Functional Connectivity in Parkinson’s Disease

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Introduction

Parkinson’s disease (PD) includes both motor symptoms and cognitive symptoms spanning memory, visuospatial, and attentional domains and is characterized by systematic dopaminergic deficits.

Dopamine has previously been implicated in salience network function. The salience network (SAL), which includes the anterior cingulate cortex (ACC) and bilateral anterior insula (AI), is thought to facilitate detection of environmental stimuli and plays a critical role in switching between the default mode network (DMN) and frontoparietal central executive network (CEN).

Additionally, the default mode network (DMN) in Parkinson’s Disease (PD) exhibits decreased deactivation in posterior nodes relative to healthy controls during a short-term memory task.

Here, we investigate functional connectivity in the salience and default mode networks at rest as well as activation during performance of an attention-demanding task.

Methods

Participants: 18 PD patients (mean age=65.3, SD=9.6), 11 Controls (mean age=54.6, SD=7.9).

2 sessions of T2*-weighted whole-brain data for each participant were acquired on a Philips Achieva 3.0T MRI using an EPI sequence (TR=2.4s, TE=25ms, FA=79, FOV=240x120x240mm, 3mm isotropic voxels).

In each session, participants completed a 12-minute eyes-open resting state scan with fixation prior to six 6-minute runs of the Attentional Network Task (ANT). Data from both sessions were combined for the present analyses.

Resting state analyses are presented here for a subset of participants (N=13 PD, 8 Controls).

Results

Attention Network Test

Prior to analyses, data were corrected for motion, and high pass filtered at 100Hz. Then, scanner spikes were removed from the data prior to slice-time correction and spatial smoothing (fwhm=5.0mm).

Resting state data were submitted to a temporally-concatenated group independent components analysis using FSL’s MELODIC. Resulting spatial maps for the salience and default mode networks from this group-average analysis were used to generate subject-specific versions of the spatial maps, which were compared between groups. Group differences were evaluated using FSL’s GLM tool and randomise permutation-testing tool.

ANT data were analyzed using an event-related model in which onsets for each cue and target were convolved with a double-gamma HRF using FSL’s FEAT. Error trials were modeled separately but not analyzed.

Conclusions

Our resting state analyses showed increased connectivity between putamen and the salience network in PD. This finding may be related to altered connectivity in the basal ganglia previously observed in PD using FDG PET. Taken together with evidence for dopamine related SAL function, this suggests that cognitive impairments in PD could result from ineffective network switching because of altered SAL integrity.

PD patients also exhibited altered functional connectivity within the DMN compared to controls.

Despite equivalent behavioral performance on the ANT, PD patients exhibited less deactivation of the posterior DMN (PCC) in response to specific orienting cues.

Given that our patients were in the early stages of PD progression, our results suggest that altered functional connectivity may precede PD-related cognitive decline.

Future Directions

Following the baseline scans reported here, PD patients complete 12 weeks of treatment with an acetylcholinesterase inhibitor (galantamine) followed by an additional scanning session.

We will explore whether cholinergic intervention normalizes SAL and DMN connectivity at rest and suppression of posterior DMN in response to spatial cues.

References


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