BOLD changes in somatosensory cortex of malnourished rats

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Introduction. Malnutrition is a major public health problem in developing countries. Its incidence is increasing and the mortality rate is still high. Experimental animal models using rats and mice have been widely used to study this health problem. Functional Magnetic Resonance Imaging (fMRI) provides a method for mapping brain functional activity based on the blood oxygen level-dependent effect (BOLD). In this work, we described the pattern of BOLD changes caused by the trigeminal nerve stimulation to investigate the effects on brain activity of malnutrition in rats. To provoke malnutrition, the food competition method was applied [1]. This method consists in inducing malnutrition during lactation through food competition. A large number of pups cannot be sufficiently fed by one nursing mother. Then, a delay in weight increase is observed even if there is plenty milk available. The vibrissae-barrel axis is an attractive model for studying structure, function, development and plasticity within the somatosensory cortex, due to the functional and morphological correlation between the vibrissae and the barrels [2]. BOLD responses of control and malnourished rats were compared and discussed.

Material and Methods. Twelve male Wistar rats aged 18 to 21 days, equally divided into control (41.94±4.9g) and experimental (29.09±3.3g) groups, were induced with 1.5-2% isoflurane in O2. The anaesthetic was administered at 1.5 to 2% with 2l/min of O2. The rat's head and ears were fixed with a Varian stereotactic frame to minimise motion artefacts and to supply anaesthetic during the fMRI experiment. ECG and breathing monitoring, and rat's temperature control were done with a small animal monitoring and gating system (Model 1025, SA Instruments, NY, USA). The right trigeminal nerve was stimulated using percutaneously inserted stainless steel electrodes, the cathode positioned in the whiskers and the anode inserted in the masticatory muscles. The trigeminal nerve was stimulated using a stimulator with 10 ms constant current pulses (500 mV and 2 mA) applied every second (Grass S-48 Stimulator, Grass Technologies, RI, USA) at 1Hz. 60s OFF was alternated with 60s ON periods. All experiments were performed on a 7T/21cm Varian system (Varian, Inc, Palto Alto, CA) equipped with DirectDrive technology and a transceiver 16-rung birdcage coil (16 cm long and a 6.5 cm diameter). Rat's brain axial images were acquired using a standard gradient echo sequence and the following parameters: TR/TE=107.82/3.8 ms, Flip angle=20^0, FOV=30x30mm, matrix size= 128x128, thickness=0.3mm, and NEX=1.

Results. Image stacks were digitally process using SPMMouse [3] to determine regions of interest in the somatosensory cortex where neuronal activity is expected to happen. Control and experimental data were then fitted to a non-linear regression over time and the results are shown in Fig. 1. Nonlinearity of the BOLD response is observed for both groups. There is great similarity in the pattern of BOLD response for both groups. These results showed a great concordance with results already reported by Silva and Korestky [4]. The BOLD responses display a similar time delay for both groups and reach their maximum value at 5 seconds into the stimulation. Experimental group results suggest larger oxygen consumption when compared with the control group. Fig. 2.a) shows the averaged BOLD signal intensity time course for the control and experimental groups. A sign change can be observed between the regions I and II of Fig. 2.a), roughly after 12 s for both cases. This has been already reported as a negative BOLD response and it is caused by inhibition mechanisms [5]. A student t test was run to investigate statistical independence of the measurements of the response amplitude. At the 0.05 level, the difference of the population means ($mean_{control}$=384 ± 108 & $mean_{exp}$= 504 ± 198) is significantly different than the test difference. In order to quantify the BOLD response of the malnourished rats, the method reported in [6] was used. Then, the response amplitudes were calculated from the peak of BOLD response intensity. Additionally, the response integral was defined as the product of the amplitude and the full width at half maximum (FWHM) for both groups of rats as shown in Fig. 2.b). The response integral values are 4235.80 and 5503.22 for the control and malnourished rats, respectively. This parameter indicates a clear increment in the neuronal activity for the malnourished rats.

Conclusions. This fMRI study is the first performed in rats and illustrates a similar pattern of BOLD responses between malnourished and control rats. An increment on the BOLD signal can be appreciated for the malnourished rats for the first 10 s. Negative BOLD responses can be seen for the two groups of rats and are caused by inhibition mechanisms. Vascular nonlinearities are the major contribution to the observed nonlinearities and they are neuronal in origin.

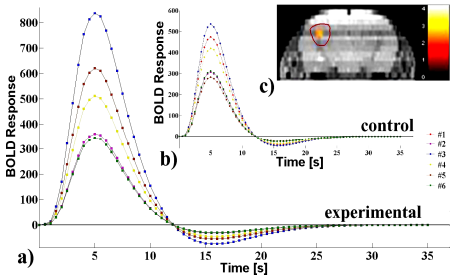

Figure 1. BOLD changes in somatosensory cortex (c) during the left trigeminal nerve stimulation for control (b) and experimental (a) .groups.

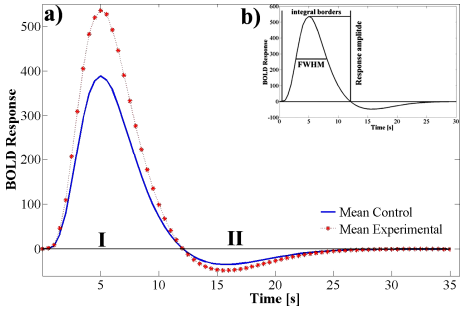

Figure 2. a) Averaged BOLD signal intensity time course for control (solid line) and experimental (*) groups, b) Representative averaged time course (illustration purpose).

Acknowledgement. R. M. thanks the CONACyT Mexico for Ph. D. scholarships. email: arog@xanum.uam.mx. **References**. [1]. Ortiz R. et al. Med. Sci. Res. 1996;24:843. [2]. Just N. et al. 16th ISMRM. 2008: . [3]. Sawiak SJ. et. al. 17th ISMRM. 2009:1086. [4]. Silva AC, Koretsky AP. PNAS. 2002;99:15182. [5]. Vandervliet E. et al. ESMRMB. 2006:624. [6]. Yesilyrut B. et al. MRI. 2008;26:853.