



Propofol induction reduces the capacity for neural information integration: Implications for the mechanism of consciousness and general anesthesia

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ABSTRACT

The cognitive unbinding paradigm suggests that the synthesis of neural information is attenuated by general anesthesia. Here, we analyzed the functional organization of brain activities in the conscious and anesthetized states, based on functional segregation and integration. Electroencephalography (EEG) recordings were obtained from 14 subjects undergoing induction of general anesthesia with propofol. We quantified changes in mean information integration capacity in each band of the EEG. After induction with propofol, mean information integration capacity was reduced most prominently in the γ band of the EEG ($p = .0001$). Furthermore, we demonstrate that loss of consciousness is reflected by the breakdown of the spatiotemporal organization of γ waves. We conclude that induction of general anesthesia with propofol reduces the capacity for information integration in the brain. These data directly support the information integration theory of consciousness and the cognitive unbinding paradigm of general anesthesia.

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1. Introduction

Numerous theories and recent data suggest that the synthesis of cognitive information is an essential requirement for consciousness (Crick & Koch, 1995; Hameroff, 1996; Mashour, 2004, 2006; Singer, 1996). Integrative neural activities such as recurrent processing from higher to lower cortical areas, as well as coherent 40 Hz oscillations, have been associated with higher cognitive function or consciousness (Mashour, 2006). There has been a particular focus on functional and effective connectivity of the thalamocortical and corticocortical systems due to their ability to integrate the activities of functionally diverse cognitive modules (Tononi & Sporns, 2003; Tononi, 2004). Accordingly, Tononi's "information integration theory" formalizes this synthetic property as the neural basis of consciousness. Tononi has created a mathematical model of the capacity for information integration, denoted as Φ , which is increased in systems maintaining consciousness (e.g., thalamocortical processes) and decreased in those that do not (e.g., cerebellar processes, sleep).

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Since the integration or binding of neural processes is deemed essential to the generation of conscious states, it has been suggested that the “unbinding” of these processes may be essential to the generation of unconscious states (John & Pritchep, 2005; Mashour, 2004, 2006). The cognitive unbinding paradigm of general anesthesia suggests that cognitive activity does not need to be eliminated, but simply disintegrated, for general anesthetics to interrupt consciousness. There has been indirect evidence and support of this theory. Anesthetic-mediated loss of consciousness has been associated with decoherence of activity around 40 Hz using quantitative EEG (John et al., 2001), loss of thalamocortical connectivity using positron emission tomography (PET) (Alkire, Haier, & Fallon, 2000), and loss of functional connectivity using magnetic resonance imaging (MRI) (Peltier et al., 2005). These findings are consistent with the loss of effective cortical connectivity associated with sleep (Massimini et al., 2005). What has not yet been reported is a direct measure of the capacity for neural information integration in the conscious and anesthetized state. A decrease in Φ associated with the induction of general anesthesia would be a direct demonstration of the importance of information integration in conscious processes and would support cognitive unbinding as one mechanism of anesthetic-mediated unconsciousness. The task is to translate these theoretical paradigms into empirical studies in humans. In order to accomplish this, we developed a novel method of human EEG reconstructions in state space.

State space (or phase space) is the space in which all possible states of a dynamic system (such as the anesthetized brain) can be represented. In state space, each parameter of a system is represented as an axis of a multi-dimensional space. Consider a classic example from physics: the swinging pendulum. The location of the pendulum can be plotted in structural space, but its overall behavior as a system is plotted in state space. The back-and-forth motion in “real space” is what we would actually see if a pendulum were swinging. The state space of the swinging pendulum, however, would show the oscillating behavior of the system using the parameters of position and velocity, unfolding over the parameter of time. This behavior would translate to a sine wave plotted in three dimensions, which represent the three parameters. When a system converges to a typical behavior, the corresponding sets in state space are referred to as the attracting sets or *attractor*. Attractors may be linear or non-linear: when they are described by fractal rather than Euclidean geometry, they are said to be *strange attractors*.

Functional integration (“binding”) and segregation in the brain are fundamental principles of neural organization (Hameroff, 1996; Mashour, 2004; Tononi & Sporns, 2003; Tononi, 2004). Here we assumed that the functional integration and segregation of the brain is different in conscious and anesthetized states. In order to investigate this functional organization in conscious and unconscious states, we developed a new method based on the information integration theory and state space reconstruction method. By using the state space reconstruction method, a complex combination of several functional segregations and integrations in the brain can be represented as a point in a state space. Furthermore, the temporal evolution of such combinations can be reconstructed as a trajectory, much like the sine wave of the pendulum’s behavior moves forward in time. With this reconstructed trajectory in a state space, we can consider cognitive states as a dynamic problem of spatiotemporal functional organization of the brain. This technique also enables quantification of the functional characteristics in conscious and anesthetized brain with several measures in nonlinear science. For example, the dimension of a reconstructed state space corresponds to the degree of freedom of a system.

