tasures. As well as Akt phosphorylation via the tropomyosin receptor kinase signaling pathway, p75NTR has been shown to increase phosphorylated Akt in some systems using the neurotrophin NGE. In figure 4C, when DIV-5 cultures were treated with control small interfering ribonucleic acid, the isoflurane treated cultures had a higher level of p75NTR than control cultures. p75NTR staining of cultures or Western blot analysis of p75NTR levels would allow this hypothesis to be further investigated.

In addition to the regulation of tPA secretion, p75NTR levels are also an important determinant of isoflurane-mediated neuronal changes. In summary, there may be a two-part mechanism to the isoflurane-mediated neuronal response, an increase in p75NTR levels, and a decrease in tPA release, a threshold of which is required to obtain the isoflurane-mediated neuronal changes.

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apoptotic pathway. Use of immunoprecipitation experiments at different developmental time points after receptor agonism may explain whether this is an alteration in receptor signaling or changes in receptor expression with age. What does appear to be known is that p75NTR expression and signaling is not only temporally but also spatially dependent on some unknown intracellular mechanism. Studies to characterize p75NTR expression and its coupling with known partners (e.g., Trk) at varying ages are currently underway in our laboratory. The expectation is that these studies will provide more detail about the mechanisms by which isoflurane injures developing neurons.

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Difficult Mask Ventilation and Neuromuscular Blockade

To the Editor.—We read with interest the article by Kheterpal et al.1 regarding impossible mask ventilation. This is a very important but rare event, and this large study gives us a clear idea about its incidence and, for the first time, what the associated risk factors are.

We note that in all but 4 of the 77 cases of impossible mask ventilation, the patients had received neuromuscular blockade “in the process of induction or management of the airway,” with succinylcholine being used in 65 patients and a nondepolarizing agent in the remaining patients. However, it is not clear at what stage of airway management that the neuromuscular block was administered in these cases—was it before difficulty with mask ventilation being encountered or given after problems occurred to improve the situation, and did ventilation indeed improve? Furthermore, only 19 patients (25%) proved difficult to intubate, which suggests that there was opportunity for improving the conditions for mask ventilation. Kheterpal et al. do go on to discuss the problem in assessing the role of muscle relaxants in mask ventilation difficulties, but the documentation for each case did not include an assessment of mask ventilation before and after neuromuscular blockade. It would be interesting to note if there is a difference in the incidence of impossible mask ventilation with or without neuromuscular blockade being given at induction (before attempts at mask ventilation). This may be an area for further investigation, although as with this study, a large population sample would be required.

In our experience, optimum depth of anesthesia and neuromuscular blockade provide the best conditions for both mask ventilation and tracheal intubation (in patients in whom an awake technique, transtracheal catheter, or awake tracheostomy are not indicated). Neuromuscular blockade given at induction and before attempts at mask ventilation is the most common practice in our institution for patients requiring tracheal intubation. In addition, we have found that using intermittent positive pressure ventilation by means of a Penlon Nuffield 200 ventilator (Penlon Ltd., Abingdon, United Kingdom) while holding a mask is beneficial for assessment of adequacy of mask ventilation and also useful for training. This approach has the advantage of allowing a two-handed mask technique for more challenging airways and continual monitoring of airway pressure from the pressure gauge on the ventilator. Monitoring airway pressure in this way provides an objective measure of the seal that is achieved with the mask and patency of the airway. Mask technique can then be optimized by reference to clinical signs (e.g., chest expansion), airway pressure/peak pressure, and capnography. We also encourage initial management of the airway without use of an oropharyngeal/Guedel airway to improve and optimize these fundamental airway skills. Mask ventilation is our core skill, and we believe subjective and objective assessment throughout training is required to maintain this art and limit airway disasters.

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