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Propofol weakens alpha oscillation phase locking between hippocampus and prefrontal cortex

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Background

Interactions between hippocampus (hip) and prefrontal cortex (pFC) are associated with mnemonic processes. pFC has been linked to working memory, capable to store information for some seconds. To be remembered, items must be shifted into the hip. Synchronized θ-oscillations seem essential for interactions between these areas, i.e., a functioning amnestic pathway [1]. To evaluate θ-synchrony changes between pFC and hip, the phase locking value *PLV* was calculated during control and at hypnotic propofol concentrations. Changes in *PLV* may represent an anesthetic-induced effect on hip-pFC interactions, possibly reflection amnestic actions. Since narrower frequency ranges may be beneficial for detection of synchronization effects, one wide and 2 narrow frequency bands in the θ-range were used.

Methods

Nine local field potential (LFP) sets from wild type mice were recorded with 20 kHz at control and hypnotic propofol concentrations (30 mg/kg) from 4-channel multi-electrode arrays located in pFC (layer II) and hip. Representative episodes of 5 s were extracted from each recording and filtered to 5-15 Hz, 4-8 Hz or 8-12 Hz after down sampling to 250 Hz. PLV calculation [2] is based on phase differences between LFPs from hip and pFC.

The LFPs' complex representation was derived from the Hilbert transform. The real part is the original signal and the imaginary part is the 90° phase shifted original signal. The analytic phase $\varphi(t)$ of a signal $x(t)$ is $\varphi(t)=\arctan(\mathrm{Im}(x(t))/\mathrm{Re}(x(t)))$. The phase difference is $\Phi(t)=\varphi_{hip}(t)-\varphi_{PFC}(t)$ and $PLV=(1/N)|\Sigma\exp(i\Phi(t))|$. *PLV* was calculated for all hip/pFC channel combinations from 5 non overlapping 1s episodes (N=250) of the 5s segment and averaged. For statistical analysis, *PLV* of all channel combinations of one data set were also averaged, leading to 9 *PLV* at control and with propofol. Wilcoxon signed rank test was used (significant: p<0.05) as well as the effect size measure Hedges' g [3].

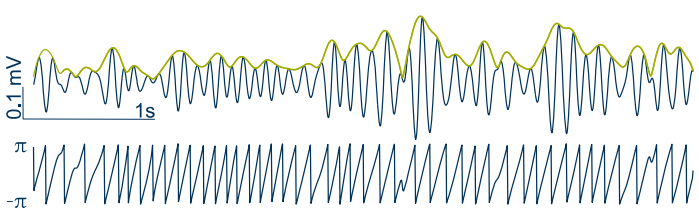

Figure 1: Based on the exemplary LFP that was filtered to the 8-12 Hz range (1st row, blue trace) the analytic amplitude, i.e., the signal envelope (1st row, orange trace) and the analytic phase (2nd row) can be derived using HT.

Results

	PLV control	PLV propofol	p	Hedges' g
	mean ± sem	mean ± sem	(signed rank)	(95% confidence intervals)
5-15 Hz	0.53 ± 0.05	0.38 ± 0.04	0.164	1.05 (0.12-2.62)
4-8 Hz	0.48 ± 0.05	0.47 ± 0.04	1	0.09 (-0.99 1.18)
8-12 Hz	0.58 ± 0.04	0.37 ± 0.03	0.004	1.80 (1.20 3.06)

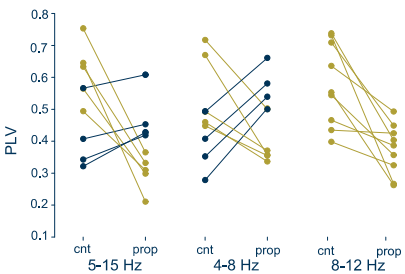

Figure 2: Change of PLV in the defined frequency ranges for the single experiments

Conclusions

Propofol negatively influences *PLV* in the 8-12 Hz range. A *PLV* close to 1 indicates little variation of phase differences. If the variation increases *PLV* tends towards 0. Our data indicate that propofol causes a bigger variation in phase differences leading to decreased phase locking and hence possibly impaired communication between hip and pFC. Based on the results we suggest that the usually chosen θ-ranges of 5-15Hz, 4-12Hz, etc. may be too wide to determine significant oscillation effects. Here, e.g., in the 5-15Hz range no significant effect by means of the signed rank test but a strong effect by means of Hedges' g can be observed. In the narrower 4-8Hz frequency range no effect was observed, but in the 8-12Hz band the effect was significant. This militates for analyses in smaller frequency bands. The negative effect of propofol on *PLV* may be associated with anesthetic-induced amnesia.

References

[1]Anesthesiology,2010,113:48–57; [2]Hum Brain Mapp,1999,8:194–208; [3]EJN,2011,34:1887–1894