There is a precedent for using state space and EEG to study consciousness and anesthesia. Watt and Hameroff (1988) demonstrated that state space analysis of EEG reveals distinct attractors and dimensions for distinct states of consciousness, while van den Broek et al. (2006) showed that dimensionality and complexity are measures of anesthetic depth. Finally, Walling and Hicks (2006) found that emergence from sevoflurane was associated with a transition from an ordered attractor of unconsciousness to a chaotic strange attractor of wakefulness. Of interest, they deemed emergence from anesthesia as a “cognitive rebinding.” These previous studies considered the dynamic properties of single EEG channel or the average of single EEG channels’ properties. In contrast, we take into account the spatiotemporal organization of segregated functions. Each segregated function was determined by a computational method, called “minimum information bipartition”, as a cluster of EEG channels.

Here, we report that the information integration capacity (Φ) of subjects is significantly reduced after induction with propofol. We also show the spatiotemporal organization of segregated functions is distinct in states of consciousness and general anesthesia. This distinctive feature appears only in the γ band, which has been associated with cognitive information processing in the brain.

2. Methods

2.1. Subjects

After obtaining the approval of the Institutional Review Board of Asan Medical Center (Seoul, Korea) and written informed consent, we studied 14 patients, aged 20–80 years, who were scheduled for stomach surgery. Given the higher incidence of gastric cancer in this region and associated early screening, patients were identified prior to any signs or symptoms of mechanical obstruction and were therefore scheduled for elective cases with routine induction of anesthesia. All patients were American Society of Anesthesiologists (ASA) physical status 1 or 2. Patients were excluded from the study if they had known allergy to propofol (Diprivan[®], AstraZeneca, London, UK), had abnormal preoperative renal and hepatic function, had a history of drug or alcohol abuse, psychiatric disorder, or had a body weight that was not within 30% of ideal.

2.2. Study design

Patients fasted for 8 h before drug administration. No pre-medication was given before surgery. An 18-gauge angio-catheter was placed in a vein of the forearm area. Patients were monitored with electrocardiography, pulse oximetry, end-tidal carbon dioxide concentration and non-invasive blood pressure measurement. The EEG activity of eight monopolar channels (Fp1, Fp2, F3, F4, P3, P4, T7 and T8 referenced by A2) was recorded by qEEG-8 (LXE3208, Laxtha Inc., Daejeon, Korea) with a sampling frequency of 256 Hz. Baseline EEG activity was recorded for 5 min before the intravenous bolus of 2.0 mg/kg of propofol. During the intravenous bolus of propofol, EEG activity was recorded continuously up to 10 min after administration.

Time to loss of consciousness (LOC) was determined every 5 s by the loss of response to verbal command. If patients were not able to ventilate spontaneously due to injection of propofol, lungs were manually ventilated with 100% oxygen *via* face-mask, to maintain an end-tidal carbon dioxide concentration of 35–45 mm Hg. Manual ventilation was discontinued when the spontaneous respiratory rate exceeded 12 breaths per minute and end-tidal carbon dioxide was less than 45 mm Hg. Upon completion of the measurement of EEG activity, patients received an effect-site target propofol concentration of 3 $\mu\text{g/ml}$ in combination with a target remifentanyl concentration of 5 ng/ml and rocuronium 0.6 mg/kg to facilitate orotracheal intubation. After surgery, nurses conducted observation and management in the post-anesthesia care unit (PACU) and, subsequently, the ward.

2.3. State space reconstruction for states of consciousness

We developed a new method to reconstruct states of global brain functions, using the EEG recorded from surface electrodes. The reconstructed trajectory in a state space reflects the temporal evolution of functional segregation and integration patterns underlying neural activities. This method is based on two hypotheses: (1) that a combinatorial pattern of specific brain functions reflects a state of consciousness, and (2) that a specific brain function can be estimated by an EEG complex that consists of two causally independent sub-clusters of EEG determined by the minimum information bipartition (MIB) method (Sporns, Tononi, & Edelman, 2000; Tononi & Sporns, 2003; Tononi, 2004). The second hypothesis is based on the idea that if a cluster of EEG is functionally distinguishable from another cluster of EEG, it may be playing a distinct functional role in the brain.

