Consciousness, Anesthesia, and Neural Synchrony

Imagine being ensconced in a plush seat, about to experience an evening with your favorite symphony orchestra. The musicians are assembled on the stage and many are playing their instruments, pausing occasionally to tune a string or ruffle through the pages of the score. Now imagine that all of the musicians are rehearsing their part individually and independently... the sound swells as an unsettling crescendo scales a jagged peak of dissonance. The conductor finally emerges from behind the heavy red curtain and steps onto the podium. The cacophony collapses to silence as two arms are raised. A baton is set into motion and then suddenly you hear music.

It should be clear from this description that the difference between cacophony and symphony does not necessarily relate to the number of musicians playing, or the decibel level, or the processing of the musical score: the difference is coordination in time. At the close of the 20th century, such coordination was suggested to be critical for generating the music of the mind, as neural synchrony became a strong contender for the correlate of conscious perception. In this issue of Anesthesiology, Li et al.1 describe a study of electrocorticography in animals that shows an increase in neural synchrony after induction of general anesthesia. This and other recent studies prompt a discussion of neural synchrony and how it may play a role both in consciousness and anesthetic-induced unconsciousness.

Terminology and Measurement of Neural Synchrony

Before discussing the relationship of neural synchrony to states of consciousness, it will be helpful to clarify some terms and modes of measurement. Note that the following descriptions serve only as simplified shorthand for what are obviously complex topics.

- **Scale of Neurophysiologic Recording:** With respect to the analysis of neural synchrony, the time series of interest can be derived from single unit recording (spike activity/action potentials), local field potentials (summation of many neurons), electrocorticography (on the surface of the cortex), or electroencephalography (on the surface of the scalp). The study by Li et al. focuses on electrocorticography in sheep. By comparison, a recent study of propofol in humans included multiple scales of recording and was thus able to analyze neural spike activity in relation to the phase of slow oscillations.2

- **Range of Synchronous Activity:** The coordination of neural activity can be identified within a particular region (short-range synchrony) or more globally between different regions (long-range synchrony).3 The study by Li et al. focuses on local or short-range synchrony.

- **Measure of Synchrony:** Correlation is a linear measure in the time domain that is often used to determine covariance of spike activity.4 Coherence is a linear measure in the spectral domain that is often used to determine synchrony of neural signals. Coherence is sensitive to the phase and the amplitude of the potential, whereas phase synchrony—a nonlinear measure—is intended to reflect only phase relationships.5 The study by Li et al. employed measures of both coherence and phase synchrony.

- **Origin of Synchrony:** Synchrony can be externally prompted by a stimulus, resulting in a “stimulus-locked” synchrony and possibly followed by a delayed, internally generated “induced” synchrony.5 Alternatively, neural synchrony can result exclusively from internal sources.

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*This Editorial View accompanies the following article: Li D, Voss LJ, Steigh JW, Li X: Effects of volatile anesthetic agents on cerebral cortical synchronization in sheep. Anesthesiology 2013; 119:81–8.*
• **Flexibility of Synchrony:** This is a heuristic designation that can be used when evaluating the literature. Flexible synchrony may transiently occur in response to a specific sensory stimulus, while inflexible synchrony may be persistent and impervious to incoming stimuli.

**Neural Synchrony and States of Consciousness**

In the late 1990s, there was excitement in the field of neuroscience regarding the potential role of synchrony as a neural correlate of consciousness. Neural synchrony was thought to provide a flexible method of (1) unifying the activities of spatially separated brain regions and (2) amplifying the salience of a neural response. It was proposed that “temporal binding” was the strategy by which the brain could unify a perception after the initial parceling of sensory input into distinct modalities mediated by distinct sensory cortices. A seminal study in 1999 by Rodriguez et al. was one of the first to demonstrate that conscious perception was associated with an increase in long-range phase synchrony in the gamma frequency at approximately 230 ms after the presentation of a visual stimulus.

Although there have been data supporting this finding, other investigations have demonstrated that neural synchrony may not be a general mechanism for feature binding. Fair enough—alternative strategies for binding and consciousness exist. Furthermore, more recent efforts have been directed at distinguishing among the neural prerequisites, neural substrates, and neural consequences of a conscious event. It is not yet clear whether synchrony is an active substrate or a prerequisite. However, there are several other arguments against a critical role of synchrony in the generation of consciousness that are more pertinent to the work of Li et al. and others investigating mechanisms of anesthesia. First, one can have “hypersynchrony” in the case of a seizure, but be decidedly unconscious. Second, neural synchrony (including gamma phase synchrony) can persist or even be increased during general anesthesia. Li et al. used electrocorticography (i.e., recordings from the cortex) of sheep during the waking state as well as during various depths of general anesthesia with volatile anesthetics. They found that local synchrony in the alpha (8–13 Hz) and beta (13–30 Hz) bandwidths was directly related to cortical depression—deeper anesthesia was associated with reduced cortical activation and increased synchrony. These findings are generally consistent with several recent studies of propofol-induced hypersynchrony in the alpha band and advance the field by demonstrating similar phenomena with multiple volatile anesthetics. Do these results exclude the possibility of neural synchrony being involved in conscious processing? Not necessarily. The local synchrony observed by Li et al. and others may inhibit or reflect an inhibition of the long-range synchrony that is thought to be important for consciousness and that appears to be differentially impaired during general anesthesia.

It is hopefully becoming clear how neural synchrony can be a double-edged sword with respect to consciousness. We must distinguish between local/short-range and global/long-range synchrony, recognizing that there can be an increase in one during anesthesia (e.g., short range) with a decrease in the other (e.g., long range). Second, it must be recognized that consciousness appears to be associated with a flexible synchrony rather than the stereotyped behavior observed during general anesthesia. Thinking of it in this way, an increase in synchrony, per se, would not necessarily be consistent with an increased capacity for conscious processing. This leads to the third point, which is sometimes neglected in current discussions of neural synchrony and consciousness: in the study by Rodriguez et al., the increased long-range gamma synchrony that correlated with conscious perception (at 230 ms) was followed by what appeared to be an “active desynchronization” (around 500 ms). In other words, it was a transient synchrony that correlated well with consciousness. Synchrony is therefore an element in the temporal organization of neuronal activity, but should not be regarded as equivalent to temporal organization.

**Conclusion**

Data regarding synchrony and states of consciousness might appear contradictory because simultaneous neuronal events can—depending on their characteristics—facilitate or inhibit conscious perception. The work of Li et al. supports a body of emerging evidence suggesting that “increased neural synchrony” may be an important neurophysiologic feature and possible mechanism of anesthetic-induced unconsciousness. When evaluating the literature, however, it is important to remember that “increased neural synchrony” could mean (among numerous options) the following:

1. Flexible and transient long-range phase synchrony in the gamma bandwidth followed by active desynchronization, which is associated with consciousness.

or

2. Inflexible and persistent phase synchrony in the alpha bandwidth, which is associated with anesthetic-induced unconsciousness.

The specific characteristics of neural synchrony—and how best to measure them in the anesthetized state—will be critical to consider as we further investigate the role of temporal coordination in consciousness and general anesthesia.

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**References**