Identification of Parkinson's disease patients based on resting-state between-network connectivity

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Introduction:

Parkinson's disease (PD) is the second most common neurodegenerative disorder. Diagnosis is based on clinical history and neurological examinations (1), and may at times be challenging. Diagnostic accuracy of movement disorder experts is 79.6% at the initial visit. Non-experts are 73.8% accurate (2). A robust biomarker might be beneficial in certain diagnostic dilemmas.

Given the interplay of e.g. motor and non-motor symptoms, and functional connectivity changes found within and across different functional networks (3,4), we hypothesize, that functional connectivity can be used as a neuroimaging biomarker.

We evaluated a data-driven, model-based classification approach to discriminate idiopathic PD patients from healthy controls (HC) based on between-network connectivity in whole-brain resting-state functional MRI (rs-fMRI).

Methods:

Whole-brain rs-fMRI (EPI, TR 2.2 s, TE 30 ms, flip angle 90°, resolution 3.1 mm3, acquisition time ~11 min) was assessed in 42 PD patients (medical OFF), and 47 HC matched for age and gender.

fMRI data was preprocessed using FSL 5.0.8 (5), including motion correction, slice timing correction, 5 mm spatial smoothing, intensity normalization, high-pass filtering (150 s) and ICA-based noise-removal using FIX (6) with the standard training dataset and recommended settings shown to be robust for PD (7). EPIs were registered to MNI152 standard space applying linear and non-linear transformations.

Between-network connectivity based on full and L2-regularized partial correlation measures (FSLNets) were computed for each subject using canonical functional network parcellations with different dimensionalities based on independent component analysis from two large population-based samples: The Human Connectome Project (HCP, 15/25/50/100/200 networks) and 1000BRAINS (15/25/50/70 networks) (8,9). A Boosted Logistic Regression model was trained on the correlation matrices using 20 repeats of 10-fold stratified cross-validation (R, caret and caTools). The number of iterations was fixed at 100, then optimized for the best model. Accuracy was aggregated over the validation folds. Sensitivity and specificity were calculated for the optimized model.

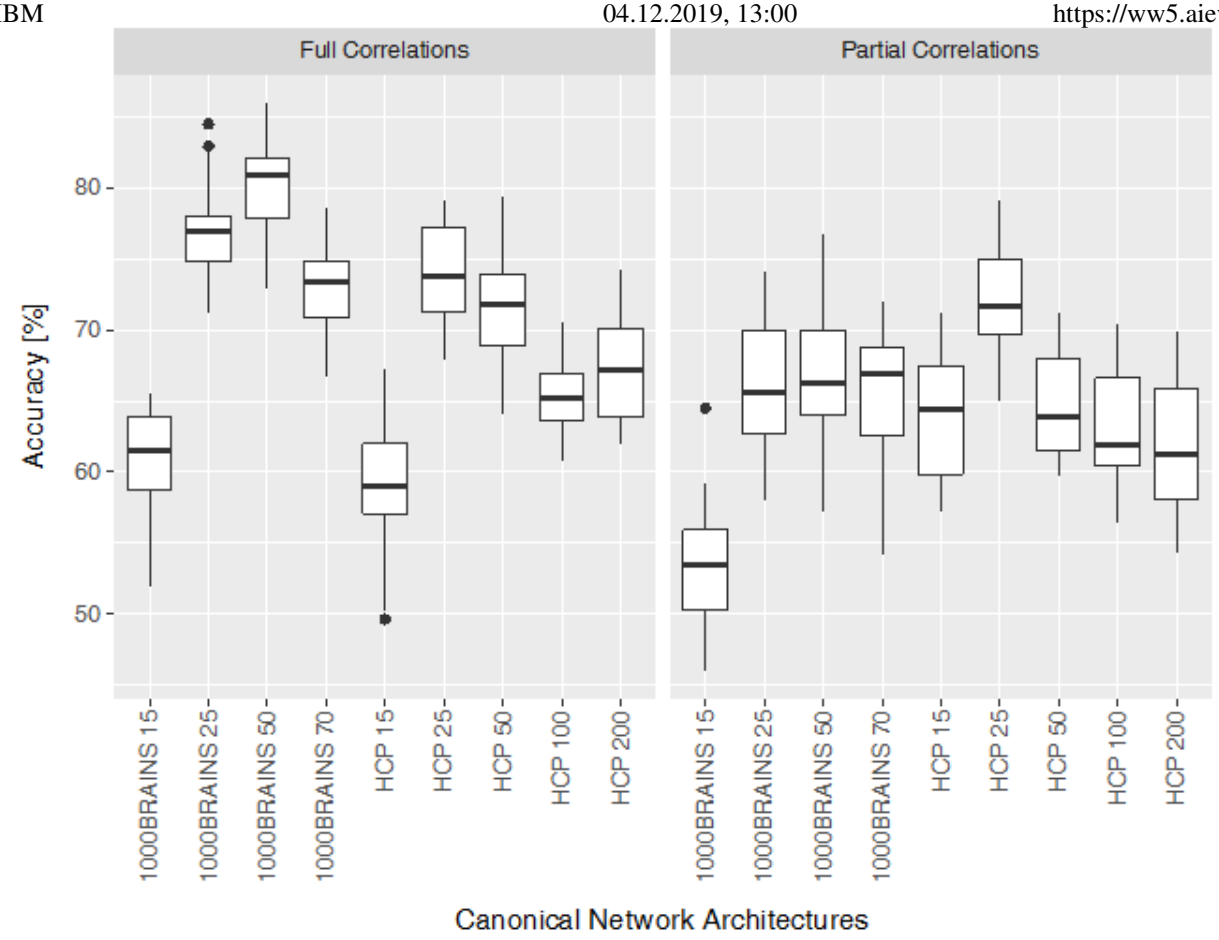
Feature importance was evaluated for the optimized model. Since no model-specific metric is available, we chose to only evaluate the top three features in a "filter" approach by a ROC-curve analysis to gain insights into the model (10).