In a given subset of EEG channels, the MIB method defines a subset of EEG channels, called ‘EEG complex Φ ’, which is determined by searching out the minimum information bipartition among all possible bipartitions. The bipartition of EEG channels may reflect the functional segregation within a given subset. The value of Φ is defined by the effective information across the informational weakest link of a given set and is associated with the amount of information it can integrate between segregated sub-clusters. Therefore, an EEG complex, which satisfies the functional segregation and integration at the same time, corresponds to a specific brain function and is the locus at which information is integrated (Tononi, 2004; Tononi & Sporns, 2003). This process of finding an EEG complex in a subset of EEG channels continues to all possible subsets of EEG channels (see Appendix A: Method).

Taking into account the spatiotemporal organization of segregated functions, the state space reconstruction method was used. Fig. 1(a) and (b) illustrate how to construct the state space and a state vector in the space with three EEG complexes and their Φ values. In a state space, a type of EEG complex and its value Φ are set as an axis of the state space and the coordinate value of the axis. We segmented the EEG into 500 ms long windows, overlapping by 400 ms, with the window size set to cover the presumed time unit of cognitive binding (Edelman, 2003). Fig. 1(e) shows the trajectory $\bar{\Phi}$ in the state space, composed with a sequence of the EEG complexes appeared during the recording period. In Fig. 1(e), the number of axes of the state space (dimension) was set as the total number of different types of EEG complexes occurred during the whole EEG period. Each coordinate and its value were occupied with the 30 top ranked EEG complexes occurred in the window.

In order to make the axes orthogonal and to take the principle component from the trajectory, the singular value decomposition (SVD) was applied to the trajectory (Fig. 1(f)). In these data, the 30 primary principle axes of the projected trajectory, $S\bar{\Phi}$, were used for the dimension analysis (see Appendix A: Method).

2.4. Mean information integration (MII) capacity

To define the mean information integration (MII) capacity for a subject (in Fig. 2(b)), the three-minute long EEG periods were selected in the conscious and the unconscious states and they were segmented into 500 ms as above. The mean information integration (MII) capacity was defined as the mean value for the top 30 ranked EEG complexes taken from all windows and the total number of EEG complexes used for the mean is 53,850 for 1795 windows over 3 min. Fig. 2(b) showed the MII capacities for the various spectral band EEGs (δ : 0.5–4 Hz, θ : 4–8 Hz, α : 8–13 Hz, β : 13–35 Hz, γ : 35–55 Hz, all: 0.5–55 Hz). The same averaging process was carried out for each band pass filtered EEG.

As comparative measures, the average mutual information (AMI) and the absolute power spectrum for each band pass filtered EEGs were calculated in the same windowing condition and averaging process over the windows as above. For each window, the AMI was defined as the mean of mutual information values of all pairs of EEG channels and the absolute power spectrum was defined as the mean of the absolute powers in all EEG channels (Fig. 2(c) and (d)) (Modde-meijer, 1989).

