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Commentary

GABA inhibitory network: A requirement of maintenance of consciousness

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In this EBioMedicine manuscript [1], Dr. Guo and colleagues report that the isoflurane-induced loss of consciousness was associated with numerous interesting phenomena, including general decay of GABA input onto each cortical neuron subtype, and diverse glutamate transient in both excitatory and inhibitory interneurons. By using *in vivo* two-photon imaging with high spatiotemporal resolution and recently developed genetically-encoded neurotransmitter indicators [2], the authors systematically investigate the dynamics of cortical neurotransmitters in a cell type-specific manner during anesthetic-induced unconsciousness which occurred transitorily within tens of seconds. They found a general decreased GABA transmission among pyramidal neurons as well as Parvalbumin (PV), somatostatin-expressing (SOM) and Vasoactive Intestinal Polypeptide (VIP) interneurons. In contrast, glutamate transmission was almost preserved on pyramidal neurons but reduced on PV, SOM, and VIP interneurons. Furthermore, VIP neuronal activity was delayed, and PV neuronal activity was strongly inhibited and highly synchronized. The authors conclude that anesthetic-induced unconsciousness is a state with a disrupted excitatory-inhibitory network, and that the functional inhibitory network is required in the maintenance of consciousness.

The findings presented in this manuscript provide an original experimental paradigm for *in vivo* imaging under anesthesia with high spatiotemporal resolution. The findings of GABA/glutamate/calcium dynamics under isoflurane anesthesia provide evidence for the understanding of anesthesia-associated cortical dysconnectivity [3] (feedforward and feedback) as well as information disintegration theory [4]. Anesthetic-induced unconsciousness is associated with the dysfunction of the cortical information integration through the breakdown of the cortico-cortical long-range connectivity. This study refers to the intracolumnar information disintegration under isoflurane anesthesia.

(1) As a major medical breakthrough, anesthesia allows us to lose consciousness during surgery and other painful procedures. However, how anesthetic drugs work is a mystery and with that, they also high light the mystery of consciousness itself. This paper provides new insights for scientists specializing in the field of anesthesia and consciousness to understand the cortical mechanisms of anesthetic-induced unconsciousness [5]. The study is important in the area of anesthesia and anesthesia mechanisms, since unraveling the mechanism of anesthesia will contribute to the development of new anesthetics and the improvement of anesthesia monitoring tools and safety.

Another important issue that has not been adequately addressed in previous studies is the clarification of how neurotransmitter and neuromodulator systems [6,7], as well as other high-order cortical regions [8], are implicated in anesthesia. Previously, GABA and Nucleus accumbens (NAc) neurons expressing dopamine D1 receptors have been shown to modulate states of consciousness and control wakefulness [9]. While the clinical utility of current studies has yet to be established, studies like the one by Dr. Guo and colleagues are informative and certain to promote the investigation of multidimensional cortical network dynamics [10] under anesthesia comprehensively utilizing the basic and clinical technology.

Contributors section

YZ conceived and wrote the entire MS.

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Declaration of Competing Interest

The author declares no conflict of interest.

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