Disturbed Coherence of Information Processes as Revealed by Intrinsic Functional Connectivity during Propofol Anesthesia

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Introduction Process-coherence theories have been proposed by anesthesiologists about how general anesthetics achieve anesthesia and cause a loss of consciousness [1-3]. These theories have been based on clinical observations of neuronal activity in sleep, epileptic, or vegetative patients [4,5]. It has been difficult to test hypotheses involving disruptions in the coherence of neural activity until very recently with the development of techniques for reliably assessing intrinsic functional connectivity contrast (ICC) by our group and others [6,7]. In this work, we used intrinsic function connectivity contrast power [7] to quantify changes in communications between neural networks, upon administration of Propofol, and test the hypothesis of process-coherence theories of anesthesia.

Materials and Methods Twenty eight healthy subjects (19-35 years) underwent MR sessions in which resting state fMRI/BOLD acquisitions for intrinsic functional connectivity with and without the administration of Propofol at the plasma concentration of 2μg/ml. Propofol i.v. infusion was administered through a target-controlled infusion pump (Stanpump, Stanford University, Palo Alto, CA) based on the age, sex, weight and height of the subject. MRI data were acquired on a 3T whole-body scanner Trio (Siemens Medical Systems, Erlangen, Germany) with a 12-channel phased-array head coil. During pre-anesthesia and Propofol anesthesia, two functional BOLD runs of 210 volumes each were acquired using a T2*-sensitive gradient-recalled, single-shot echo-planar imaging pulse sequence (TR = 2 s, TE = 30 ms, FOV = 256x256 mm², flip angle = 90°, matrix size 64x64). Each volume consisted of 33 AC-PC aligned slices, with a slice thickness of 4mm and no gap. Steady-state fMRI/BOLD data were slice-time and motion corrected using SPM5. At each voxel the BOLD signal was low-pass filtered (cut-off frequency: 0.08 Hz) and the 6 motion parameters, the mean signals of white matter and CSF, and linear and quadratic drifts were regressed from the data. The mean time course signals from the white matter and CSF signals were removed from the BOLD time courses. For each experimental condition (i.e. pre-anesthesia and Propofol anesthesia) the two functional runs were concatenated after the removal of the mean value and the ICC power measure was computed applying a correlation threshold of 0.25. Bioimage Suite was employed for multi-subject integration.

Results and Discussion Significant increases and decreases in ICC were observed in different regions of the brain during propofol anesthesia (Figs. A & B). Increases in ICC by Propofol occurred extensively in the parietal, occipital, and medial prefrontal cortex, whereas decreases were distributed primarily along the precentral gyri, the ventral frontal and temporal lobe. More specifically, cuneus and precuneus, primary visual, motor areas and their associative areas, anterior and posterior cingular cortex showed increases in ICC upon administration of Propofol; the ventral medial/lateral frontal gyrus (BA 8-11, BA 32, BA 45 and 46), primary auditory, all areas along precentral gyri and suppar temporal cortex were among the regions where ICC was most suppressed. The spatial pattern of the ICC changes induced by Propofol in this study is very similar to that previously reported by our group during Sevoflurane administration in humans [7], and more importantly, the networks with the largest increase in ICC essentially comprised the default-mode network (DMN) [8], which has been related to the unconscious states in previous clinical practice [4,5]. These results indicate increased cross talk between the DMN components during anesthesia might make them ignore the input of external stimulation into the DMN.

Conclusion There has been speculation that anesthesia and sleep might share some common neuronal mechanisms. The functional significance of the default mode of the brain has been attributed to evolutionary survival for continuously screening the ambient information and preparation to respond whenever necessary. The results in this study demonstrate enhancement of synchronous oscillations in the DMN in the presence of Propofol. Such increases in synchronous oscillations may be a prerequisite for producing sleepiness and unconsciousness.


![Fig. Changes in ICC induced by Propofol, p<0.05 corrected. (A) Coronal slices and (B) 3-slice view.](image)