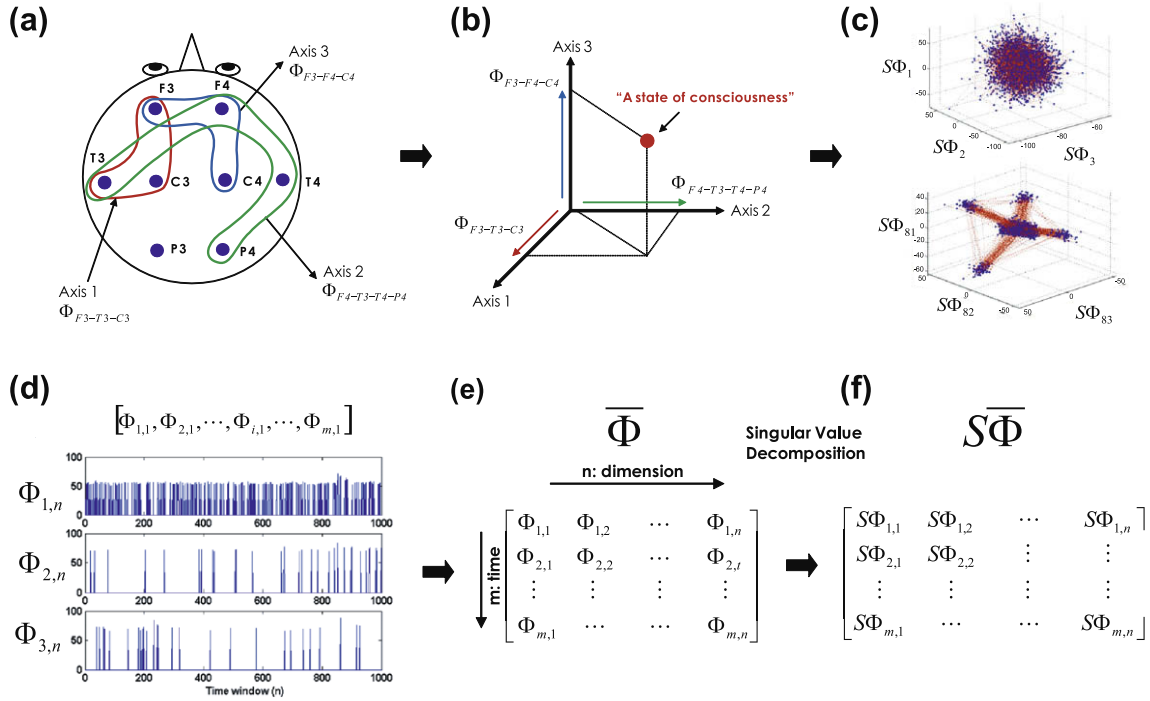


Fig. 1. Schematic of state space reconstruction from multi-channel EEG. (a) Three primary EEG complexes determined by the minimum information bipartition method. (b) The three EEG complexes were used to construct the state space. In practice, all types of EEG complexes observed during the EEG recording were used to construct the state space of consciousness. (c) Two trajectories, composed of two different EEG complex sets, show distinctive transition processes. (Upper figure) Trajectory of three higher ranked EEG complexes. (Lower figure) Trajectory of the three lower ranked EEG complexes. (d) Time evolution of three primary EEG complexes. (e) Sequences of the EEG complexes occurring during the recording period were used to construct the trajectory in the state space. (f) Orthogonal axes of the state space, as determined by singular value decomposition.

2.5. Takens estimation

The takens estimator was used to estimate the correlation dimension of the reconstructed trajectory in the state space. It is a maximum likelihood estimator for the correlation dimension, d_2 , which is less sensitive to the choice of scaling region in the determination of dimension (Castro, 1997; Takens, 1985). The upper cutoff distance, R_0 , which is the unique parameter, is set at 5% of the standard deviation of the values of the highest ranked EEG complex through searching the parameter region.

2.6. Phase randomized surrogate data

The 28 randomized data sets were generated from the EEGs of 14 subjects (two randomized data sets per subject), in order to show that the reconstructed trajectory of original EEG is not random. The data were randomized in phase but the amplitudes were adjusted as those of the original EEG (Kugiumtzis, 2000). The Takens estimation of dimension was calculated under the same conditions for both data groups and the original data set was statistically compared with the random data set, considering the randomness but not the determinism of it as conventional surrogate data test.

3. Results

3.1. State space reconstructions

Fig. 1(a) and (b) demonstrate state space construction from multi-channel EEG. Fig. 1(a) depicts three representative EEG complexes, determined by the MIB method, while Fig. 1(b) depicts the point reconstructed by the three EEG complexes. Fig. 1(c) shows the two trajectories, which represent different dynamics of different EEG complexes. Fig. 1(d) shows the sequences of the three EEG complexes selected from a subject. Fig. 1(e) and (f) demonstrate a state space and the decomposed space by the singular value decomposition method to make the axes orthogonal.

3.2. Mean information integration (MII) capacity is reduced during general anesthesia

The MII capacity was calculated for the EEGs recorded from the 14 subjects. Following the administration of propofol, EEG was recorded continuously for up to 10 min. A notch filter and 0.5–70 Hz band-pass filter were applied to EEG. Three minute segments of artifact-free EEG were selected to represent the conscious and unconscious states (Fig. 2(a)). Since the information integration theory suggests that consciousness corresponds to the capacity of a system to integrate information, we calculated the mean information integration capacity Φ of the subjects in the conscious and unconscious state. We found that general anesthesia corresponded to a reduction of information integration capacity of the γ band (35–50 Hz) (Fig. 2(b)). The other bands also showed significant changes of the mean information integration capacity, but relatively less than that of the γ band. The δ and the α bands were reduced, while the whole frequency band was increased after loss of consciousness (Fig. 2(b)) (δ (0.5–4 Hz, $p = .005$), θ (4–8 Hz, $p = .1$), α (8–13 Hz, $p = .005$), β (13–35 Hz, $p = .07$), γ (35–50 Hz, $p = .0001$) whole frequency band (0.5–50 Hz, $p = .005$), Wilcoxon signed rank test).

As comparative measures, the power spectrum of the δ band was significantly increased ($p < .01$, Wilcoxon signed rank test), while the power spectra of α , β , γ and whole frequency bands showed a tendency to decrease. As a similar measure based on information theory, the average mutual information also tended to be reduced in most frequency bands, especially in θ , α , β and the whole frequency bands ($p < .01$, Wilcoxon signed rank test), but the γ band did not reach statistical significance ($p = .08$, Wilcoxon signed rank test).

