Propofol-Induced Reduction of Functional Connectivity in Large-Scale Brain Networks Defined at Fine Spatial Scales

Xiaolin Liu[1], Kathryn K. Lauer[2], B. Douglas Ward[1], Jeffrey R. Binder[3], Shi-Jiang Li[1], and Anthony G. Hudetz[2]

[1]*Biophysics, Medical College of Wisconsin, Milwaukee, Wisconsin, United States,* [2]*Anesthesiology, Medical College of Wisconsin, Milwaukee, Wisconsin, United States,* [3]*Neurology, Medical College of Wisconsin, Milwaukee, Wisconsin, United States*

Target audience: neuroscientist, anesthesiologist, fMRI analyst

Purpose: Theoretical and experimental advances have suggested that consciousness emerges from brain function as a network phenomenon.[1,2] Neural processes supporting conscious perception integrate information from endogenous and exogenous sources in large-scale brain networks and make the computational result globally accessible across the brain.[3] Anesthetics may suppress consciousness by globally disrupting functional interactions within and between brain networks. The details of this process remain incompletely understood due, in part, to limitations in the current neuroimaging brain parcellation approaches used to estimate the topological, structural and functional features of brain network organization at fine spatial resolutions.[4] In a recent study, we proposed a new combined anatomical-functional parcellation algorithm for defining brain networks at arbitrary spatial scales using functional magnetic resonance imaging (fMRI).[5] The goal of the current study is to extend this approach to determine global changes in brain functional connectivity during propofol sedation at two sedation levels as compared to wakefulness and recovery. We hypothesized that propofol sedation is accompanied by a profound global reduction of functional connectivity in the brain networks.

Methods: Resting-state blood oxygen level-dependent (BOLD) fluctuations (3T GE Signa scanner, repetition time 2s, 3.5-mm isotropic voxels) were measured from 11 healthy volunteers (8 men and 3 women; aged 23 to 34) during four 15-min runs in wakeful baseline, propofol-induced light sedation and deep sedation, and recovery. In deep sedation, volunteers showed no response to verbal commands (OAAS score 2-1). After standard imaging preprocessing procedures, hierarchical clustering was performed with all voxels in each of the 116 standard anatomical structures defined by a template.[6] The constituent nodes of the brain networks were defined as clusters of voxels sharing a similar hemodynamic temporal correlation in one run and spatially confined by individual anatomical boundaries. By varying a global threshold that determines the final cluster formation, the networks can be flexibly defined at any arbitrary spatial scale or at any total number of network nodes (**Fig. 1A**). Group comparison of node connectivity between the states of consciousness was performed by aligning the defined network nodes (at each spatial scale) of all runs in all study volunteers to a reference 3-dimensional node coordinate obtained from a representative volunteer in wakeful baseline based on a nearest neighbor node-to-node alignment principle.

Results: The distribution of network nodes demonstrated a general trend of interhemispheric symmetry across the examined spatial scales and conditions in all subjects. Condition comparisons are shown in Figure 1 at the spatial scale of 1000 nodes ($P<0.0001$). Node pairs showing significant reduction in connectivity relative to baseline wakefulness increased from light sedation (**Fig. 1B**, 150 pairs) to deep sedation (**Fig. 1C**, 378) and decreased at the recovery of consciousness (**Fig. 1D**, 82). Of all node connections showing significant reduction in wakefulness > deep sedation comparison, 56% involved the frontal lobe, 29% the parietal lobe, 26% cortical-subcortical connectivity, 23% the cerebellum, 9% frontal-parietal connectivity, and 41% interhemispheric connectivity. Similar results were present at other spatial scales (e.g. 300, 500 and 2000 network nodes).

Discussion and Conclusion: The findings support the hypothesis that propofol sedation and its deepening are associated with a global reduction of brain functional connectivity. Reduced node connectivity in deep sedation showed different degrees of involvement of cortical and subcortical systems. The proposed approach represents a way of comprehensively characterizing complex functional and behavioral changes in sensory, attentional, cognitive and motor systems of the brain during anesthetic sedation.

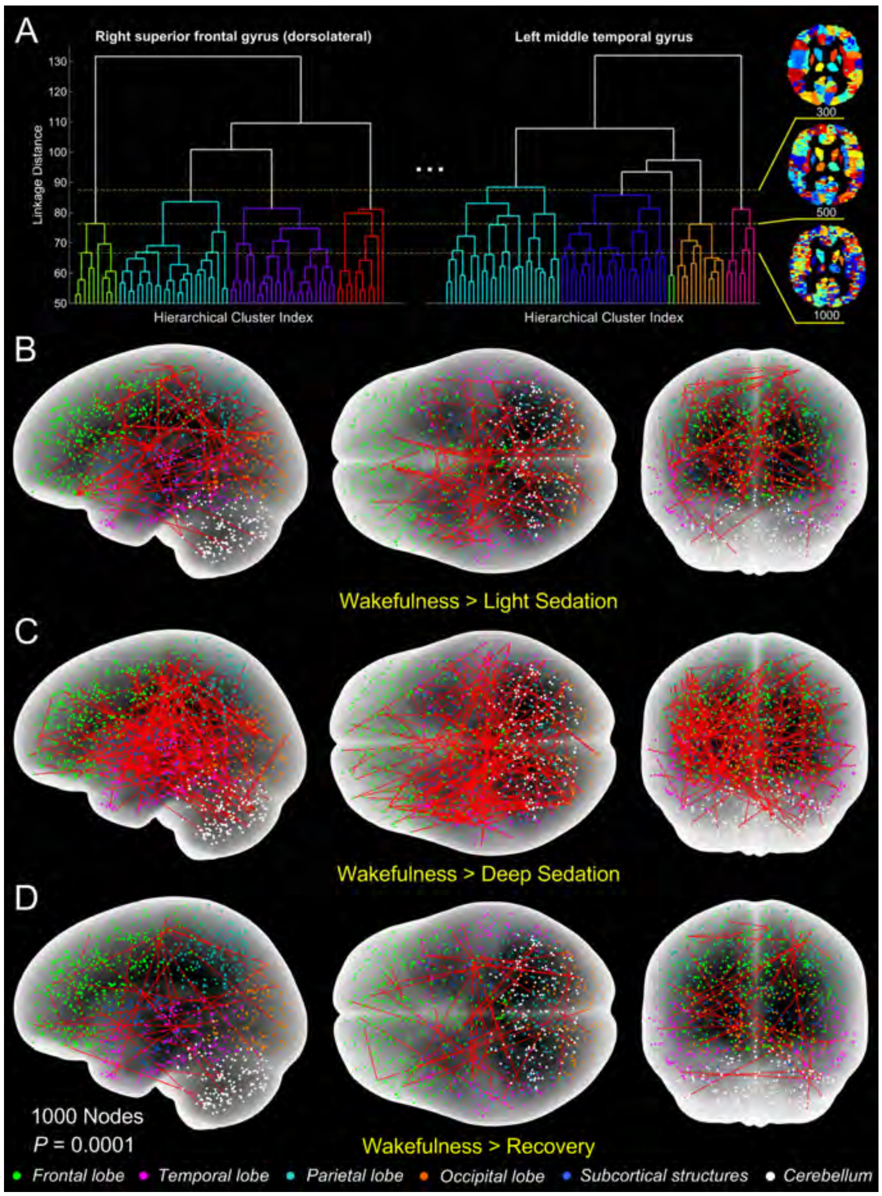

Figure 1. (*A*) A combined anatomical-functional brain parcellation algorithm. (*B-E*) Condition comparisons of network node connectivity (at the1000-node scale) by two-sample *t*-test.

References:

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