Perfusion networks in Parkinson's disease revealed using Arterial Spin Labeling

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Aim: To distinguish those with Parkinson's disease (PD) from healthy controls by the expression of a characteristic Arterial Spin Labeling (ASL)-derived perfusion network.

Methods: Pseudo-continuous ASL was used on a 3T GE HDx scanner with a 3D fast gradient echo spiral sequence[1] to investigate CBF perfusion. Forty-four PD patients (mean age±sd: 68.1±9.1 years; 34 males) and 26 healthy controls (67.7±9.5; 18 males) completed neuropsychological tests of global mental status (Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA)), motor assessment (Hoehn & Yahr (H&Y), UPDRS-III) and MRI scans. Each CBF map was normalized to a probabilistic elderly template[2] using SPM5 and smoothed with a 10mm isotropic Gaussian kernel. Principal component analysis (PCA) of the entire data set produced a set of characteristic perfusion covariance patterns represented via principal components (PCs). The expression of each of the first seven PCs in each individual was entered into a stepwise logistic regression to determine those which significantly contributed ($p<0.05$) to the differentiation of PD from control. A linear combination of the significant components was then used to create a PD-related perfusion network. The expression of the PD network in each individual was correlated with neuropsychological scores and disease severity and further examined with ROC analysis. Leave-one-out cross validation was used to assess reliability of the network.

Results:

Components 1, 2, 4, and 6, explaining 24.9%, 9.4%, 5.7%, and 3.7% of the variance respectively, significantly contributed to differentiating PD from control. The resultant PD-related network (Figure 1a) was characterized by decreased perfusion in PD versus controls in bilateral posterior parietal-occipital regions, posterior medial cortex, precentral and bilateral middle frontal gyri, and left caudate. Preserved perfusion occurred in bilateral globus pallidus. ROC analysis yielded an area under the curve of 0.85 (Figure 1b). Expression of the network in the PD group significantly correlated with MoCA ($r = -0.54$, $p < 0.001$) and MMSE ($r = -0.39$, $p = 0.01$) as well as age, disease duration, and severity ($r>0.30$, $p<0.05$; H&Y Spearman's rho=0.46, p=0.002). Motor impairment (UPDRS-III) showed a non-significant correlation ($r=0.29$, $p = 0.06$). Leave-one-out cross validation showed a classification accuracy of 78.6% (sensitivity: 86.4%, specificity: 65.4%).

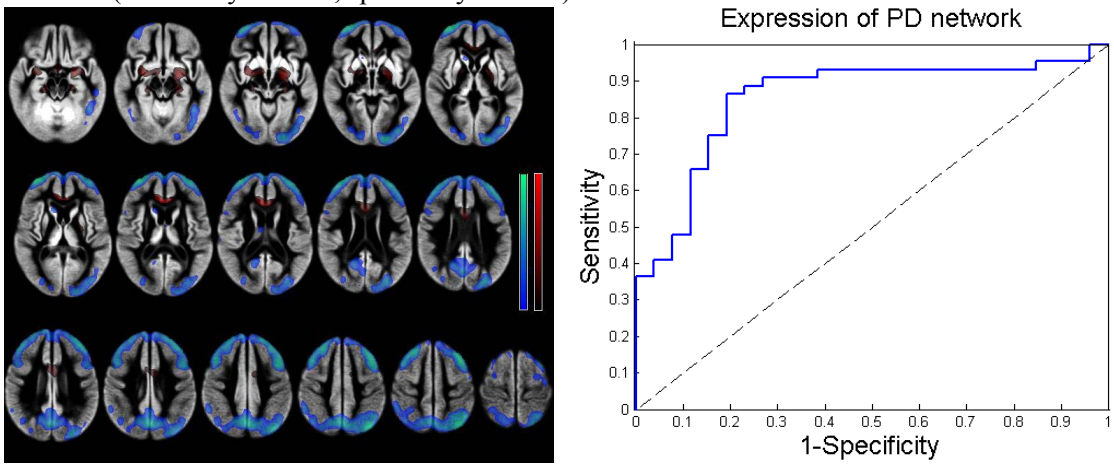

Figure 1: a) PD-related perfusion network. Blue indicates areas of decreased perfusion in PD vs. controls, red denotes highly preserved perfusion. Display shows voxels which significantly contribute to the network at $p<0.01$ (colour bars: $z = \pm [2.3\ 5.0]$). b) ROC curve: AUC = 0.85.

Concluding Remarks:

Radiotracer studies by others suggest separate motor and cognitive metabolic/perfusion patterns in PD[3]. In this study, none of the ASL-derived individual components showed a unique association with motor or cognitive measures. However the resultant perfusion network which optimally distinguished PD from control correlated with disease duration and cognitive status in the PD group. Cross validation of the PD-related network showed generalization to a wider population. This network approach provides a promising marker to objectively gauge disease severity and serves as a potential method to longitudinally track disease progression.

References:

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