3.3. Dynamic properties of human consciousness

Fig. 3 demonstrates that conscious and anesthetized states are associated with distinctive dynamic properties as brain states evolve over time. In Fig. 3(a) and (b), the correlation dimension of the γ band EEG in the conscious state (blue

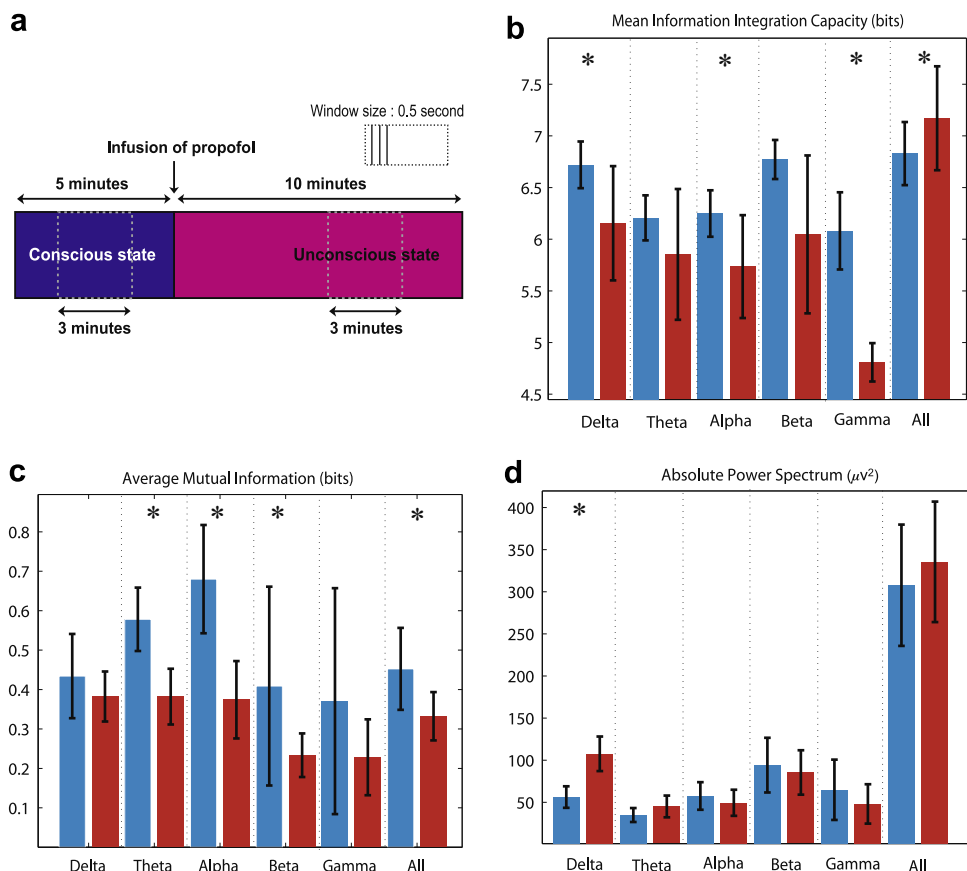


Fig. 2. General anesthesia reduces information integration. (a) Schematic of the anesthesia experiment. The three minute long EEG periods were selected for analysis before and after the injection of propofol. (b) The mean information integration (MII) capacity (measured in bits), (c) average mutual information (AMI) (measured in bits), and (d) absolute power spectrum (measured in μV^2) for various spectral bands in the conscious and the unconscious states. “*” marker indicates significant change after loss of consciousness (Wilcoxon signed rank test, $p < .01$) Blue:conscious state; Red: unconscious state.

