

# Supporting Information

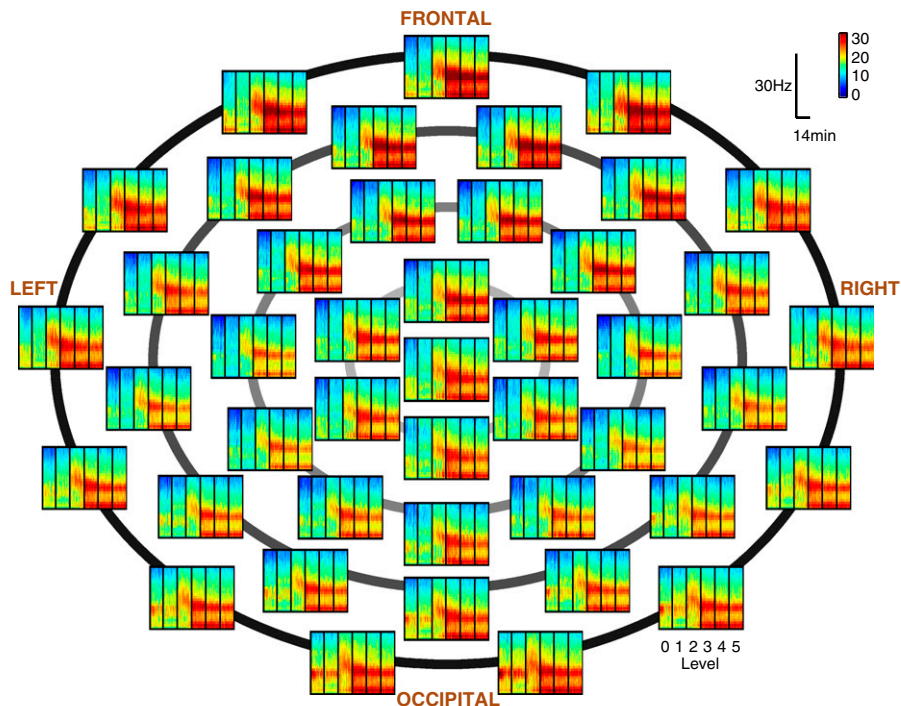
Cimenser et al. 10.1073/pnas.1017041108

## SI Materials and Methods

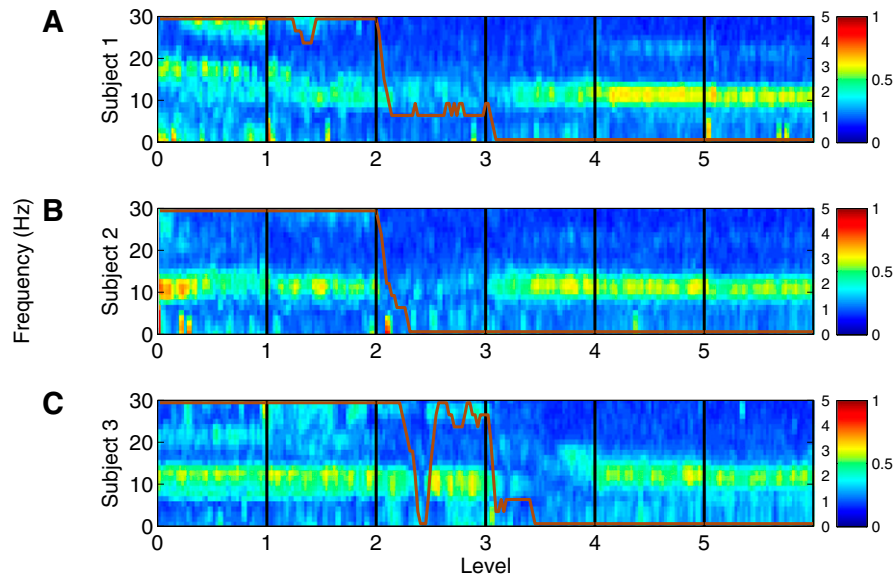
The study was approved by the Human Research Committee at Massachusetts General Hospital. The data from two healthy female subjects and one healthy male subject are reported here. Informed consent was obtained from all of the subjects. All of the subjects were American Society of Anesthesiology Physical Status 1 with Mallampati Class I airway anatomy. All subjects were required to take nothing by mouth for 8 h before start of the study. Immediately before the study a urine toxic screen was performed to document that no additional drugs had been taken by the subject that could confound the electrophysiological and behavioral effects observed in response to the administration of propofol. Female subjects received a urine pregnancy test to rule out the possibility of a pregnancy. Before the start of the study, a 64-lead EEG cap was applied to the head of each subject. Physiological monitors for general anesthesia included electrocardiogram and pulse oximeter. A radial arterial line was inserted to continuously monitor blood pressure. While the subject was conscious, breathing and respiration were monitored by the attending anesthesiologist. Once the oxygen mask was applied to the subject's face when he or she began to lose consciousness, capnography was used to monitor breathing and respiration. If the subject became apneic, ventilation was assisted by the attending anesthesiologist. Before receiving propofol, each subject breathed room air. Once propofol was administered, oxygen was administered by mask at a concentration of 30%. A minimum of three anesthesiologists were present during the study.

