Isoflurane reduces glutamatergic transmission in neurons in the spinal cord superficial dorsal horn: evidence for a presynaptic site of an analgesic action.

Abstract:
The minimum alveolar concentration (MAC) of a volatile anesthetic defines anesthetic potency in terms of a suppressed motor response to a noxious stimulus. Therefore, the MAC of an anesthetic might in part reflect depression of motor neuron excitability. In the present study we evaluated the effect of isoflurane (ISO) on neurons in the substantia gelatinosa driven synaptically by putative nociceptive inputs in an in vitro spinal cord preparation of the rat. Whole-cell patch-clamp recordings were performed in neurons with their soma in the substantia gelatinosa of transverse rat spinal cord slices. We investigated the effect of ISO on excitatory postsynaptic currents (EPSC) evoked by dorsal root stimulation (eEPSC), spontaneous (sEPSC), and miniature (mEPSC) EPSC. ISO reversibly reduced the amplitude of eEPSC to 39% +/- 22% versus control. ISO decreased the frequency of sEPSC and mEPSC to 39% +/- 26% and 63% +/- 7%. Neither the amplitudes nor the kinetics of mEPSC and sEPSC were altered by ISO. We conclude that ISO depresses glutamatergic synaptic transmission of putative nociceptive primary-afferent inputs, presumably by reducing the release of the excitatory transmitter. This effect may contribute to an antinociceptive action of volatile anesthetics at the spinal cord level.
IMPLICATIONS: The present electrophysiological in vitro experiments provide evidence that the volatile anesthetic isoflurane reduces excitatory transmitter release at the first site of synaptic integration of nociceptive inputs, the spinal cord superficial dorsal horn. This effect may contribute to the anesthetic action of volatile anesthetics at the spinal cord level.