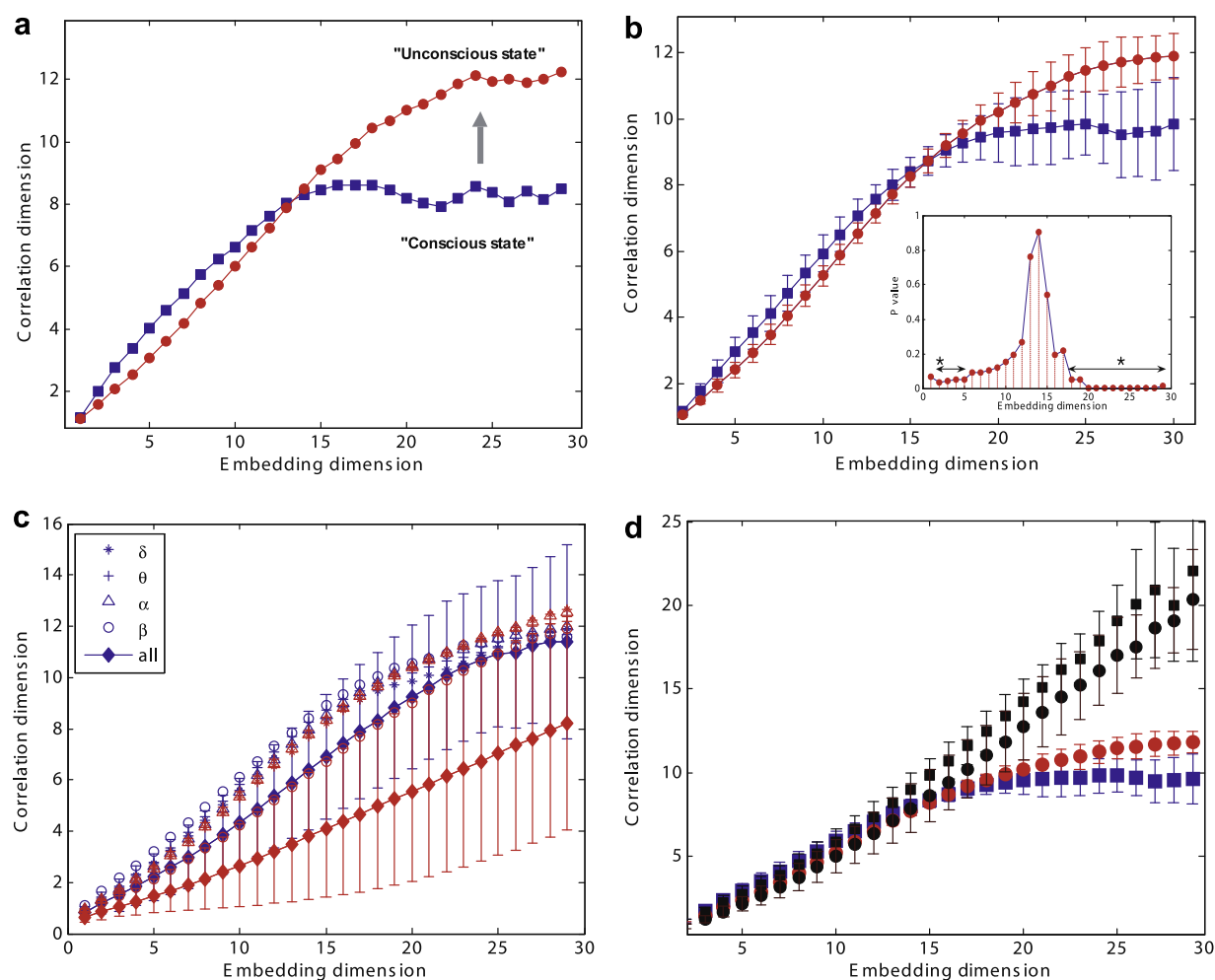


Fig. 3. Differential dimensionalities reflect the dynamic properties of conscious and anesthetized states. (a) The dimensionality of the trajectory constructed by the γ band in the conscious state was increased after loss of consciousness (blue square: conscious state, red circle: unconscious state). (b) The mean correlation dimensions of the conscious and unconscious states for 14 subjects (blue square: conscious state, red circle: unconscious state). The conscious state showed a lower dimensional structure, saturating at about 9.7 of the mean correlation dimension. The inset shows the p -values of the Wilcoxon signed rank test at each embedding dimension (* indicates that $p < .05$). (c) The mean correlation dimensions of various spectral bands such as δ , θ , α , β and raw EEG (blue color: conscious state, red color: unconscious state). Error bars denote the standard deviation of the correlation dimension of raw EEG. (d) Application of the surrogate test to the γ band EEG. The randomized data (black circle and black square) are clearly distinguished from the original data (red circles and blue squares, respectively) in the estimation of the correlating dimension. The mark and error bars at each embedding dimension indicate the mean and standard deviation of the correlation dimension values for the 14 subjects.

square) has a flat region, saturating at around 15 of the embedding dimension, which indicates a lower dimensional structure of the trajectory. In contrast, the correlation dimension of the unconscious state (red square in Fig. 3(b)) is not saturated until the end of the embedding dimension, which indicates that the actual correlation dimension would be much higher. This finding suggests randomness. The mean correlation dimensions of the trajectories constructed by the γ band EEG in the conscious and the unconscious states are significantly distinguished from 18 of the embedding dimensions ($p < .01$, Wilcoxon signed rank test, the inset of Fig. 3(b)). This characteristic dynamic property of the γ band EEG appears in 10 out of 14 subjects. Such a lower dimensional dynamic property appears only in the γ band EEG and is not found in the other spectral bands (Fig. 3(c)).