Propofol (2,6 di-isopropyl phenol) was administered to the subject using a computer-controlled Stanpump infusion to achieve successive target effect site concentrations of 1, 2, 3, 4, and 5  $\mu\text{g}/\text{mL}$  (Fig. 1A, main text). The experiment began with no drug administration (level 0). Each effect site concentration was maintained for  $\approx 14$  min. During the infusion of propofol, at some point (in level 2 or level 3, depending on the subject), the subjects lost consciousness as determined by cessation in the responses to the auditory task.

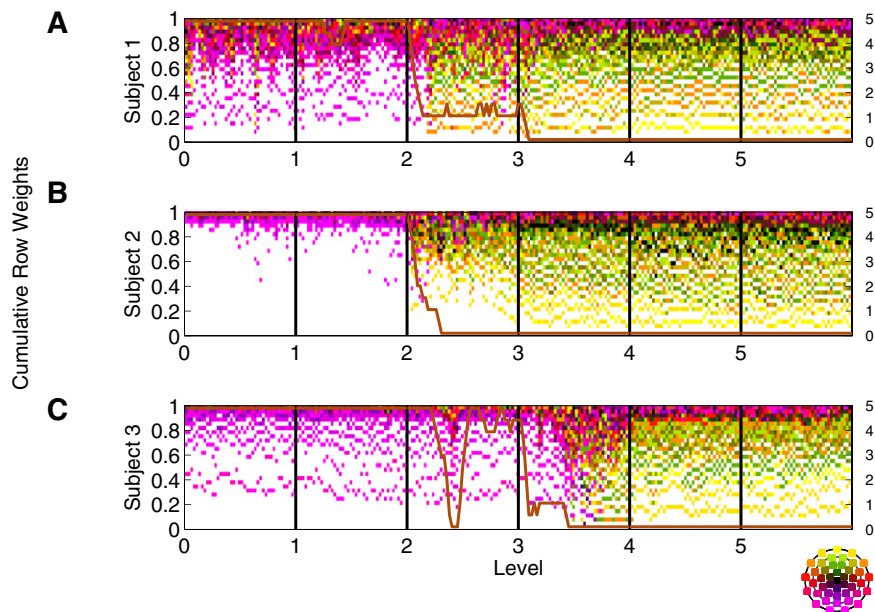
To assess level of consciousness, each subject was continually required to respond to a series of computer-administered binary tasks. The task consisted of identifying a superposition of tones, a neutral word (such as bed, chair, clock, and desk), or the subject's name. If the subject heard the tones or a neutral word, he/she pressed the left button. For his/her name he/she pressed the right button. The superposed tones were presented for 2 s, and 2 s were allowed for the response. For the word or name task, 4 s were allowed for presentation of the task and subject response. A trial consisted of five stimuli that were presented every 4 s: 0th, 4th, 8th, 12th, and 16th seconds of a trial (Fig. 1C, main text). The stimuli consisted of four superposed tones and one word or a name. A trial ended at the 20th second or by the last response, whichever was first. The end of a trial marked the beginning of the next trial. For the purposes of our analysis, we report here the number of correct responses per each trial ( $\approx 20$  s) as a score of 0, 1, 2, 3, 4, and 5. Subjects were asked to keep their eyes closed during the entire experiment. For each level, as identified by the targeted propofol concentration, there were 42 trials.



