Foregoing Anesthesia Entirely: Resting-State Functional MRI of Completely Awake Rats

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RATIONALE: Functional magnetic resonance imaging (fMRI) is commonly used in characterizing normal brain networks in resting state (rsfMRI). There is vast literature linking changes in fMRI networks with disease states. In the context of disease models connectivity changes have been proposed as a sensitive measure of brain vulnerability or plasticity [1]. However, several fMRI studies on animal models of AD have been confounded by the use of anesthesia during imaging acquisition. Rodent fMRI protocols designed to acquire images from awake animals routinely utilize anesthesia to restrain animals in the MRIs from which they are allowed to wake [2]. Given the well characterized anesthesia effects on normal brain hemodynamics and the utilization of blood oxygenated level determined (BOLD) contrast for fMRI, being able to image conscious animals without any anesthesia interference provides significant advantages**.** **AIMS AND HYPOTHESIS**: We tested the feasibility of training Sprague Dawley rats to undergo awake rsfMRI acquisition without exposure to anesthesia. We expect that conscious acquisitions will result in a stronger global connectivity of the DMN, without a significant signal deterioration induced by head movements. **METHODS**: This study was approved by McGill University Research Ethics Board. Sprague-Dawley rats (N=6; males only; 227.7±10.2g) were trained for over a period of 2 weeks. Each training session consisted of an increasing exposure time to an individual custom designed cradle to constrain animals in the scanner (Biospect 70/30 USR, Bruker, Billerica, MA). Animals were rewarded with chocolate pellets. Functional BOLD images were acquired for each training day. The same animals underwent an additional BOLD acquisition conducted with 2% isoflurane anesthesia in medical air. For each scan, strength of DMN connectivity was measured using cross-correlation method with a seed point located in the anterior cingulate. The effect of anesthesia was estimated by voxel-wise t-statistical analysis conducted with fMRIstat for Matlab. **RESULTS**: Unacceptable movement artifacts were observed in three rats. For the three successful rats, significant reduction of absolute movements (x, y and z directions) was observed as early as the second day of scanning and reaching a minimum at the fourth day of scanning. In addition, at the fourth day, the amount of movement was comparable between awake and anesthetized animals. Finally, in anesthetized animals the DMN connectivity was reduced in the medial prefrontal and temporal cortices, as well as in striatal, thalamic and pontine nuclei (see Fig. 1). No differences were observed in the contrast [awake < anesthetized]. **DISCUSSION**: Although the present technique shows favourable results regarding brain network organization, the large rate of animal refractory to the training was high. Acquiring conscious connectivity data is a work in progress that will certainly reduce the distance between human and animal research.

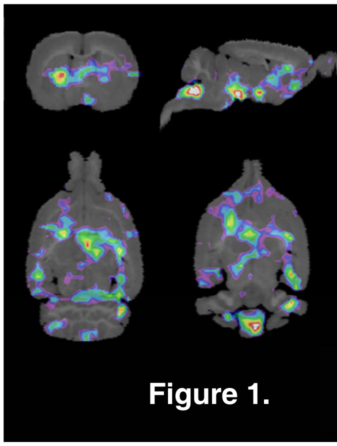

Figure 1.

1. Greicius, M.D., et al., *Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI.* Proc Natl Acad Sci U S A, 2004. **101**(13): p. 4637-42.
2. King, J.A., et al., *Procedure for minimizing stress for fMRI studies in conscious rats.* J Neurosci Methods, 2005. **148**(2): p. 154-60.