Functional Networks and their Modulation by Cortisol as Investigated by Pseudo Continuous Arterial Spin Labeling (pCASL)

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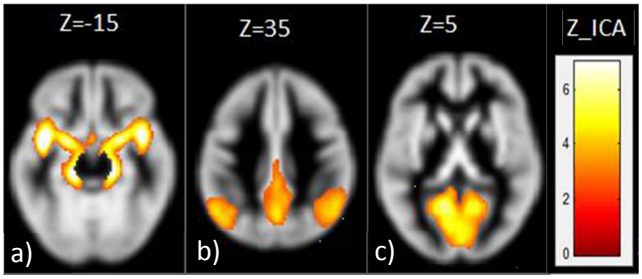
Introduction: The investigation of functionally connected networks (FCN) exhibiting synchronized low frequency fluctuations is of growing interest for a wide range of basic and clinical research questions. FCNs representing motor, auditory and visual systems and also higher cognitive functions [1] and emotional processing [2] have been described. Cortisol, the so-called stress hormone, modulates numerous cognitive and emotional brain functions [3] via receptors located in the cortex, limbic system, hippocampus, thalamus, and hypothalamus [4]. As the cortisol level is fluctuating in a diurnal rhythm, it might alter network connectivity and/or network metabolism. Indeed, variation in the cortisol level led to changes in regional metabolism [5] and cerebral blood flow (CBF) [6, 7] in healthy individuals. In the present study we investigated the effect of different cortisol levels on CBF in FCNs using arterial spin labeling (ASL) since it allows to identify FCNs [8, 9] as well as to quantify CBF (in [ml/100g/min]) within the same measurement session.

Methods: 54 subjects were assigned to three groups according to the cortisol level: H) ASL measurement at 2 pm 1 hour after oral administration of 20 mg hydrocortisone (high cortisol level); M) ASL measurement at 8 am (medium cortisol); and L) placebo administration before ASL session at 2 pm (low cortisol). Saliva cortisol level analysis revealed a significant group effect ($F(2, 50)=20.9$, $p<.000001$; Fig. 2). Imaging was performed in a 3T Siemens Magnetom Trio TIM system equipped with a 12-channel head coil. The pCASL parameters were: 13 slices, 6.5mm slice thickness, FOV=230x230mm^2, matrix=128x128, TR/TE=3500/18ms and FA=25°. A balanced labeling technique [10, 11] was used with a mean slice-selective gradient (Gz) of 0.6 mT/m and a pulse (Hanning window-shaped RF pulse) for a total labeling duration of 1.72 s. The labeling plane was positioned 90 mm below the isocenter of the imaging region and the post-labeling delay ω was 1100ms. 50 label/control-pairs were acquired. In addition, a 3D T1-weighted structural scan was run (modified driven equilibrium fourier transform (mdeft) sequences: 176 sagittal slices with 1.0mm thickness, voxel size = 1x1x1mm3, TR/TE = 7.92/2.48ms, FA = 16°, FOV = 256x256mm2, matrix size=256x256mm, and Ti = 910ms for an optimal contrast-to-noise ratio) [12]. Matlab/SPM8 was used for preprocessing of imaging data and calculation of absolute CBF maps. ASL images were motion corrected and CBF was quantified using a single-compartment model (T1blood 1650ms, labeling efficiency 0.85, blood-tissue partition coefficient 0.9). CBF images were coregistered to the T1 images, normalized into standard MNI space and smoothed with an 8mm FWHM Gaussian kernel. FCNs were identified by means of the group ICA of fMRI Toolbox (GIFT) [13].

Results: The FCNs displaying the spatial pattern of the medial-temporal network (MTN) and the default mode network (DMN) were selected as well as the occipital visual network (OVN) as control region (Fig. 1). CBF was quantified for these networks. There was no difference in global CBF between groups. We found significant CBF differences between all the FCNs (main effect of FCN: $F(2, 74)=77.94$, $p<.00001$) with the CBF values in the MTN being the lowest and the ones in the DMN being the highest. Group M showed significantly higher CBF in the DMN ($p<.01$) compared to group L (Fig. 2).

Fig. 1) ICA maps of the whole ASL data set; a) MTN, b) DMN, c) OVN



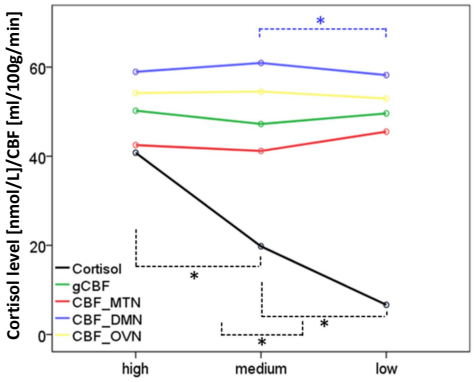


Fig. 2) Average cortisol level (black line) and mean CBF in the different FCNs per group (high cortisol (H); medium cortisol (M); low cortisol (L)

Conclusions: Applying ICA on ASL data in order to identify CBF functional connectivity is a novel approach to evaluate network activity differences in terms of absolute network CBF, which allows the quantification of inter-individual differences. We found a positive correlation between cortisol level and CBF which is consistent [7] but also controversial to the existing literature [4, 5, 6]. As this effect was shown only in the DMN (no effect in the MTN or OVN) between the groups M and L, but not between H and M, or H and L, we suggest that not cortisol level might be the influencing variable but rather daytime: as the M group was measured in the morning, the subjects might have been in a more relaxed state and thus their DMN more active. This result would indicate that cortisol level has no particular impact on the different FCNs at a resting state. However, distinct FCNs show different levels of CBF.

References:

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