Carry-over effects of gaseous anaesthesia on fMRI response and tissue oxygen levels in the rat brain

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Introduction

Alpha-chloralose is thought to preserve the coupling between neuronal, vascular and metabolic responses to somatosensory stimuli [1-4], and is the standard anaesthetic agent used in many functional magnetic resonance imaging (fMRI) studies in the rat [1-5]. However, α-chloralose has poor analgesic properties, and surgical preparation (e.g. cannulation of a blood vessels or implantation of electrodes into the forepaw) prior to the fMRI experiment is performed under different anaesthetics (usually inhalational anaesthetics such as halothane or isoflurane) [1-3]. The change of anaesthetics regime affects tissue and vascular responsiveness, but very few reports address this problem. In order to assess the effects of anaesthetics switch-over on tissue metabolism, and to determine the time needed to regain robust and stable fMRI response to somatosensory stimuli, we measured brain partial oxygen pressure, cerebral blood flow and BOLD signal changes during and after transition from isoflurane to α-chloralose in a forepaw stimulation paradigm in the rat.

Methods

Experiments are carried out in accordance with the European Communities Council Directive of 24 November 1986 (86/609/EEC), and Italian legislation regarding animal use (DL 116/1992).Experiments were conducted in two separate groups, one for the measurement of pO2 and CBF, the other for the assessment of MR BOLD signal changes, both under a forepaw stimulation protocol during anaesthetics transition. Male Sprague-Dawley rats (250-350g) were anaesthetised with Isoflurane (5% induction, 2-3% during surgery). Animals were mechanically ventilated under neuromuscular blocker (d-Tubocurarine 0.25 mg/kg in bolus followed by a continuous infusion at 0.25 mg/kg. hr). Subsequently, anaesthesia was changed to α-chloralose (bolus i.v. of 50 mg/kg followed by a continuous infusion at 40 mg/kg. hr). Cerebral activation was induced through electrical stimulation (2Hz, 2mA, 0.3ms) with sub dermal electrodes placed above the wrist. Repeated stimulations of the forepaw were applied (3min OFF-45s ON). In the first cohort (n=7), brain oxygen pressure and cerebral blood flow were continuously measured for two hours after switching to α-chloralose using a dual pO2/Laser-Doppler-Flow probe (Oxylite, Oxford Optronix) inserted in the layer IV of the cortex. The same protocol was used in the second group (n = 2, 250-350g) in which we acquired MRI data using a Bruker Avance 4.7T system, a 72mm birdcage resonator for RF transmit and a quadrature surface receive coil (Bruker, Ettlingen, Germany). BOLD signal was assessed using the GEPI sequence: matrix 64x64; FOV 40mm; slice thickness 1mm in one slice positioned 5 mm caudal to the rhinal fissure, TE=25ms; TR=3000ms. Statistical maps were obtained using Stimulate [6]. The region of interest was chosen as the significant activated voxels (t-test between rest and activated times after 90 min) in the contralateral side to the stimulationFig.1B).

Results

Switching from isoflurane to α-chloralose resulted in a decrease in brain oxygen pressure and blood flow baseline (-76 ± 14% and -63 ± 8 % respectively Fig. 1A), reaching a steady state after 92 ± 24 min. and 81 ± 37 min. respectively. Similarly, fMRI signal intensity decreased by about 10 %, with a latency of 85-90 min. to reach steady state. The brain reactivity to forepaw stimulation was very low under isoflurane and increased after injection of α-chloralose to reach a maximum at 60 ± 26 min. and 93 ± 32 min for CBF and pO_2, respectively (Fig. 1B). Similarly, BOLD response increased after the switch-over to α-chloralose, and reached steady state after 80 min (Fig1C).

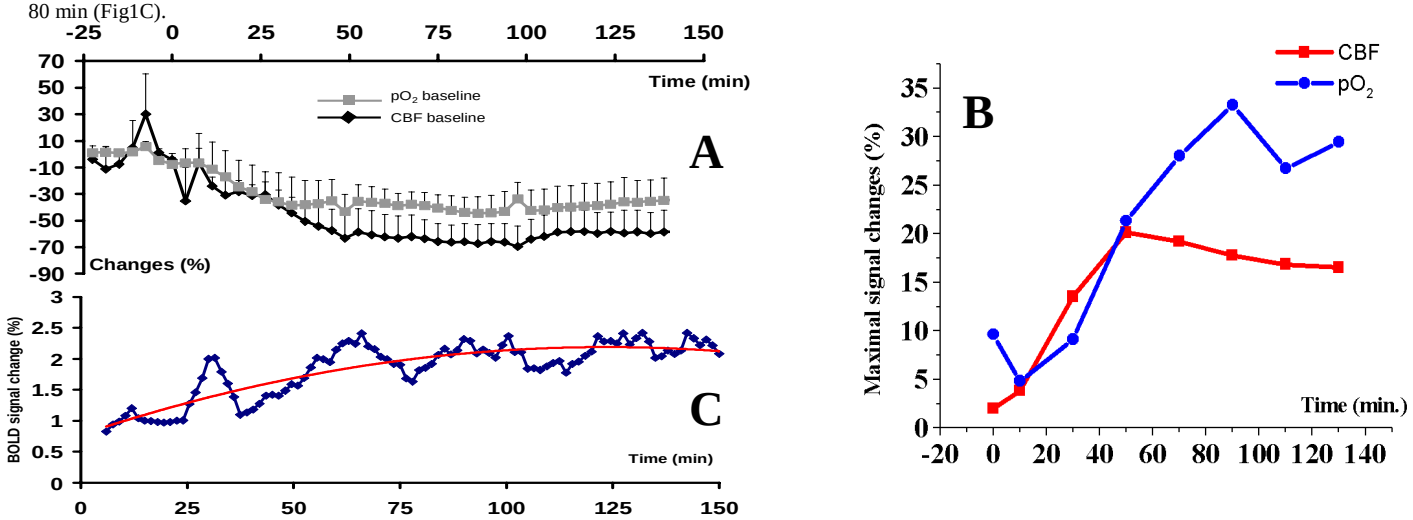

Fig. 1: Brain oxygen pressure (pO_2), cerebral blood flow (CBF) and BOLD signal in the somatosensory cortex during anaesthesia transition from Isoflurane (2%) to α-chloralose (50 mg/kg + 40 mg/kg.hr). A: Average time course of pO_2 and CBF baseline (N = 4). B: Corresponding evolution of brain reactivity for CBF and pO_2 evoked by controlateral forepaw stimulation. C: Time course of BOLD signal reactivity induced by forepaw stimulation (N = 2). Red curve represents the trendline guide for the eye. In all figures time zero represents the injection of α-chloralose and the stop of Isoflurane anaesthesia.

Discussion and conclusion

We have shown that switching from isoflurane to α-chloralose anaesthesia affects baseline BOLD and CBF, and tissue partial pressure of oxygen, as well as response to somatosensory stimulation. A new steady state in baseline and responsiveness is observed after at least 90 min upon changing anaesthetics. Acquisition of fMRI data before the new steady state is reached might result in erratic and inconsistent responses. Other gaseous anaesthetics characterised by longer wash-out and recovery times, (e.g. halothane [7]) may require an even longer stabilisation time.

References

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