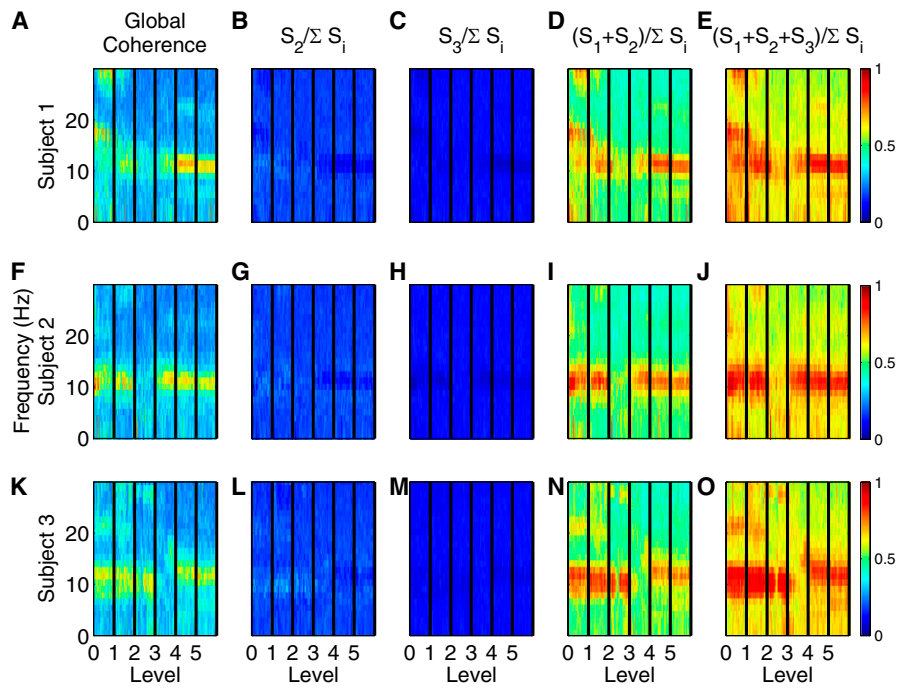
**Fig. S1.** Spectrograms of the voltages from the electrode sites in Fig. 1B (main text) using an average reference. The five different propofol levels are demarcated as in Fig. 2. x axis, time (0–84 min); y axis, frequency (0–30 Hz).



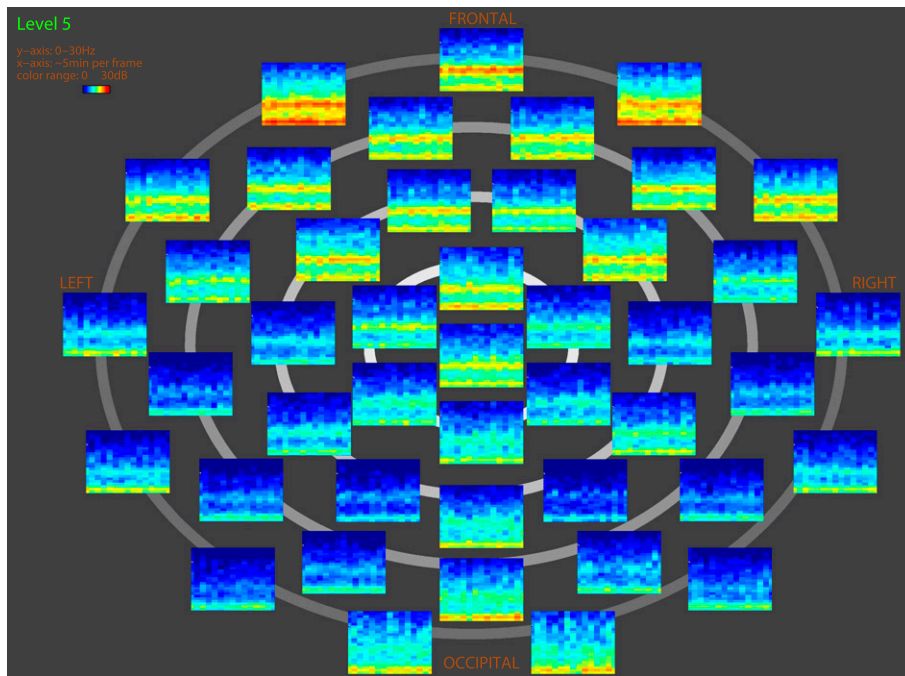
**Fig. S2.** (A–C) Time course of the global coherence with greater smoothing than in Fig. 4. Global coherence is estimated from a cross-spectral matrix averaged over twice the number of segments,  $K = 32$ , instead of  $K = 16$  (*Materials and Methods*), and further averaged over a triplet of frequencies at  $f - 1$  Hz,  $f$ , and  $f + 1$  Hz, instead of a single frequency  $f$ . The color coding is as in Fig. 4.



**Fig. S3.** (A–C) Time course of the cumulative sum of the row weights showing the contribution of each electrode site (Fig. 1B) to the leading eigenvector (Fig. S2) at frequency band (10–12) Hz. The color coding is as in Fig. 6.



**Fig. S4.** Fraction of total power contained in the leading eigenvectors. Ratios of the (A, F, and K) leading eigenvalue (global coherence), (B, G and L) second eigenvalue, (C, H, and M) third eigenvalue, (D, I, and N) sum of the first two eigenvalues, and (E, J, and O) sum of the first three eigenvalues to the sum of all eigenvalues are shown. The color coding is as in Fig. 4.



**Movie S1.** Spectral dynamics of the radial current density estimated from the electrode sites in Fig. 1B. x axis: time ( $\approx$ 5 min per frame); y axis: frequency (0–30 Hz). Different propofol levels (Fig. 1A) are demarcated.

[Movie S1](#)