# Alpha band connectivity of the frontal EEG associates with consciousness during target controlled infusion of dexmedetomidine and propofol in healthy subjects

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## Background and Goal of Study

Current depth-of-anaesthesia monitors cannot reliably differentiate unconsciousness from deep sedation. In the search for better EEG signatures, we compared connectivity changes induced by dexmedetomidine and propofol until loss of consciousness (LOC) in a highly standardized setting.

## Materials and Methods

After ethical approval (ClinicalTrials.gov Identifier: NCT01889004), 47 healthy male subjects were randomised to receive dexmedetomidine (n=23) or propofol (n=24) through target controlled infusion, starting from 1.0 ng/ml and 1.0 µg/ml, respectively, and then titrated with 0.25−0.50 stepwise increments at 7 min intervals until loss of responsiveness (LOR). LOR was defined as subjects' inability to press handles upon requests presented via headphones. After achieving LOR, an attempt was made to awaken the subjects with a loud voice or mild physical stimulation without changing the drug infusion. After possible awakening (return of responsiveness, ROR), the subjects were permitted to subside (or maintain if unarousable) unresponsive, and the target concentration was increased by 50 % to achieve presumable LOC. EEG signal was collected at 64 sites, and EEG spectra and weighted (wPLI) and directed phase lag index (dPLI) between different brain areas processed offline using custom-written functions in MATLAB and linked mastoid reference. Data were analysed using repeated measures analysis of variance (RM ANOVA) followed by paired comparisons corrected for multiple comparison (Bonferroni).

## Results

The mean (SD) measured drug concentration for LOR was 2.10 (0.67) ng/ml dexmedetomidine and 1.67 (0.62) µg/ml for propofol. Eighteen (78%) and 10 (42%) subjects were arousable from the LOR state (i.e, achieved ROR) in the dexmedetomidine and propofol groups, respectively. Apparent connectivity changes were seen in the alpha band (8-14 Hz), and topographic analysis revealed that especially in and between the prefrontal-frontal areas the connectivity measures showed state dependent changes (**Figures 1-2**). Prefrontal-frontal wPLI increased and dPLI turned more negative (suggesting that prefrontal "lagged" the frontal signal) towards LOC (**Figure 3**), and were reverted in subjects who could be aroused during constant drug infusion (**Figure 4**).

