Melatonin Ameliorates Neurotoxicity Induced by Sevoflurane in Young Mice by Enhancing Glutamate Transmission and Synaptic Plasticity in the Hippocampus

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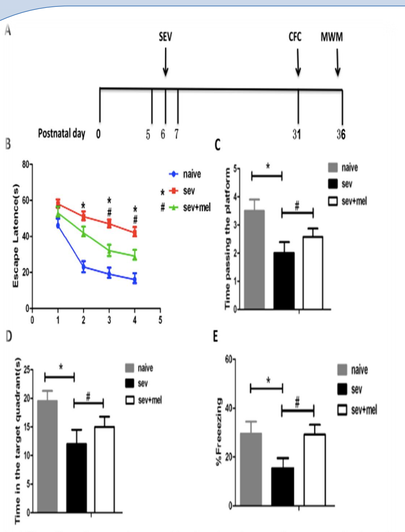
Backgroud: Children with multiple exposures to anesthesia and surgery may have an increased risk of developing cognitive impairment. Sevoflurane is a commonly used anesthetic in children. Previous studies have shown that anesthesia with sevoflurane can induce neurotoxicity in the brain tissues of adult young mice. However, the exact molecular mechanism is elusive. Melatonin is the major secretory product of the pineal gland, and has a cellular protective effect in cerebrovascular and neurodegenerative diseases. We therefore set out to assess the potential therapeutic effect of melatonin in young mice anesthesia by sevoflurane.

Methods: Six day-old wild-type (WT) were exposed to 3% sevoflurane 2 h daily for 3 days. Cognitive function in the mice was determined at postnatal day 36 by using a Morris water maze. Golgi staining demonstrated that the effects of neuronal synaptic plasticity. Finally, we investigated the glutamatergic transmission in the hippocampus after sevoflurane induction and melatonin treatment, used by Western blot and vitro electrophysiological measurement of spontaneous excitatory postsynaptic currents (sEPSCs).

Results: Melatonin increased learning and memory function in young mice compared treatment by sevoflurane. And melatonin alleviated the sevoflurane -induced impairment of the synaptic plasticity in the hippocampus. Moreover, melatonin mitigated the sevoflurane-induced reduction in postsynaptic density-95 levels in the neurons. We found that melatonin treatment significantly relieved the impaired glutamatergic receptors in the hippocampus after sevoflurane treatment by significantly increasing NMDAR and AMPAR expression. In electrophysiological experiments, sevoflurane significantly decreased the frequency and ampitude of sEPSCs, and Melatonin blocked these sevoflurane-induced effects.

Conclusion: These results suggest that sevoflurane may induce cognitive impairment in young mice, which can be mitigated by melatonin. These findings should promote more studies to determine the neurotoxicity and suggests melatonin play an important role of anesthesia in the developing brain.



ig.1 The effect of neonatal on cognitive function after sevoflurane anesthesia and melatonin treatment.

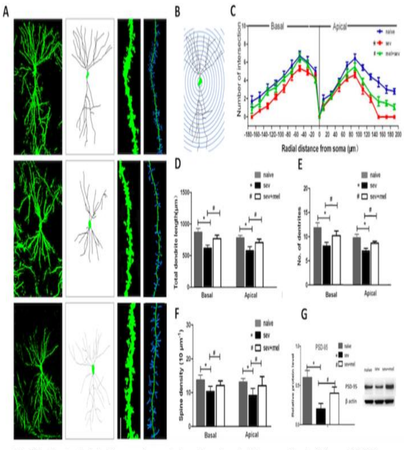


Fig.2 Melatonin alleviated the sevoflurane-induced impairment of the synaptic plasticity and PSD95 expression in the Hip. Representative neurons and dendrites labelled by Golgi staining and imaged by confocal microscopy in reflection mode. Scale bar = 5 μm.

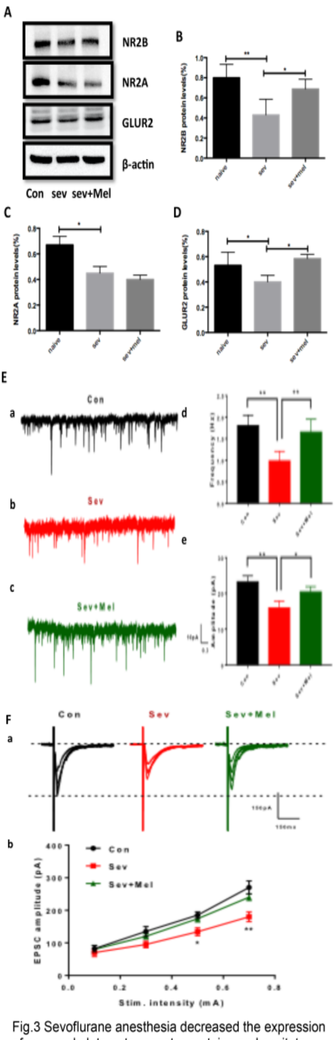


Fig.3 Sevoflurane anesthesia decreased the expression of neuronal glutamate receptor proteins and excitatory synaptic transmission function.