Propofol and Cellular Calcium Homeostasis

To the Editor.—In an interesting paper, Jensen et al.1 described the effects of propofol on the cytosolic-free calcium concentration ([Ca"2+]i) and on the cytoskeletal organization in neurons and astrocytes. The authors concluded that propofol induces an increase in [Ca"2+]i, and therefore a change in the organization of actin filaments. A large part of the discussion concerned the mechanisms of this [Ca"2+]i increase. However, the authors did not provide a consistent explanation for their findings.

At least three processes are involved in [Ca"2+]i regulation: (1) the transmembrane Ca"2+ influx through voltage-activated Ca"2+ channels, (2) the release of Ca"2+ from intracellular stores (e.g., mitochondria or endoplasmic reticulum), and (3) the clearance of cytosolic Ca"2+ by reuptake in the intracellular stores or extrusion in the extracellular medium. The authors found two components of the [Ca"2+]i increase: an increased influx of extracellular Ca"2+ and a release of Ca"2+ from intracellular stores.

Propofol has been found to inhibit transmembrane Ca"2+ current in myocytes and neurons.2,5 Nevertheless, a nonspecific membrane-estivating effect could be involved in the extracellular Ca"2+ influx. The most interesting point concerns the release of Ca"2+ from intracellular stores. The authors cite the work of Eriksson on rat liver mitochondria.6 In this study, the author demonstrated that propofol could inhibit Ca"2+ release from mitochondria.7 This finding appears for Jensen et al. to be contradictory with their own results. We studied the effects of propofol on Ca"2+ transport in mitochondria. As previously reported by Eriksson in liver mitochondria, we have shown in heart mitochondria that propofol inhibits the permeability transition pore and the mitochondrial Ca"2+ release.8 At higher concentrations (>100 µM), an uncoupling effect of propofol can decrease the mitochondrial Ca"2+ uptake through the potential-dependent Ca"2+ uniport.

We think that these data and those of Eriksson do not contradict the results of Jensen et al. In their study, the increase in [Ca"2+]i after addition of propofol could be due to a release from another intracellular store like the endoplasmic reticulum. Recently, Hossain et al.9 reported that some anesthetics (halothane, isoflurane, octanol) increase [Ca"2+]i by inducing a leak of Ca"2+ from IP3-sensitive stores (e.g., endoplasmic reticulum). In the case of propofol, it seems important to test the same hypothesis to explain the results of Jensen et al.

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References

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