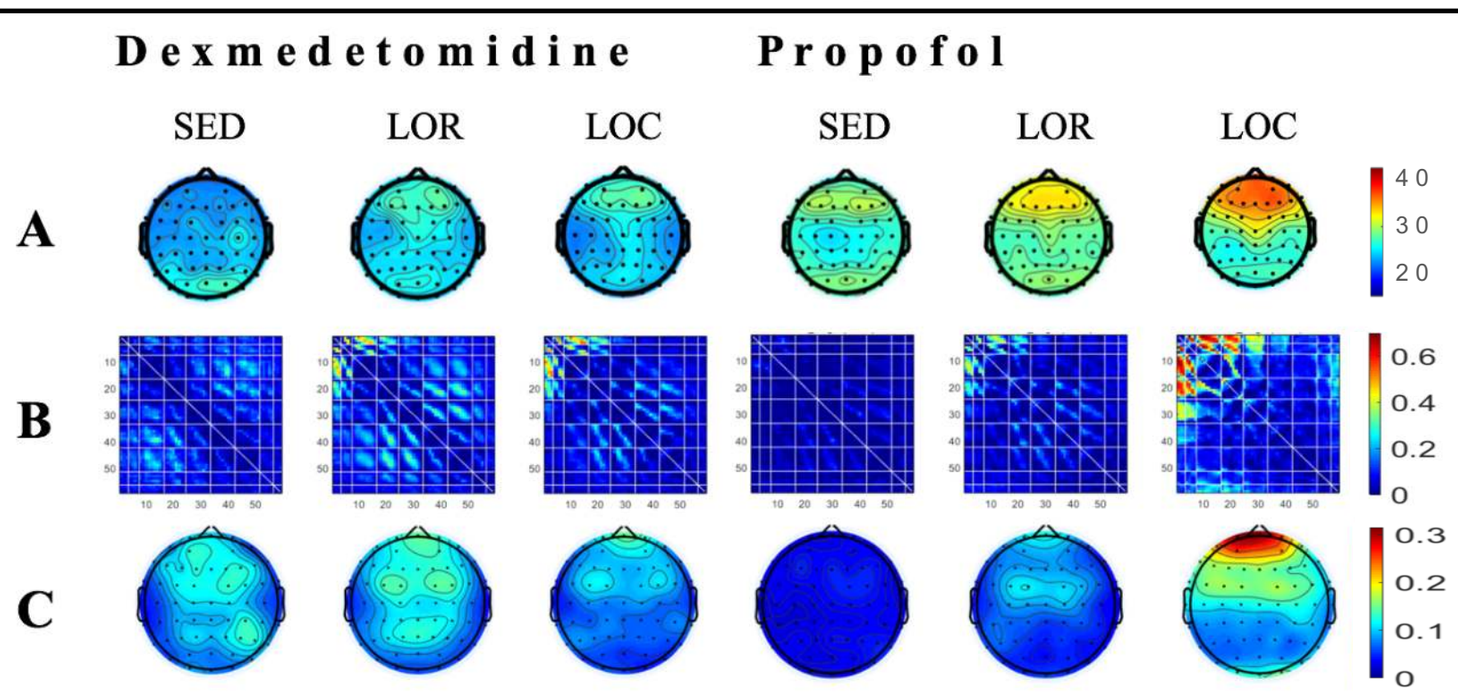


**Figure 1** **A.** Spectral powers (dB) of alpha band (8-14 Hz). **B.** wPLI matrix in alpha band between all channel pairs (low numbers = frontal). **C.** Mean alpha band wPLI in each channel over all channel pairs.

