

Integrative *in vivo* approaches to studying anaesthetic mechanisms

David Carr. Imperial College London, London, United Kingdom.

Although modern general anaesthesia has been used for over 100 years in medical and veterinary practice, the mechanisms of how such a wide variety of pharmacological agents induce reversible loss of consciousness are not completely known. Given that loss of consciousness can only be measured in live animals, *in vivo* experiments therefore provide the most optimal setting for the elucidation of such unknowns.

Electroencephalographic (EEG) methods have been widely used in both research and clinical settings to monitor anaesthetic depth for surgical and non-surgical procedures in humans and animals. The technique relies on recording network activity of synchronously oscillating neurons in the mammalian brain. The utility of the technique is that it can provide a real-time measure of brain activity on millisecond timescales.

We recorded the EEG activity of C57Bl/6 mice chronically implanted with gold-plated electrodes in response to increasing doses of the volatile anaesthetic halothane. We recapitulated experiments that show a prominent theta oscillation (centred at 5 Hz) in the EEG and found this effect to be sensitive to muscarinic antagonism with systemically administered atropine.

There is evidence that this theta oscillation results from the concerted action of cholinergic and GABAergic neurotransmitter systems in the medial septum that form projections to the hippocampus. So for our further investigations we injected various pharmacological agents directly into the medial septum thus allowing a more specific neurophysiological analysis.