states are schematized in Figure 2B.

Table 2. Inter-hemispheric and Intra-hemispheric z'coherence, Statistical analyses

A. One-way ANOVA results. Inter-hemispheric z'coherence W. Vs. Anesthetized States									
	rM1-lM1			**rS1-lS1**			**rV2-lV2**		
Frequency	**df**	**F**	**p**	**df**	**F**	**P**	**df**	**F**	**p**
Delta	2,7	14.66	0.001*	2,7	15.80	0.001*	2,7	2.876	0.113
Theta	2,7	2.711	0.131	2,7	9.36	0.007*	2,7	6.458	0.027*
Sigma	2,7	2.515	0.152	2,7	26.16	0.001*	2,7	5.624	0.042*
Beta	2,7	0.353	0.588	2,7	8.086	0.005*	2,7	6.524	0.023*
LG	2,7	1.436	0.270	2,7	1.179	0.333	2,7	4.058	0.048*
HG	2,7	2.635	0.141	2,7	37.30	<0.001*	2,7	10.24	0.012*
HFO	2,7	0.311	0.672	2,7	32.77	<0.001*	2,7	3.789	0.088
B. Adjusted p values. Inter-hemispheric z'coherence W. Vs. Anesthetized States									
	rM1-lM1			**rS1-lS1**			**rV2-lV2**		
Frequency	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**
Delta	0.018*	0.732	0.050*	0.002*	0.258	0.205	N/A	N/A	N/A
Theta	N/A	N/A	N/A	0.087	0.026*	0.772	0.151	0.399	0.814
Sigma	N/A	N/A	N/A	0.064	0.002*	0.288	0.290	0.400	0.814
Beta	N/A	N/A	N/A	0.104	0.104	0.928	0.399	0.241	0.725
LG	N/A	N/A	N/A	N/A	N/A	N/A	0.399	0.399	0.814
HG	N/A	N/A	N/A	0.002*	0.007*	0.894	0.131	0.233	0.814
HFO	N/A	N/A	N/A	0.003*	0.007*	0.737	N/A	N/A	N/A
C. Paired student t test with adjusted p values. Inter-hemispheric z'coherence NREM sleep Vs. NREMure									
	rM1-lM1			**rS1-lS1**			**rV2-lV2**		
Frequency	**df**	**t**	p	**df**	**t**	p	**df**	**t**	**p**
Delta	7	0.952	0.915	8	0.913	0.406	7	0.521	0.854
Theta	7	0.114	0.991	8	3.795	0.026	7	4.988	0.011
Sigma	7	0.123	0.991	8	7.540	0.001	7	4.675	0.014
Beta	7	1.022	0.916	8	5.417	0.005	7	3.714	0.037
LG	7	0.958	0.916	8	6.142	0.003	7	2.875	0.092
HG	7	1.029	0.916	8	3.806	0.026	7	0.844	0.811
HFO	7	1.461	0.766	8	1.317	0.406	7	0.373	0.854
D. Paired student t test with adjusted p values. Inter-hemispheric z'coherence REM sleep Vs. REMure									
	rM1-lM1			**rS1-lS1**			**rV2-lV2**		
Frequency	**df**	**t**	**p**	**df**	**t**	**P**	**df**	**t**	**p**
Delta	7	0.120	0.907	8	2.435	0.169	7	0.127	0976
Theta	7	0.969	0.597	8	6.023	0.003	7	4.403	0.018

