General Anesthesia and the Cortex

Communication Breakdown?

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There is a growing body of evidence to suggest that depression or functional disconnection of frontal–parietal networks occurs during general anesthesia.[1] If fully confirmed, this would be an important advance for anesthesiology because it could help us (1) understand how our anesthetic drugs act to cause unconsciousness, and (2) monitor the effects of our anesthetic drugs in the clinical setting. The hypothesis that general anesthesia is a kind of "communication breakdown" between the front and back of the brain could be a parsimonious approach that informs both mechanistic understanding and clinical care. However, most studies of the frontal–parietal network during anesthesia have been conducted with functional magnetic resonance imaging (with slower time scales) or electroencephalography (with fuzzy spatial relationships). How do these findings hold up when assessing a neurophysiologic time scale in well-defined circuits across the frontal–parietal network? In this issue of Anesthesiology, Ma *et al.*[2] report the study of a specific neurophysiologic relationship across the oculomotor circuit—a well-defined and structurally connected tract from the frontal cortex to parietal cortex—on the surface of the primate brain. They find, contrary to what would be predicted based on past studies in humans and rodents, that propofol *increases* long-range functional coupling of neural activity across this frontal–parietal circuit. Their work prompts the question of whether general anesthesia really is a state of communication breakdown across the cortex and what the implications are for clinical monitoring.

"[Is] general anesthesia really a state of communication breakdown across the cortex? [What are] the implications for clinical monitoring?"

One compelling reason to think that communication across frontal–parietal networks is an important substrate of general anesthetics is that functional connectivity between frontal and parietal cortices has been found to be disrupted during propofol, sevoflurane, *and* ketamine anesthesia,[3] arguing for a common correlate or mediator of diverse anesthetic drugs. This is true in humans based on methods involving electroencephalography[4] and functional magnetic resonance imaging.[5–7] A recent neuroimaging study in nonhuman primates also demonstrated a suppression of functional connectivity across the prefrontal and posterior parietal cortex during propofol, sevoflurane, and ketamine anesthesia.[8] Of relevance to Ma *et al.*, this neuroimaging study of monkeys showed that connectivity patterns during anesthesia tend to converge on specific structural connections, as opposed to the broader repertoire of functional connectivity patterns observed in the waking state that might extend beyond structural highways. However, ketamine anesthesia is also associated with interrupted somatosensory information transfer between the structurally connected primary sensory cortex (in the parietal lobe) and primary motor cortex (in the frontal lobe).[9] This finding has been supported by work in human electocorticography, showing disruptions of cortical coherence across similar sensorimotor regions during propofol anesthesia.[10] Thus, anesthetics with distinct mechanisms do, indeed, suppress coherence and information transfer across structurally connected frontal–parietal networks. Taken in context, the study of Ma *et al.* demonstrates that assessment of frontal–parietal connectivity patterns depends on the specific circuit, even if there is a clear structural connection.

This is not the first study to identify increased frontal–parietal connectivity during general anesthesia. Although magnetic resonance imaging data and electroencephalogram-based analysis have been consistent across

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Corresponding article on page 560.

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numerous studies by independent laboratories, some analytic techniques have shown increased functional connectivity or a reversed pattern of directional influence across frontal–parietal networks.[11,12] The current study of Ma *et al*.[2] raises the question of whether this discrepancy is due to the specific analytic technique in addition to the specific brain regions analyzed. Although both might contribute, evidence is strong for the latter because Ma *et al*. analyzed other densely connected areas and found similar results. It is also critical to note that increased functional connectivity does not necessarily imply that there is an overall increase of information exchange between the frontal and parietal cortices. Excessively high functional connectivity could also be associated with a reduction of information transfer by isolating the circuit or reducing its repertoire of responses. Recent work in general anesthesia and disorders of consciousness suggests that there is a "sweet spot" that balances cortical dynamics and functional connectivity to maintain normal levels of consciousness.[13]

The work of Ma *et al*.[2] adds to the literature by demonstrating that densely connected brain regions in the frontal–parietal network do not manifest the expected reduction of functional connectivity. This study refines the frontal–parietal hypothesis by suggesting a dependence on the specific circuit analyzed and serves as a reminder that complex anesthetic mechanisms and brain dynamics cannot be trivially reduced to a single functional connectivity pattern. This prompts a careful reconsideration of the role of frontal–parietal networks in anesthetic-induced unconsciousness and highlights the need to consider circuit specificity in network-based approaches[14] to understanding or monitoring general anesthesia.

Competing Interests

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