Isoflurane Enhances and Depresses Synaptic Coupling

Background/Introduction: Anesthetics are known to depress synaptic transmission, and this effect is thought to underlie the uncoupling of brain regions seen with cortical EEG recordings. We tested the hypothesis that anesthetic-induced depression of synapses leads to uncoupling of electrical activity between frontal cortex and hippocampus.

Methods: The present study used electrophysiologically-guided electrode implants to record Schaffer-collateral to CA1 neuron mono-synaptic responses, as well as frontal cortical micro-EEG signals. Rats were allowed to recover from surgery and then isoflurane effects were characterized after several days (>7) to several months (<7) later. Simultaneous recordings of cortical and hippocampal micro-EEG signals, evoked synaptic responses, anesthetic concentration, vital signs and behavior were made.

Results: Loss of consciousness, measured as righting reflex, was consistently associated with increased synchronized delta activity, in hippocampus and cortex, as well as a novel ~15 Hz rhythmic oscillation produced by isoflurane in hippocampal micro-EEG recordings. Surgical anesthesia, measured as loss of tail-clamp reflex, was observed on the transition to burst-suppression activity in both hippocampal and cortical micro-EEG signals. Isoflurane produced a concentration-dependent depression of mono-synaptic responses: at surgical anesthetic depths, excitatory postsynaptic potentials were depressed by 26.6 ± 4.2 % ($n=5$; $p<0.001$) of control amplitudes, but surprisingly, coupling between cortex and hippocampus was further enhanced.

Conclusion: Clearly, our hypothesis was wrong, since increased coupling between brain regions was observed at the same time that mono-synaptic responses were depressed. We demonstrate for the first time that cortical-hippocampal coupling is increased at both low (loss of consciousness) and at high surgical concentrations of isoflurane.

Support: Anesthesia Department at Stanford University, the NIH (R01GM095653 to MBM and R01GM101497 to RAP) and NSERC (A9935 to BHB).