Title: Level of consciousness is dissociable from cortical connectivity

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Abstract:

Several studies across multiple species suggest that frontal-parietal functional connectivity is a correlate of wakefulness that is disrupted during anesthetic-induced unconsciousness. However, it is not understood if anesthetic-induced disruption in cortical connectivity correlates with unconsciousness (i.e., a state effect) or the presence of anesthetic drugs in the brain (i.e., a drug effect). We recently demonstrated that reverse dialysis of the cholinergic agonist carbachol into the prefrontal cortex during sevoflurane anesthesia (1.9-2.4%) produced signs of wakefulness and electroencephalographic activation in male Sprague-Dawley rats (n=11), whereas reverse dialysis of noradrenaline produced only electroencephalographic activation (n=11). Reverse dialysis of either carbachol (n=11) or noradrenaline (n=11) into two areas of parietal cortex was sufficient to produce electroencephalographic activation but likewise failed to produce any signs of wakefulness. If frontal-parietal connectivity is a correlate of wakefulness, then it should be restored in rats following cholinergic stimulation-induced wakefulness (i.e, prefrontal cortex + carbachol) despite the presence of anesthesia. To investigate this, we analyzed normalized symbolic transfer entropy, a measure of directed connectivity, between ipsilateral frontal and parietal channels before, during, and after sevoflurane and carbachol/noradrenaline infusion into prefrontal and posterior parietal cortices. We focused our analyses on the gamma frequency bandwidth (25-155 Hz) because a recent study from our lab demonstrated high gamma (85-155 Hz) connectivity as a correlate of wakefulness. Consistent with our previous data, sevoflurane-induced unconsciousness was characterized by a bidirectional suppression of frontal-parietal high gamma connectivity. However, the frontal-parietal high gamma connectivity remained depressed in all experimental conditions/cohorts, despite the appearance of wake-like behaviors following carbachol infusion into prefrontal cortex, then returned after discontinuation of the anesthetic. This dissociation between level of consciousness and cortical connectivity motivates a reconsideration of the role of frontal-parietal connectivity in consciousness and anesthesia.