

Pattern of alterations in motor circuit resting state fcMRI in Parkinson's Disease patients due to medication and forced exercise

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Introduction:

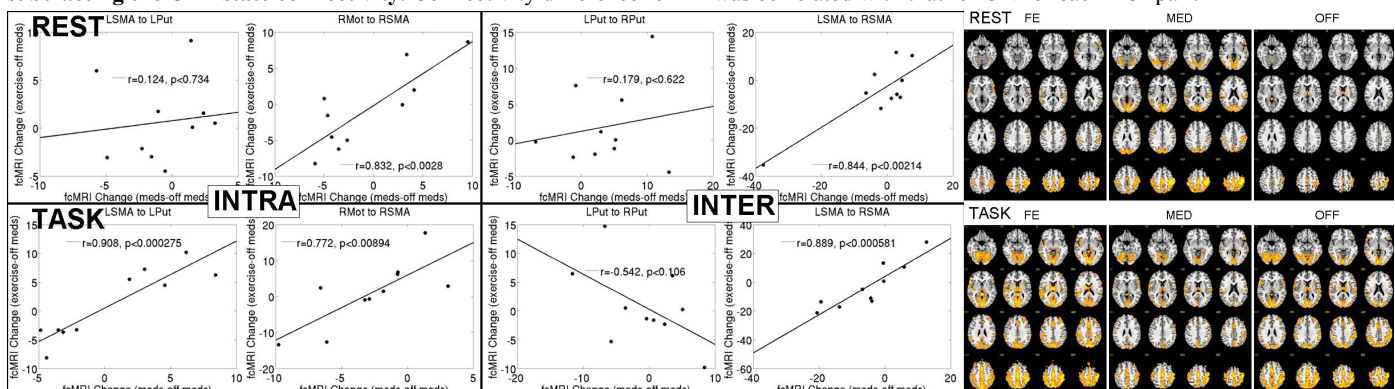
Parkinson's Disease (PD) is a progressive neurologic disorder primarily characterized by altered motor function. As the disease progresses, medication has a diminishing effectiveness in controlling symptoms in most patients, leading to increased dose or in some patients, invasive surgical procedures such as deep brain stimulation. An assisted bicycle pedaling exercise paradigm (rate is controlled to be above the voluntary pedaling level) has been found to have similar effect as medication on motor symptoms [1] and on functional activation [2]. Functional connectivity MRI (fcMRI) has been used to examine resting connectivity between brain regions in PD patients as a result of medication therapy[3,4]. This technique affords the ability to look at how strongly nodes of the motor circuit communicate with each other, and can provide insight into the complementary effects of various therapies. Here we present results from a group study comparing the effect of controlled-rate aerobic exercise and medication therapy on fcMRI of the motor circuit in PD patients (compared to the off-medication state), with bilateral motor fMRI, resting fcMRI and continuous motor fcMRI. We find that in many important nodes of the motor circuit, the observed changes in functional connectivity effected by forced exercise and medication are positively correlated. Although this positive correlation was observed both at rest and while continuously tapping, the correlation was stronger while measuring connectivity in the tapping state.

Methods:

10 mild to moderate PD patients (6 male) between the ages of 44 and 79 were recruited for a series of 3 identical scanning sessions: off medication (OFF), on medication (ON, and off medication with forced exercise (FE), with the order of conditions randomized across subjects. In each session, subjects were scanned in an IRB-approved protocol at 3T using a bitebar to reduce head motion, in a 12-ch receive head coil. Scans included T1-MPRAGE, a bilateral complex finger tapping fMRI EPI scan, a resting connectivity fcMRI scan and a unilateral (with most affected hand) continuous motor performance fingertip force tracking (visual display feedback) task during task connectivity fcMRI. EPI scans were identical (apart from duration) at 2x2x4mm voxels, 1954 Hz/pix BW, 31 axial slices, TR/TE/FA=2800/29/80. fMRI and fcMRI data were corrected as described in [5] and the fMRI student's t-map was coregistered to the connectivity scans. ROIs were drawn on the MPRAGE for bilateral putamen (Put), globus pallidus (Gp), thalamus (Thal), supplementary motor area (SMA), and primary motor cortex (Mot) and were coregistered to connectivity scans. Seed-based correlation connectivity maps and values were determined using fMRI activation and ROIs as described in [5]. Inter-hemispheric fcMRI determined between left and right sides of same brain region, intra-hemispheric fcMRI determined between pairs of ROIs on same side of brain. Correlation of low-pass filtered reference timeseries were converted to t-scores, which represent our fcMRI connectivity metric between two ROIs. **Difference in connectivity as function of FE or ON state was referenced to OFF state by subtracting the OFF state connectivity.** Connectivity difference for FE was correlated with that for ON for each ROI pair.

Table shows linear correlation of FE (minus OFF) to MED (minus OFF) connectivity, and p-values. Significant values highlighted.

	Resting correlation	p-value	Task (const) correlation	p-value
RSMA-GP	0.600	0.067	0.705	0.023
LSMA-PUT	0.124	0.734	0.908	3.00E-04
RSMA-PUT	0.102	0.780	0.749	0.013
RMOT-SMA	0.832	2.80E-03	0.772	8.90E-03
RMOT-GP	0.357	0.311	0.837	2.50E-03
LMOT-PUT	0.613	0.060	0.851	1.80E-03
L/R MOT	0.387	0.269	0.658	0.039
L/R PUT	0.179	0.622	-0.542	0.106
L/R GP	0.568	0.087	0.694	0.026
L/R SMA	0.844	2.10E-03	0.889	6.00E-04



Results and Discussion:

The connectivity between most nodes of the motor circuit is altered in a similar way by both exercise and medication, and this similarity is strengthened during continuous performance of a motor task. This suggests that forced exercise and medication may have the same underlying mechanisms on most of the motor circuit.

References: 1) Ridgel et al, Neurorehabil Neural Repair, 2009;23:600-8, 2) Phillips et al, ISMRM 2009, 3) Baudrexel et al, ISMRM 2010, 4) Yang et al, ISMRM 2010, 5) Lowe et al, HBM 2008;29:818-827