To test the randomness of the trajectory of original data, we compared it with the randomized data set, which randomly shuffled the elements of each axis in the reconstructed space. The original data could be clearly distinguished from the randomized data set from around 15 of the embedding dimensions (Fig. 3(d)), indicating that human brain functions are not completely random and they may have certain metastable structures. This test also showed that the lower dimensional dynamic structure was not due to the finite length of trajectory but due to the correlation of trajectory.

4. Discussion

Here, we report that the general anesthetic propofol is associated with a decrease in the capacity for information integration in the human brain. Our data further suggest that states of human consciousness and unconsciousness are directly associated with the information integration capacity of γ waves. These data agree well with the predictions of the information integration theory of consciousness (Tononi & Sporns, 2003; Tononi, 2004), as well as the cognitive unbinding paradigm of general anesthesia (John & Prichep, 2005; Mashour, 2004, 2006). There are several important limitations that must be taken into account. First, these data suggest correlation, but not causation of consciousness and general anesthesia. Our data do not shed light on the hard problem of consciousness, but do point us in the direction of potentially fruitful methods of exploring functional neural correlates in humans. Second, our focus was limited to the γ band of EEG, since 40 Hz oscillations have been associated with conscious activity. Furthermore, the temporal dynamic analysis illustrated in Fig. 3 did not reveal characteristic changes for the other EEG waveforms. Third, further studies are required to exclude the possibility of γ band decoherence resulting from an artifact of decreased signal-to-noise, although our further analyses suggests that this is not the case. As evidenced by the δ band, signal power and information integration are not directly linked. Finally, our data are restricted to the intravenous agent propofol used at the induction of anesthesia. Further studies are required to assess whether these findings can be generalized to other intravenous induction agents, as well as inhalational agents commonly used for maintenance of anesthesia. Additionally, a return of information integration after recovery from anesthesia would also strengthen our findings.

Another important finding in this report is the further insight into how global brain states dynamically change over time. Our data suggest that conscious and unconscious states have distinct temporal attributes: a lower dimensional process (associated with consciousness) and a random-like process (associated with unconsciousness). The change in correlation dimension is the opposite of that found by Walling and Hicks (2006). This is likely attributable to our use of multi-channel EEG versus single-channel EEG. Their approach reflected one region of brain function, while ours reflects the cooperation of multiple different regions. Thus, the higher dimension associated with unconsciousness found in the current study may originate from the complexity of individual and uncoupled cognitive modules during general anesthesia, as opposed to the more highly ordered and integrated cognitive structure of consciousness.

The neuroanatomic structure of the human brain has a scale-free network structure, which has fractal properties (Buzsaki et al., 2004; Song, Havlin, & Makse, 2005). Thus, when global cognitive information is integrated in such an anatomic structure, the functional property of cognitive information integration would have fractal attributes in the spatial integration (Passingham, Stephan, & Kotter, 2002). Furthermore, a state of consciousness, which may contain a fractal structure spatially, is succeeded by other discrete and relatively stable structures through a rapid transitive process. It has been postulated that the transition is carried out by a metastable process, by which the individual parts of the brain are coordinated autonomously and changed adaptively with the ever-changing environment (Bressler & Kelso, 2001; Fingelkurts, 2004). The lower dimensionality of the trajectory constructed with global γ waves indicates a temporal correlation in the transition process. Therefore, it could be argued that a state of consciousness is organized with a specific spatiotemporal structure of γ waves in the brain. Furthermore, such global spatiotemporal organization of the cognitive information may be constructed under the context of the past state and the expectation for the future state. We posit that this is a characteristic dynamic property of human consciousness.

In contrast, as consciousness fades, communication between different parts of the cerebral cortex breaks down (Massimini et al., 2005) and this breakdown may cause the loss of the scale-free attribute in the spatial information integration. The destruction of the “shortcut” between distant cortical areas also reduces global information integration capacity, giving rise to a loss of brain adaptability to the external stimuli on various scales (Sporns et al., 2004; Sporns, 2006). The interruption of the lower-dimension structure indicates a disruption of temporal correlation in the transition process of brain states. We posit that the breakdown of the spatiotemporal organization of cognitive information is a characteristic property of human unconsciousness.

