Is It Feasible of Prophylactic α5 GABA<sub>A</sub> Receptor Blockade for Preventing POCD?

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GAMMA-AMINOBUTYRIC ACID (GABA) is the chief inhibitory neurotransmitter in the mammalian central nervous system (CNS). It plays a role in regulating neuronal excitability throughout the nervous system. Also GABA activation is considered as the basis of general anesthesia including intravenous and inhalational anesthetics. Meanwhile, cumulating evidence indicated that GABA is the underlying mechanism of post-operative cognitive dysfunction (POCD). Based on these findings, researchers are beginning to focus on GABA as the target to treat POCD, but they ignored the role of GABA in the performance of general anesthesia, especially when the blockade of GABA was given prior to surgery. It is undoubtedly risking our patients in intra-operative awareness. Our exploratory data also verified our hypothesis in which the GABA inhibition would reduce the efficacy of inhalational anesthetics.

Keywords: Gamma-aminobutyric acid - post-operative cognition dysfunction - minimum alveolar concentration

ZUREK et al. (1) reported that α5 GABA<sub>A</sub> receptor involves in the development of postanesthetic memory deficits and they used inverse agonist of α5 GABA<sub>A</sub> receptor to mice before or after isoflurane anesthesia, and found the deficit in short-term memory was fully reversed by the inverse agonist and also the mice lacking of Gabra5 gene displayed no short-term memory deficits 24 hours after isoflurane, so the authors suggested α5 GABA<sub>A</sub> receptor can be targeted to restore isoflurane-induced memory dysfunction. The interesting finding of this study gives us the hope to avoid, at least reduce the risk of cognition impairment from inhalational anesthetics, but we still concerned whether or not it is feasible and reliable if α5 GABA<sub>A</sub> receptor was focused on as the therapeutic target prophylactically showed by the same group in their previous study (2).

General anesthesia and increasing age are two major risk factors of post-operative cognition dysfunction (POCD) (3), even the authors did not investigate the influence of age on this topic, but we still raised some other issues as follows: 1) they merely gave one minimum alveolar concentration (MAC) of isoflurane or sevoflurane and lasted for 1 hour, this regimen omitted the role of time and dosage of anesthetics on cognition; 2) although the genetically modified animals were used, we do not know the exact changing characteristic yet of the expression of α5 GABA<sub>A</sub> receptor in the central nerve system; 3) given the essential role of GABA<sub>A</sub> receptors in general anesthesia (4), we proposed that the interventions targeting on GABA<sub>A</sub> receptors would finally affect anesthetic efficacy or/and effectiveness. Even the authors did not find change in MAC after delivering of L655,708, but we detected and found the onset and awake time of anesthesia of isoflurane and sevoflurane were changed by this drug in rats at different MACs (Figure 1). Therefore, if we used these kinds of drugs before anesthesia, is it good for us and our patients when the onset and awake time of an-
esthesia shifted? This issue should be explored in further and an ascertained answer should be given because such drug may increase the risk of intraoperative awareness through attenuating general anesthesia-associated GABA inhibition.

CONFLICT OF INTEREST
None

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REFERENCES