Results:

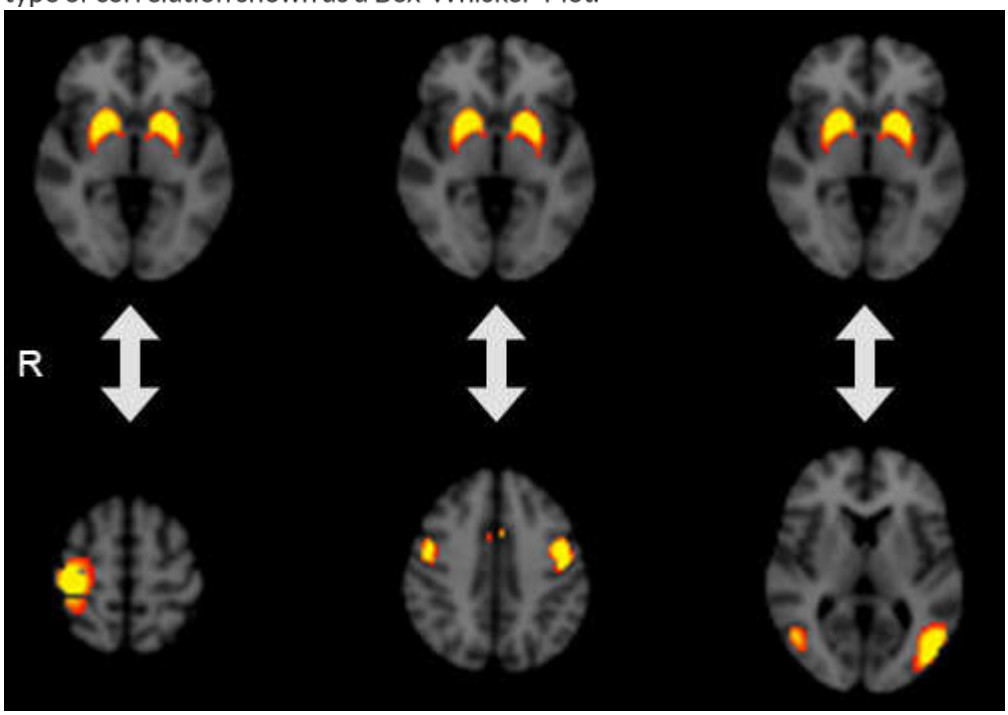
The 1000BRAINS 50-network-parcellation performed best using full correlations, with a median accuracy of 80.9% (SD 3.7, Inter-Quartile-Range (IQR) 77.8-82.1%, Fig 1). For partial correlations the HCP 25-network-parcellation performed best (median acc. 71.6%, SD 3.8, IQR 69.6-75.0%), which also performed best for full correlations within the HCP sample (median acc. 73.8%, SD 3.6, IQR 71.2-77.2%).

The optimized model (134 iterations) yielded a median acc. of 81.4% (SD 3.5, IQR 79.2-82.4%). Median sensitivity was 90.5% (SD 4.2, IQR 85.9-92.2%) and median specificity was 71.3% (SD 5.2, IQR 70.0-72.9%).

The top three features were found to be the correlations of a basal ganglia network, comprising the Putamen, Globus pallidus and ventral Thalamus, with 1) a right lateralized sensorimotor network, comprising the supplementary motor area (SMA) and the right primary sensorimotor cortex, 2) a motor-control network containing the left-dominant dorsolateral prefrontal cortex, SMA and midcingulate cortex, and 3) a bihemispherical dorsal visual network comprising areas within the parietooccipital cortex (Fig 2).



·Fig 1: Accuracies of each repeat of the cross-validation for each canonical network architecture and type of correlation shown as a Box-Whisker-Plot.



·Fig 2: The top three features of the optimized model on the 50-networks 1000BRAINS parcellation.

Conclusions:

A model-based, data-driven approach to discriminate PD patients from HC is feasible and shows very good accuracy and high sensitivity. A 50-network-parcellation performed best. Connectivity between cortical networks and a basal ganglia network contained crucial information on presence of PD. Given the

high sensitivity, such an approach may be of use in a screening setting, e.g. for testing patients with a mild, as yet unspecific movement disorder.

Disorders of the Nervous System:

Parkinson's Disease and Movement Disorders [1]

Imaging Methods:

BOLD fMRI

Modeling and Analysis Methods:

Classification and Predictive Modeling [2]
fMRI Connectivity and Network Modeling

Keywords:

ADULTS
Data analysis
FUNCTIONAL MRI
Machine Learning
Movement Disorder
MRI

[1|2]Indicates the priority used for review

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Resting state

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Patients

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Functional MRI
Computational modeling

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

FSL

Provide references using author date format

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