Activation by fasting changes diffusion parameters of the hypothalamus in the adult human brain as detected by DWI

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Introduction: Cerebral activation is associated to intracellular, extracellular and transcellular ion fluxes between neural cells, accompanied by water movements and eventually cellular swelling. DWI is excellently endowed to detect these changes in a fully non invasive manner. Indeed, a redistribution of water diffusion compartments between Fast and Slow Diffusion Pools (FDP and SDP), has been reported during visual activation[1]. Previous work in our lab demonstrated a relationship between increases in SDP and D_{slow} parameters in mice and hypothalamic activation by fasting[2]. In this new work we present a study of brain activation by fasting in human subjects detected with DWI methods.

Subjects and Methods: Healthy male (n=6) aged 24-33, were imaged in two experimental conditions, fed and after 24 h of fasting. *DWI:* Experiments were performed on a 1.5 T whole-body MR scanner (Signa, GE Healthcare, Milwaukee,WIS) in the medical centre *Resonancia Magnética Nuestra Señora del Rosario* in Madrid, Spain, equipped with a ^{1}H selective quadrature head coil. Voluntaries singed up an informed consent and image acquisitions were medically supervised by the staff of *Nuestra Señora del Rosario*. Multi b-value DWI were acquired by an expert technician (6 b-values, 200<b<1200 s/mm^2, three directions, single-shot, TR/TE=5000/91 ms, Av=4, FOV=240 mm, acquisition matrix=256x256, slice thickness 3 mm). *Data analysis:* The diffusion data set was fitted (MATLAB v7a) pixel by pixel to a biexponential model $S(b)/S(0)=SDP\cdot\exp(-b\cdot D_{slow})+FDP\cdot\exp(-b\cdot D_{fast})$, with slow (SDP) and fast (FDP) diffusion phases characterized by slow (D_{slow}) and fast (D_{fast}) diffusion coefficients. Two ROIs were studied, the hypothalamus and an area of the frontal cortex (Fig.1).

Results: Our results show significant (and directionally-dependent) differences between the mean values of SDP in the hypothalamus (Fig. 1 and 2). No significant changes between feeding conditions can be detected in the cortex, where values of the D_{slow} coefficients are different from values in the hypothalamus (Fig 2).

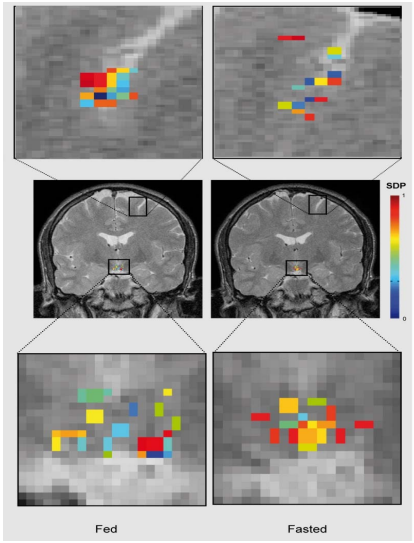

Figure1. Coronal slices containing ROIs (hypothalamus and the cortex), where H-F SDP pixel values of the fed (left) and fasted (right) have been superimposed to T2 images.

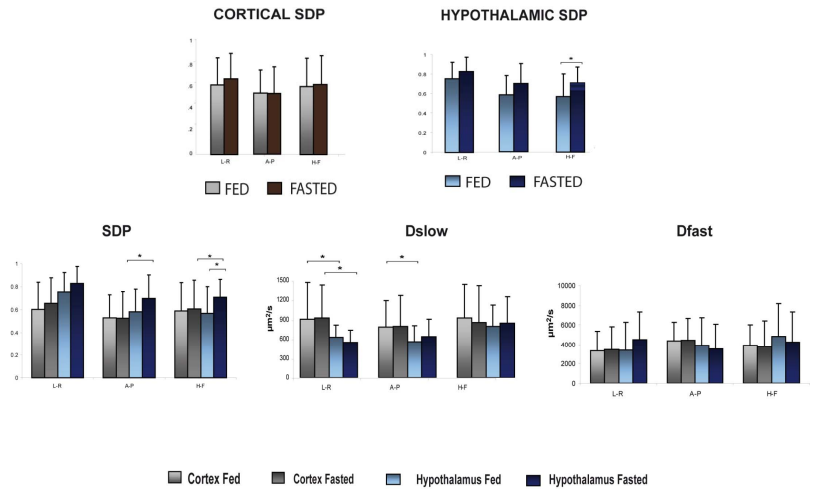

Figure2. Mean values (±SD) of hypothalamic and cortical SDP in the two feeding conditions for the three directions of diffusion (upper panels). Note the significant increase with fasting of hypothalamic SDP in H-F direction. SDP, D_{slow} and D_{fast} values in the hypothalamus (blue colours) and cortex (grey) of all subjects (bottom panels), where the significant changes between areas are depicted (*p<0.5,**p<0.01, two tails T student test)

Conclusion: We report that hypothalamic activation by fasting in adult human results in a significant increase in the hypothalamic SDP contribution, compatible with activation-induced intracellular swelling and on agreement with previous studies with animals[2].

References : [1]Le Bihan D et al. Proc. Natl. Acad.Sci 2006; *103:8263-68,*[2]Lizarbe B et al, 2-Deoxy-D-glucose mimics the effects of hypothalamic activation by fasting as detected by DWI,ISMRM submited 2012