Phase-based measures of cross-frequency coupling in brain electrical dynamics under general anesthesia

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Abstract
The state of general anesthesia (GA) is associated with an increase in spectral power of brain electrical activity recorded by scalp electroencephalograph (EEG) at frequencies below 40 Hz, including prominent spectral peaks in the slow oscillation (SO, 0.1-1 Hz) and α (8-14 Hz) bands. Because conventional power spectral analyses are insensitive to cross-frequency coupling, the relationships among the oscillations at different frequencies remain largely unexplored. Quantifying such coupling is essential for improving clinical monitoring of anesthesia as well as for understanding the neuroscience of this brain state. We tested the usefulness of two measures of cross-frequency coupling: the bispectrum-derived SynchFastSlow metric, which is sensitive to phase-phase coupling in different frequency bands, and a modulogram analysis of coupling between SO phase and α rhythm amplitude. SynchFastSlow, a metric that is used in clinical depth-of-anesthesia monitors, showed a robust correlation with the loss of consciousness at the induction of propofol GA, but we found this could be entirely accounted for by changes in the power spectrum without considering cross-frequency coupling. Modulogram analysis revealed two distinct modes of cross-frequency coupling under GA. The waking and two distinct states under GA could be discriminated by cluster analysis in a two-dimensional phase space defined by the SynchFastSlow and the preferred SO phase of α activity. Our results suggest that phase-amplitude coupling provides a robust signature of multiple stages of anesthesia induced unconsciousness, and that modulogram analysis can improve EEG based monitoring of brain state under general anesthesia.

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