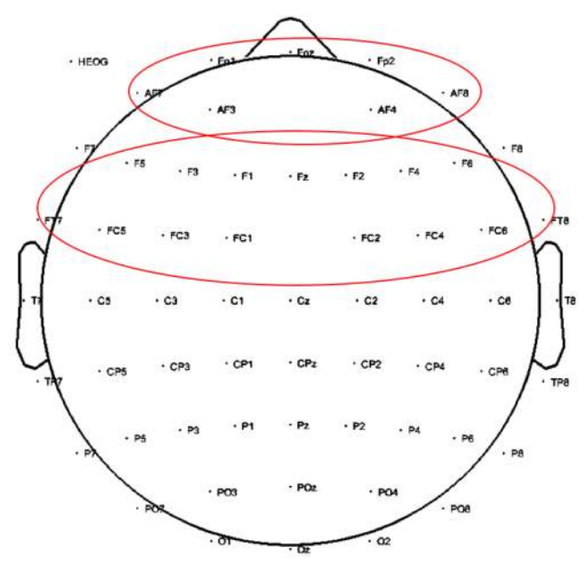


**Figure 2** EEG channels selected for prefrontal and frontal regions-of-interest.

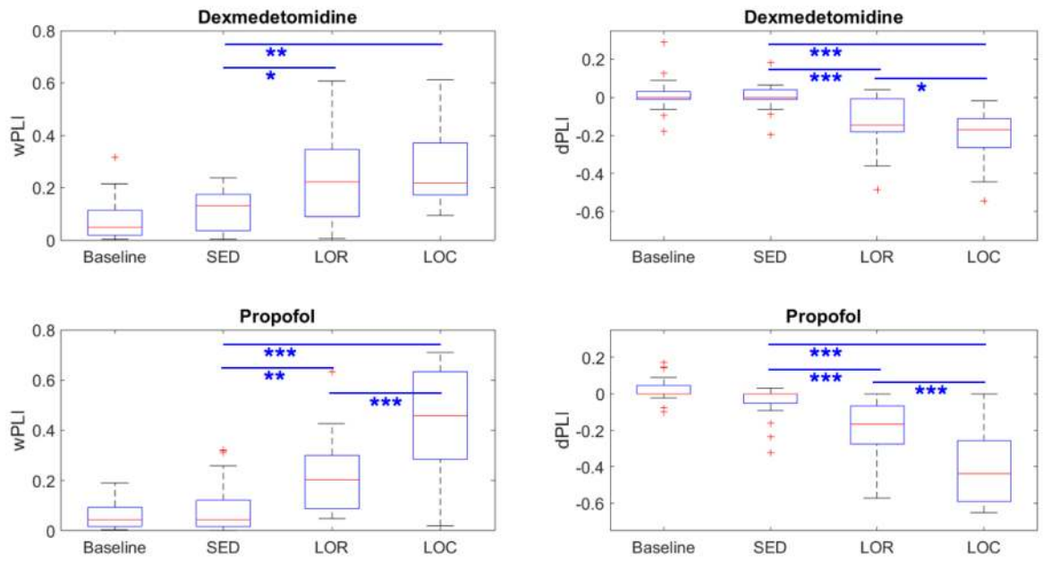


**Figure 3** Prefrontal-frontal wPLI and dPLI before and during dexmedetomidine and propofol infusions. Boxplots at baseline, deep sedation (SED), LOR and LOC states. * ($p<0.05$), ** ($p<0.01$) and *** ($p<0.001$) indicate significant differences between the SED, LOR and LOC states.

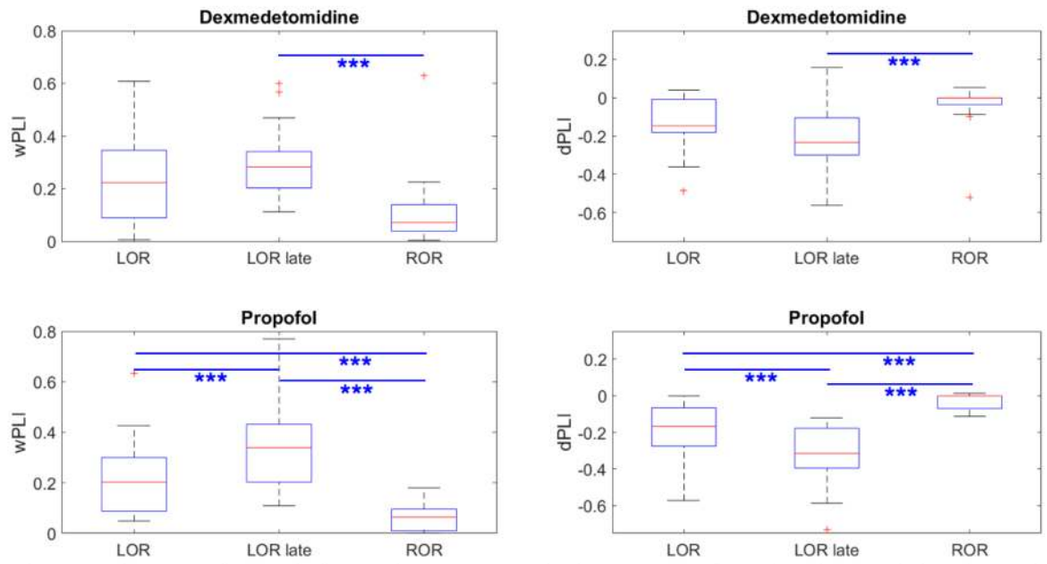


**Figure 4** Prefrontal-frontal wPLI and dPLI at LOR (early and late) and ROR in arousable subjects during constant dexmedetomidine (n=18) and propofol (n=10) infusions titrated to LOR. Data as boxplots. ***($p<0.001$) indicate significant differences between the states.

## Discussion and Conclusion

The current results are intriguing as dexmedetomidine does not seem to induce strong anteriorisation or apparent "hyper-coherence" of the EEG alpha band like propofol. Monitoring prefrontal-frontal alpha band connectivity of the EEG could be a viable alternative for developing depth-of-anaesthesia monitoring in the future.

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