With respect to anesthesiology, current theories of general anesthesia grounded in the neurophysiology of consciousness suggest that cognitive binding processes may be the functional substrate of general anesthetic mechanism, and the disorganization of cognitive information binding is a common functional outcome among different pharmacological agents (Mashour, 2006). The cognitive unbinding paradigm of general anesthesia states that anesthetics may function by interrupting various cognitive binding processes from the cellular to the global brain level, in part, by the functional uncoupling of the γ band EEG (Mashour, 2004). Our results directly support the cognitive unbinding paradigm, as propofol-induced unconsciousness is associated with the breakdown of the spatiotemporal organization of the EEG γ band. The dynamic properties of neural organization that we elucidate could be taken into account as important constraints for more realistic models of human consciousness and could be used as an indicator for defining conscious and unconscious states. If validated in future studies and with additional anesthetics, quantification and expression of information integration could have potential as the basis of a novel monitor for intraoperative awareness and anesthetic depth.

Finally, our study has methodological implications. Mashour (2006) argued that the investigation of consciousness and general anesthesia should be linked and suggested a principle of “mutual verifiability.” This principle states that (1) any proposed neural correlate of consciousness should be eliminated or altered during general anesthesia and (2) any theory of general anesthetic mechanism should relate to a neural correlate of consciousness. The present study represents a concrete example of how theories of consciousness and anesthesia can be tested empirically with an integrated methodology.

Conflicts of Interest

The authors have no conflicts to declare.

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Appendix A. Methods

A.1. Determination of EEG complexes

A subset S taken from all EEG channels, X , was partitioned into A and its complement $B(B = S - A)$. The causally effective connection between A and B was defined by effective information

$$EI(A \leftrightarrow B) = EI(A \rightarrow B) + EI(B \rightarrow A),$$

where $EI(A \rightarrow B)$ and $EI(B \rightarrow A)$ measures the causally effective connection linking A to B and B to A , respectively, by mutual information. Under Gaussian assumptions for the multi-channels EEGs, all derivations from independence among the two complementary parts A and B of a subset S of X are expressed by the covariance among the EEG channels. Therefore, $EI(A \rightarrow B)$ was calculated with the following relations,

$$EI(A \rightarrow B) = MI(A^{\max}; B),$$

$$MI(A^{\max}; B) = H(A^{\max}) + H(B) - H(A^{\max}B),$$

$$H(A) = (1/2) \ln[(2\pi e)^n |\text{COV}(A)|],$$

where A_{\max} is the independent Gaussian noises and $\text{COV}(A)$ is the covariance matrix of the EEG channels partitioned into A .

Within the subset S , we considered all possible bipartitions and found the minimum information bipartition, $\text{MIB}(S)$, for which the normalized effective information became a minimum, as well as the corresponding value of $\Phi(S)$, which quantified the capacity of the information integration of the subset S .

$$\text{MIB}(S) = \frac{EI(A \leftrightarrow B)}{\min(H^{\max}(A), H^{\max}(B))},$$

$$\Phi(S) = EI(\text{MIB}(S))$$

Originally, a subset S with $\Phi(S) > 0$ is called “complex”, if it is not included within a subset having higher Φ , but, here, in the application to EEG, the MIB subset is called “EEG complex”. The EEG complexes were searched out by using the Matlab toolbox, kindly provided by G. Tononi and O. Sporns. The main output is a list of all the EEG complexes found and their values. The top 30 EEG complexes in the list reflect the most relevant information for the global brain function, occupying about 60% of the total cumulative frequencies of EEG complexes.

The long term EEG was segmented into 500 ms EEG windows, overlapping by 400 ms. The top 30 EEG complexes ranked by its values were selected at each window and were put together into a pool of EEG complexes. Approximately 90 different types of EEG complexes were found for each subject. Thus, we determined the dimension of the state space as 90. Each type of EEG complex and its value were set as an axis and the coordinate value of the axis, respectively, in the state space. The rest of the coordinates not involved in the top 30 EEG complexes were all padded with zero.

A.2. Reconstruction of the trajectory and the state space

For the dimensional analysis, we used the five minute EEG periods in the conscious and unconscious states. From the same windowing procedure as above, 2995 windows were produced, and the trajectory and the state space were reconstructed by the EEG complexes found from these windows. To make the axes orthogonal and to take the principle components from the trajectory, the singular value decomposition was applied to the trajectory. The trajectory, M , is decomposed into $M = USV^T$, where U and V are the unitary matrices, V^T is the conjugate transpose of V , and S is a diagonal matrix whose elements are the singular values of the M , the trajectory projected to the principle axes is defined as $M_{\text{svd}} = MV$. Here, the primary principle axes (from the second to the thirtieth principle axes) of the projected trajectory, M_{svd} , were used for the dimensional analysis.

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