Sigma	7	2.309	0.323	8	7.148	0.001	7	5.203	0.008
Beta	7	0.157	0.534	8	0.990	0.584	7	3.089	0.085
LG	7	0.227	0.538	8	0.060	0.953	7	1.160	0.634
HG	7	0.124	0.534	8	1.430	0.480	7	0.204	0.976
HFO	7	0.119	0.534	8	3.699	0.038	7	2.000	0.301
E. One-way ANOVA results. Intra-hemispheric z'coherence W. Vs. Anesthetized States									
	rOB-rM1			**rM1-rS1**			**rS1-rV2**		
Frequency	**df**	**F**	**p**	**df**	**F**	**p**	**df**	**F**	**p**
Delta	2,7	11.77	0.007*	2,8	3.758	0.067	2,6	3.040	0.123
Theta	2,7	7.756	0.007*	2,8	0.434	0.564	2,6	4.956	0.046*
Sigma	2,7	7.300	0.007*	2,8	1.206	0.308	2,6	0.813	0.407
Beta	2,7	3.841	0.071	2,8	0.085	0.794	2,6	0.295	0.639
LG	2,7	1.201	0.326	2,8	1.034	0.345	2,6	0.286	0.684
HG	2,7	1.158	0.325	2,8	23.04	<0.001*	2,6	12.29	0.004*
HFO	2,7	3.217	0.094	2,8	85.11	<0.001*	2,6	7.393	0.012*
F. Adjusted p values. Intra-hemispheric z'coherence W. Vs. Anesthetized States									
	rOB-rM1			**rM1-rS1**			**rS1-rV2**		
Frequency	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**	**W vs. NREMure**	**W vs. REMure**	**NREMure vs. REMure**
Delta	0.045*	0.223	0.008*	N/A	N/A	0.205	N/A	N/A	N/A
Theta	0.065	0.223	0.223	N/A	N/A	0.772	0.154	0.845	0.077
Sigma	0.106	0.785	0.065	N/A	N/A	0.288	N/A	N/A	N/A
Beta	N/A	N/A	N/A	N/A	N/A	0.928	N/A	N/A	N/A
LG	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HG	N/A	N/A	N/A	0.001*	0.004*	0.045*	0.077	0.233	0.999
HFO	N/A	N/A	N/A	0.001*	0.004*	0.017*	0.153	0.064	0.996
G. Paired student t test with adjusted p values. Intra-hemispheric z'coherence NREM sleep Vs. NREMure									
	rOB-rM1			**rM1-rS1**			**rS1-rV2**		
Frequency	**df**	**t**	**p**	**df**	**t**	**p**	**df**	**t**	**p**
Delta	7	0.876	0.558	8	0.199	0.976	6	0.231	0.985
Theta	7	1.288	0.558	8	1.150	0.820	6	0.326	0.985
Sigma	7	1.053	0.558	8	1.037	0.820	6	1.331	0.842
Beta	7	2.057	0.437	8	1.144	0.820	6	0.726	0.942
LG	7	2.012	0.437	8	0.133	0.976	6	0.836	0.942
HG	7	1.608	0.483	8	1.243	0.820	6	0.297	0.985
HFO	7	1.769	0.473	8	1.557	0.700	6	1.128	0.885
H. Paired student t test with adjusted p values. Intra-hemispheric z'coherence REM sleep Vs. REMure									
	rOB-rM1			**rM1-rS1**			**rS1-rV2**		

Frequency	**df**	**T**	**p**	**df**	**T**	**P**	**df**	T	**p**
Delta	7	2.802	0.149	8	1.072	0.911	6	3.141	0.132
Theta	7	1.475	0.456	8	0.594	0.985	6	2.282	0.321
Sigma	7	3.473	0.071	8	0.402	0.992	6	2.035	0.369
Beta	7	1.986	0.364	8	0.204	0.992	6	0.371	0.979
LG	7	0.255	0.806	8	0.376	0.992	6	0.063	0.998
HG	7	1.124	0.507	8	0.110	0.992	6	0.021	0.998
HFO	7	1.993	0.364	8	1.129	0.911	6	1.394	0.616

Statistical analyses of interhemispheric (A-D) and intra-hemispheric (E-H) coherence. A,E. One-way repeated measures ANOVA analysis result for comparison of coherence between wakefulness and anesthetized states. B,F. Adjusted p values after Holm-Šídák *post-hoc*. We analyzed only frequency bands for which ANOVA was significant. The ones not analyzed are represented by "N/A". C,G. Statistical results from two-tailed paired Student t test comparing NREMure with NREM sleep (Holm-Šídák correction for multiple comparisons). D, H. Statistical results from two-tailed paired Student t test comparing REMure with REM sleep (Holm-Šídák correction for multiple comparisons). Data are plotted in Figure 3A and B., and differences between basal and anesthetized states are schematized in Figure 3C.

Table 3. Correlates of consciousness during anesthetized states and physiological sleep states in comparison to wakefulness

Correlates of consciousness	NREMure	NREM sleep	REMure	REM sleep
Delta power	+	+[a]	+	n/c [a]
Gamma and HFO power	-	- [a]	-	n/c [a]
Gamma and HFO coherence	-	- [a]	-	- [a]
HG FB Gamma NSTE	-	-[b]	-	-[b]
LZC	-	-	-	n/c[c]
JLZC	-	-	-	n/c[d]

EEG features suggest that urethane produces unconsciousness during both NREMure and REMure. Increase (+) or decrease (-) in comparison to wakefulness. n/c, no changes. [a]Mondino et. al (2020), [b]Pal et. al (2016), [c]Abásolo et. Al (2015), [d]Mateos et al. 2017