ASL based functional connectivity in schizophrenia relates to disease severity

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Purpose: Functional connectivity (FC) of the human brain has become a widely used method to investigate brain function. Recently, Arterial Spin Labeling (ASL) based cerebral blood flow (CBF) measurements has attained interest to estimate FC. Compared to the conventional BOLD fMRI that is a complex mixture of perfusion, metabolic and oxygenation status of the brain, the CBF measurements represent absolute quantitative brain perfusion, which is a major advantage. Especially in the diseased brain, this additional information might help to better classify the pathological alterations and explain inter-individual differences in disease symptoms and their severity.

Methods: 11 schizophrenic patients (30.5±6.3years; 9M/2F) were investigated with pCASL [1,2] (Isocenter of the readout slices was 90mm above labeling plane, balanced labeling with mean Gz of 0.6mT/m and 60 Hanning window-shaped RF pulses (RF duration 600µs with 900µs gap, FA = 25°, bandwidth 3004Hz/pixel), labeling duration (τ) = 1.72s, post-labeling delay (PLD) = 1.25s, TR/TE = 3000/18ms, EPI readout with 20slices, 6mm slice thickness, 1mm gap, FOV = 230mm2, matrix size = 128x128, 50 label and control pairs) and BOLD fMRI (EPI sequence with TR/TE 1980ms/30ms, 32 slices, 252 volumes, 3×3×3mm3, gap thickness 0.75mm, matrix size 64×64, FOV 192×192mm2). In addition, a high resolution T1 weighted MDEFT sequence was acquired (modified driven equilibrium Fourier transform [3], TR/TE 2300ms/3.93ms, 176slices, slice thickness 1.0mm, FOV 256×256mm2). Furthermore, all patients were interviewed by a trained psychologist to assess PANSS scores.
BOLD images were slice time and motion corrected to the T1 image, normalized into standard MNI space and smoothed with an 8mm FWHM Gaussian kernel. ASL data was motion corrected, then CBF was estimated with a single compartment model [4] (T1blood 1650ms, labelling efficiency 0.85, blood-tissue partition coefficient 0.9). Quantified CBF images were then co-registered, normalized and smoothed similar to the BOLD images. T1 images were segmented into grey and white matter (GM/WM) and the thresholded GM map was used as a mask in the subsequent analyses. Normalized BOLD and CBF images were then separately subjected to a group ICA (GIFT toolbox [5]) to compute Group Components (GC; 24 and 15 components for BOLD and CBF respectively) and single subject components (SC). In both datasets the Default Mode Network (DMN) was visually identified. Similarity of GCs and SCs was calculated as the spatial correlation coefficient. In addition, CBF within the global GM and in the ASL-DMN was computed and analysed for possible relation to spatial similarity or disease severity using Pearson and partial correlation analyses with GM-CBF as control variable.

Results: In the BOLD and the ASL dataset a highly similar GC representing the DMN could be identified (r=0.56, p<0.001/ Figure1 top row). The SCs' spatial comparison between the two methods revealed a high degree of agreement in spatial similarity, with one outlier (Figure1, lower left). Furthermore, the spatial similarity of the ASL-SCs to the ASL-GC was negatively correlated to the PANSS positive scores (r=-0.66, p=0.03; Figure1, lower right). A partial correlation between SC's ASL-DMN and DMN-CBF (using GM-CBF as control variable) yielded a negative trend (r=0.61, p=0.06).

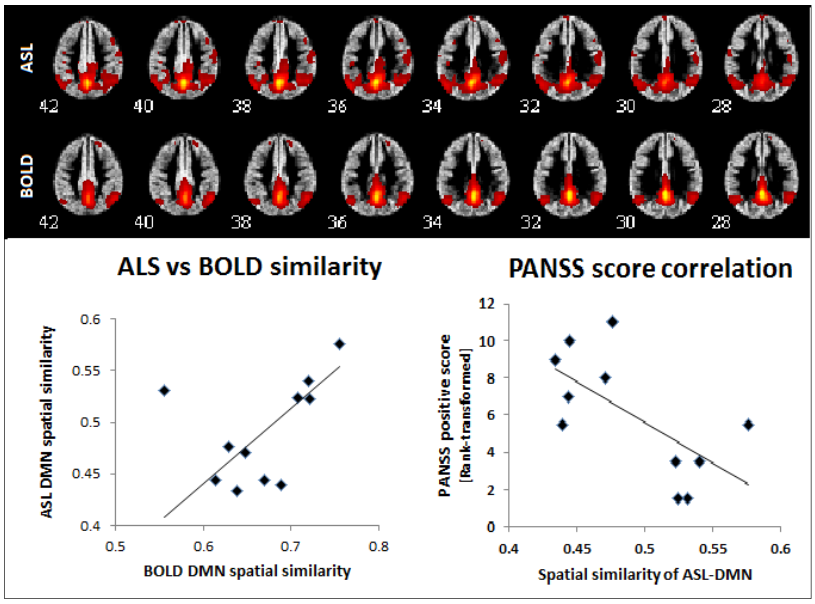

Figure1:(upper part) DMN identified based on ASL-CBF or fMRI BOLD; data thresholded at z=1.5. (lower left) scatter plot for spatial similarity of individuals' SCs to the respective GCs (BOLD/ASL). (lower right) scatter plot for ASL-DMN spatial similarity and PANSS positive scores.

Discussion: Our results indicate that using ASL data, similar information about spatial pattern of the DMN can be achieved as compared to BOLD based analyses. ASL yields the advantage to gather additional information about the absolute perfusion of the brain and network. Moreover, the degree of similarity of an individuals' DMN (SC) to the GC may reflects the severity of specific disease symptoms as assessed by PANSS positive. Thus it could be argued that spatial altered DMN in schizophrenia reflects deficits of an individual to integrate external stimuli and internal cognition to a whole concept and in self-monitoring. Furthermore, the increased CBF in the altered DMNs suggests a state of hyperactivity that may relate to how processing errors occur due to constant overload.

References:

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