

The profound effects of numbing agents

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A large proteomics study on the brains of newborn mice provides more evidence that numbing drugs often used in obstetric or pediatric medicine can have profound and long-term negative effects, even after minimal exposure.

This study, appearing in the December issue of *Molecular and Cellular Proteomics*, highlights the delicate state of the developing nervous system and reinforces the use of caution when administering sedatives, anesthetics, and anti-convulsants to pregnant women or infants.

Compounds that either block excitatory NMDA receptors or activate inhibitory GABA receptors in the brain are clinically useful as anesthetics or for treating disorders like seizures and insomnia. However, just like other chemicals that produce similar mind-soothing effects (e.g. alcohol), excessive use can be detrimental –particularly in still-developing individuals.

To examine how far-reaching the physiologic effects of such 'numbing' drugs (sedatives, hypnotics, analgesics) are, Angela Kaindl and colleagues treated 6-day old mice with two doses of either the NMDA receptor blocker dizocilpine or the GABA receptor activator Phenobarbital and then analyzed subsequent changes in brain protein expression.

They observed both acute and sustained effects, with protein changes in the cerebral cortex (the area controlling memory, thought, awareness, and language) evident after just 24 hours, and these changes were still

present one week and one month after the one-day drug treatment. The affected proteins are involved in crucial processes like cell growth, cell death, and the formation of neural circuits (In another recent study, the authors were able to confirm that such drug treatment negatively influences learning and memory).

A similar drug dose given to adult mice did not produce such changes, which the authors note clearly shows how susceptible infant brains are compared to adults. Importantly, this study shows that drug overuse on even one occasion (for example, during the delivery procedure) can have long-term implications.

Source: American Society for Biochemistry and Molecular Biology

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