A breathing apparatus providing improved control of FiO2 and FiCO2 for calibrated fMRI

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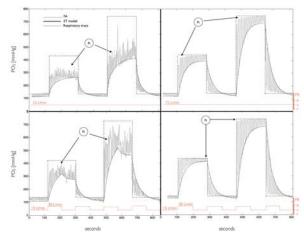
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Target audience: Researchers interested in calibrated MRI and fMRI measures of cerebrovascular reactivity to respiratory gases.

Purpose: Respiratory manipulations modulating the fractional concentration of inspired O₂ and CO₂ (FiO₂ and FiCO₂) to induce hyperoxia and/or hypercapnia as a vascular stimulus have become an important component of fMRI studies measuring the vascular as well as the metabolic function in the brain^{1,2,3}. While individualized mixing of gas concentrations to achieve prospective control of end-tidal levels is useful in certain situations, the requirements for many applications are amply met by delivering predetermined concentrations of inspired gases, so long as end-tidal values are recorded for retrospective normalization of the fMRI signal⁴. The most common practice has been to administer fixed fractional concentrations for inhalation, delivering O₂/CO₂ enriched mixtures through low-cost nonrebreathing masks commonly used in clinical oxygen therapy. However, either due to variations in the shape of the subject's face or to incomplete sealing of one-way valves used to release excess gas flow, such oxygen masks are often very leaky, hampering precise adjustments in fractional inspired concentrations and thus limiting the reproducibility of the hyperoxic/hypercapnic stimuli. One way around this limitation would be to ensure a tight seal of the face mask using surgical tape or other means. However, this approach should be avoided in a closed circuit where the gas supply directly connected to the mask because it creates a risk of asphyxia in the event that the medical gas supply is interrupted. We aimed at developing an apparatus for improved control over the fractional concentration of inspired gases which would be safe and suitable for functional MRI applications. Figure 1 - Oxygen mask vs. new circuit design

Methods: To improve control over the gases flowing in to the mask chamber, we have conceived a breathing circuit that uses a non-vented mask firmly fit to the subject's face and two high efficiency valves separating the different compartments of the circuit. To ensure the safety of subjects, we have replaced the breathing bag found in oxygen masks (Fig. 1A) by an open reservoir, through which the subject breathes room air whenever the flow of administered gases becomes insufficient. The resulting open breathing circuit (Fig. 1B) represents an inherently safe design and allows precise adjustments in the fractional concentration of inspired gases, with low flow dosages. The breathing apparatus we describe below has been implemented, using commercially available parts, to address three design criteria: to be MRIcompatible, to comfortably fit the subject when a head antenna is used for the study of the brain, and to be entirely disposable while keeping a reasonable cost of production. Parts were acquired from two different vendors: Intersurgical Inc (NY, USA) and Teleflex Medical (NC, USA) - IS and TM respectively. The circuit comprises a small non-vented face mask (IS #7193) and a dual-limb airway that is appended to the mask's frontal opening. An elbow (TM #1632 or #1624) and a triple swivel wye-piece (IS #1929) connect the limbs to the mask. A pair of valves (TM #1664/5) at the join of the limbs ensure that 1) inspired gases only come from the incoming limb, consisting of a corrugated tube (2 TM #1418 connected by TM #1960) that is preceded by a connector (TM #1642); and 2) that expired gases only flow through the outgoing limb, that can be a short corrugated tube (TM #1410). These two limbs have an open end,

Figure 2 - Oxygen mask vs. new circuit results



communicating with the exterior. While the small outgoing limb serves as an exit for expired gases, the long incoming limb serves as a gas reservoir, like the breathing bag of conventional oxygen masks. However, because of its geometry and

open end, the limb reservoir functions as a sequential container, where the bits of administered gases are stacked as they arrive at the circuit and mix much less than in a bag type of reservoir. This allows sharper transitions in fractional concentration of inspired gases using low flow dosages. We have conducted two tests (Fig. 2) using both the new circuit and a non-vented Hudson oxygen mask (#1060) in a young healthy subject (female: 32y, 1.65m, 60kg). In Test 1 the subject was given 100% O2 or 50% O2 balanced with air in two different instances lasting 3 minutes each and 3 minutes apart. Medical air was administered otherwise. Flow rates (FR) were 15 L/min during the whole manipulation. Test 2 followed the same design as Test 1 but with different FR. Upon transitions in administered concentrations (FA), FR was increased to 30 L/min for 1m:30s. The new circuit has also been tested in a fMRI experiment, where FiO₂ and FiCO₂ were modulated administering 100% O2 and 5% CO2, according to the schedule proposed by Bulte et al.³ In this test we have increased FR to 60L/min during 3 seconds upon the transitions in FA. In Figure 3 we show data obtained from two different runs in a single participant. Respiratory gases were analyzed and recorded using Biopac MP150 (Biopac Systems Inc., CA, USA). Baseline levels and changes in end-tidal (ET) partial pressures were quantified using the approach

described in ref [4].

Results: The new circuit afforded an improved correspondence between FA and FiO2, which were generally immune to differences in FR (Fig. 2). When FR was kept constant throughout the manipulation (first row) the transitions in FiO₂ were not as sharp as the switching of gases, which results from the small contamination of new input gases with gases that remained in the limb reservoir from the preceding input phase. The maneuver of increasing FR upon the switching of FA allows the replacement of gases from the preceding input by the gases constituting the new FA input; and, with that, sharper FiO2 transitions. This procedure should be as fast as possible, e.g. delivering a short bolus of the new FA and then returning to regular FR. The improved control of inspired gases afforded by our apparatus resulted in ET response waveforms that were highly reproducible (Fig. 4). In each plot, the leftmost value represents the baseline ET level of the respective gas, whereas the 4 other values represent the ET responses associated to the changes in inspired concentrations.

Conclusion: The breathing circuit we have presented allows control over fractional inspired concentrations, optimizes gas consumption, is simple, safe and suitable for fMRI applications.

References: 1) Mandell DM, et al. Mapping cerebrovascular reactivity using blood oxygen level-dependent MRI in Patients with arterial steno- occlusive disease: comparison with arterial spin labeling MRI. Stroke. 2008; 39:2021-2028. 2) Ances BM, et al. Effects of aging on cerebral blood flow, oxygen metabolism, and blood oxygenation level dependent responses to visual stimulation. HBM. 2009; 30:1120-1132. 3) Bulte DP, et al. Quantitative measurement of cerebral physiology using respiratory-calibrated MRI. NeuroImage. 2010; 60:582-591. 4) Tancredi FB, Hoge RD. Comparison of cerebral vascular reactivity measures obtained using breath-holding and CO2 inhalation. JCBFM. 2013; 33:1066-1074.

Figure 3 – O₂/CO₂ manipulations using the new circuit

