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SOCIETY FOR NEUROSCIENCE IN ANESTHESIOLOGY AND CRITICAL CARE

ARTICLE OF THE MONTH

Resting-state Network-specific Breakdown of Functional Connectivity during Ketamine Alteration of Consciousness in Volunteers

Bonhomme V, Vanhaudenhuyse A, Demertzi A, Bruno MA, Jaquet O, Bahri MA, Plenevaux A, Boly M, Boveroux P, Soddu A, Brichant JF, Maquet P, Laureys S.
Anesthesiology. 2016 Nov;125(5):873-888

Welcome to the December 2016 installment of the SNACC Article of the Month! The study presented this month is by Bonhomme *et al* and uses fMRI to look at ketamine-induced changes in the connectivity within and between resting state consciousness networks.This month's expert opinion is presented by George Mashour. George is an anesthesiologist and NIH-funded neuroscientist at the University of Michigan Medical School. His primary scholarly interest is in consciousness and the mechanisms by which general anesthetics disrupt consciousness. He is the founder and director of the Center for Consciousness Science at the University of Michigan, where he holds a number of research leadership roles. George Mashour is currently the President of SNACC.

We encourage all of our readers to tell us what they think by joining us on SNACC **LinkedIn** feed the **Twitter** feed, or the **Facebook** page.

~ Oana Maties, MD and Adrian Bohdan Pichurko, MD

Commentary

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The November issue of *Anesthesiology* has several articles of interest to the neuroscience of anesthetic-induced unconsciousness, including one on how ketamine disrupts large-scale brain networks. Ketamine has traditionally confounded generalized approaches to the mechanisms of anesthetic-induced unconsciousness because it functions so differently on so many levels. At the molecular level, it does not appear to work through the potentiation of gamma-aminobutyric acid transmission, like propofol and volatile anesthetics. Unlike virtually all

other general anesthetics and sedative-hypnotic drugs, ketamine does not metabolically depress the thalamus and in fact increases glucose metabolism. In terms of the systems neuroscience approach, ketamine activates nuclei that promote brain arousal and suppresses sleep-promoting areas. Neurophysiologically, ketamine depresses alpha power and increases gamma power of the EEG, the opposite effect of drugs like propofol or sevoflurane. So, the question remains: how does ketamine function as a general anesthetic?

In 2013, my research team and collaborators from South Korea demonstrated that ketamine disrupted brain connectivity in frontal-parietal networks in a manner that was similar to both propofol and sevoflurane. However, the studies were performed with EEG, with poor spatial resolution that did not provide a comprehensive picture of network-level activity. The article by Bonhomme et al in the November issue of Anesthesiology used fMRI, which has higher spatial resolution, to analyze networks and found results that confirmed a breakdown of frontal-parietal connectivity. As with the common finding in EEG, the results of Bonhomme and colleagues are similar to recent fMRI studies of both propofol and sevoflurane. Thus, the study provides important evidence that depression of frontal-parietal connectivity is an agent-invariant correlate—and possible mechanism—of anesthetic-induced unconsciousness. Importantly, ketamine preserved connectivity between different sensory regions (e.g., auditory and visual); these connections are disrupted during propofol and sevoflurane anesthesia. The preserved crossmodal connectivity provides insight into why patients dream or hallucinate during ketamine anesthesia, despite being disconnected from the world. Thus, the fMRI findings of this article help explain the similarities and differences of ketamine compared to more commonly-used anesthetics.