Induction with isoflurane results in faster fMRI response but weaker neuronal response in á-chloralose anesthetized rats

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INTRODUCTION

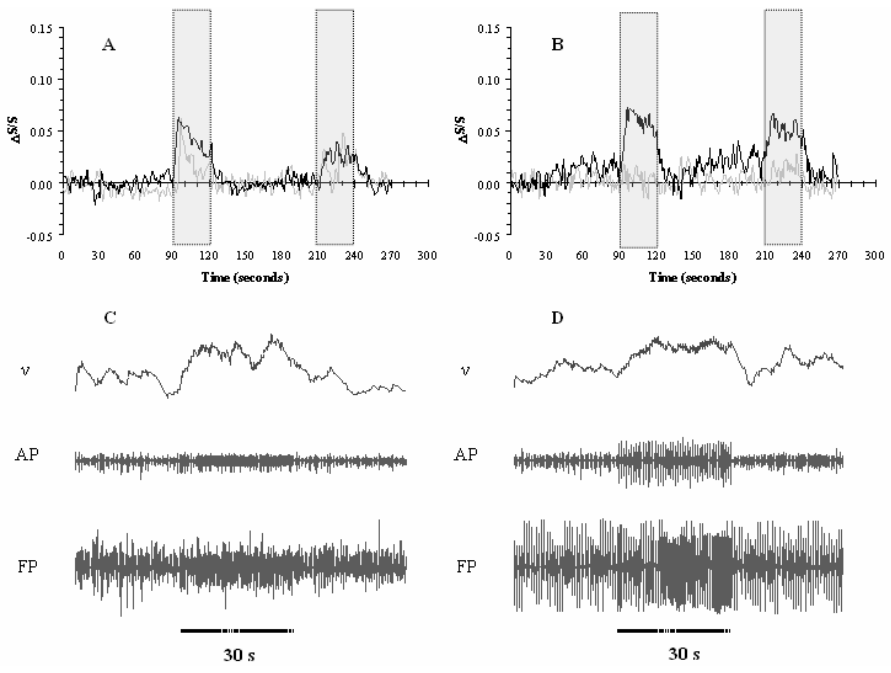
Functional brain imaging is predominantly based on changes in CBF induced by alterations in neuronal activity and is generally carried out in animals under anesthesia, usually with α-chloralose because of its minor effects on cardiovascular, respiratory, and reflex functions [1]. General anesthetics reduce neuronal activity in various regions of the mammalian central nervous system [2]. A considerable number of mechanisms have been suggested to mediate the depressant effects [3]. However it is still a matter of debate as to which molecular targets are truly relevant in producing the "true" anesthetic state [4]. Recent studies reported the relationship between the action of volatile anesthetics occurring on the molecular level and the corresponding effects on neuronal firing [5]. Prior studies have also reported that volatile anesthetics depressed action potential firing of cells in the somatosensory cortex during sensory stimulation [6]. In this study we have used two volatile anesthetics (isoflurane, halothane) and studied the time-dependent induction effects for functional studies in α-chloralose anaesthetized rats.

METHODS

Animal preparation: Sprague-Dawley rats were tracheotomized and artificially ventilated (70% N_2O, 30% O_2). During the animal preparation halothane (0.7%)/ isoflurane (0.5%) were used for induction. Intraperitoneal lines were inserted for administration of α-chloralose (46±4 mg/kg/hr) and D-tubocurarine chloride (1 mg/kg/hr). An arterial line was used for monitoring physiology (blood pH, pO_2, pCO_2) throughout the experiment. The same forepaw stimulation protocol (30 s block design; 2 mA; 0.3 ms; 3 Hz) was used for both fMRI and extracellular recordings. *fMRI measurements (n=10):* All fMRI data were obtained on a modified 9.4T Bruker horizontal-bore spectrometer (Billerica, MA) using a ^{1}H resonator/surface coil RF probe. The images were aquired with gradient echo EPI sequence (TR/TE=1000/15 ms). *Extracellular (and laser-Doppler) measurments (n=16):* The rat was placed in a stereotaxic holder on a vibration-free table inside a Faraday cage. Tiny burr holes above the contralateral and ipsilateral somatosensory regions [4.4 mm lateral and 1.0 mm anterior to bregma] were thinned and tungsten microelectrodes (FHC inc, Bowdoinham, ME) were inserted at a depth of layer 4 with stereotaxic manipulators (Kopf). The signal was then digitized (>20 kHz) with a μ-1401 interface using SPIKE-2 software [7]. The data were first filtered to action and field potentials (AP, FP) and then the spiking data were examined for spike rates (ν). The CBF was measured using a bare fiber laser-Doppler probe (Oxford Optronix, Oxford, UK).

RESULTS AND DISCUSSION

The purpose of this study was to examine the effect of isoflurane and halothane used for induction in α-chloralose anaesthetized rats. The fMRI time courses after 3 hrs (gray) and 5 hrs (black) from isoflurane induction (A) showed generally moderate levels of intra-animal reproducibility, which was lacking with halothane (B). These BOLD responses were supported by similar CBF responses measured with laser-Doppler probes (data not shown). The electrophysiology results after 5 hrs (bottom) showed changes in neuronal activity, but the alterations were far less significant with isoflurane (C) than with halothane (D). These results together suggest that while isoflurane induction may result in a faster hemodynamic response, the changes in neuronal activity are slightly depressed. These results suggest caution for interpreting results from anesthetized rats where volatile agents are used for the induction phase.



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