Disrupted Sensory Projection and Preserved Integrative Network in Propofol-Induced Anesthesia

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Introduction: Information and integration recently have been proposed to account for the essential properties of human conscious experience, providing a theoretical basis for understanding the loss of consciousness in anesthesia and other normal or pathological conditions, such as sleep, coma, and vegetative state[1, 2]. Nevertheless, the details of how information processing is disrupted in anesthesia are not well understood. Here we examined the effect of propofol on auditory stimulus-related cortical activation and integration using functional magnetic resonance imaging (fMRI) and fMRI-guided connectivity analysis. Based on the theoretical suggestion of 'information received but not perceived'[3] as a general mechanism of anesthetics, we test the hypothesis that task-defined BOLD functional connectivity in the hierarchically-organized neural networks is maintained in the waking and emergence states, sustaining auditory conscious perception, but it is disrupted at a propofol dose at which study participants no longer show conversational responses as well as mnemonic and semantic functionalities.

Methods: Eight healthy volunteers listened to 200 high-frequency words under four sequential states of consciousness: awake, sedated (0.5 ug/ml propofol plasma concentration; not considered in analysis due to its ambiguous effects), anesthetized (0.75 or 1.0 ug/ml), and emerged (a return to waking baseline) during fMRI at 1.5T. Task-induced neural activations in the blood oxygen-dependent (BOLD) signal were analyzed at each level of consciousness. Functional connectivity analysis was conducted by the cross-correlation of low-frequency (<0.1Hz) filtered BOLD time courses using seed voxels within the inferior frontal gyrus (IFG), which showed the most prominent activation under non-propofol conditions (i.e., waking and emergence) and suppression in the anesthetized state.

Results: The auditory cortex demonstrated resilient activations across all levels of propofol including anesthesia, in which subjects failed to produce conversational responses. Propofol at the high-dose reduced left-lateralized BOLD activation in the left inferior/middle frontal gyrus, precentral gyrus, middle and superior temporal cortex – regions previously found involved in mnemonic and semantic functions[4] (Fig. 1, *left*). Propofol also suppressed BOLD activation in mainly the parietal components of the "default mode network" (e.g., posterior cingulate and precuneus). In all three states of consciousness, the seed region in the IFG demonstrated robust functional connectivity with widespread frontoparietal and temporal regions including the extensive areas of the IFG, anterior insular, middle and superior frontal gyrus, premotor areas, pre/postcentral gyrus, temporal areas, precuneus, and the inferior and superior parietal lobule. Notably, in the anesthetized state, all these functional connections manifested in the conscious states were still preserved, except that the functional connectivity between the IFG seed and the areas of the primary auditory cortex was lost (Fig. 1, *right*).

Conclusion: Our results suggest that propofol disrupted the mnemonic and semantic processing of verbal inputs by preventing the auditory sensory information from propagating into the neural network of higher-order cognitive processing, which, however, maintained robust functional coupling of BOLD response. These findings indicate a differential effect of propofol anesthesia on sensory and cognitive systems and provide direct imaging evidence for information disintegration as a mechanism of anesthetic-induced unconsciousness.

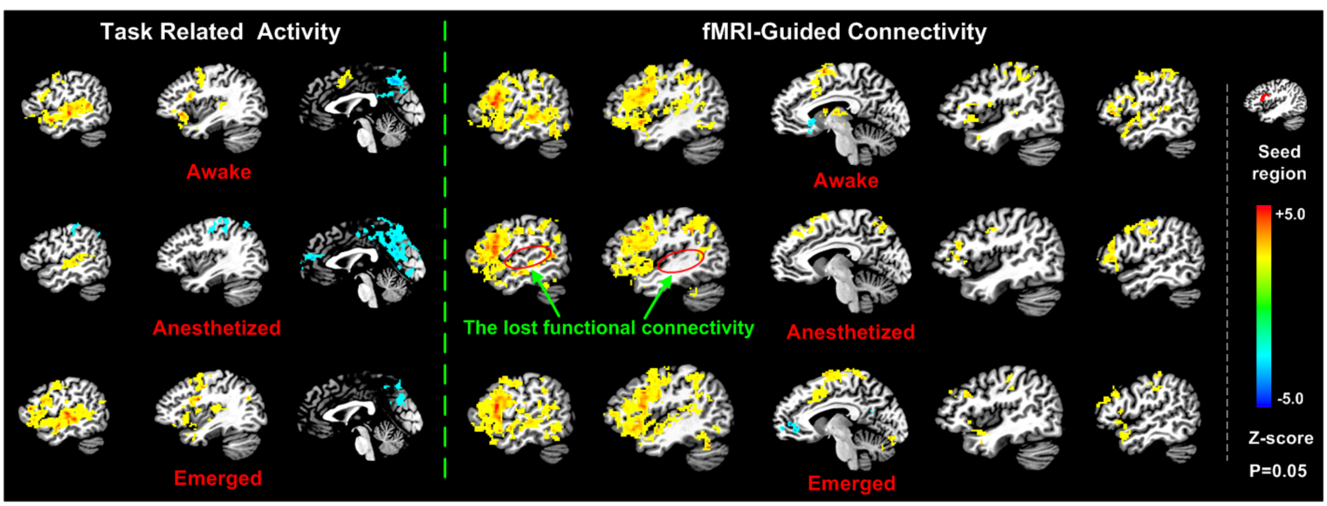

Figure 1. Verbal stimulus-related brain activation (left to the green line) and the patterns of functional connectivity (right) with a seed region drawn from a limited set of voxels in the IFG (corrected for multiple comparisons using a minimum cluster size of 1432 mm^3).

References:
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