Differences in Modulation of Intrinsic Networks During Attentional Task in Parkinson Disease

Tara Madhyastha[1,2], Mary Askren[1,2], Peter Boord[1,2], James Leverenz[3], Thomas Grabowski[1,2]
[1]Integrated Brain Imaging Center (IBIC), University of Washington, Seattle [2]Department of Radiology, University of Washington, Seattle
[3]Cleveland Lou Ruvo Center for Brain Health at Cleveland Clinic, Cleveland [4]Department of Neurology, University of Washington, Seattle

Introduction

Although idiopathic Parkinson disease (PD) is diagnosed on the basis of motor impairments caused by progressive loss of striatal dopamine, cognitive impairment and dementia are key symptoms of the disease. Typical impairments include visuospatial and executive deficits, but PD patients display a wide heterogeneity of cognitive symptoms. Disruption in multiple ascending control systems, including the dopaminergic, noradrenergic, cholinergic and serotonergic systems, contribute to the spectrum of cognitive defects in PD[1,2].

Hypothesis

- As ascending control systems lose efficacy, the ability to engage or disengage specific networks decreases
- Intrinsic network activity should be systematically altered in PD.
- These differences should be visible during performance of an attention task.

Methods

We examine data from the Attention Network Task[3] (Figure 1) obtained from 25 medicated early-stage PD patients (age 66 ± 9.7; mean H&Y stage 2.05) and 21 healthy controls (age 62 ± 10.0). Subjects were scanned twice, 2-3 weeks apart. Magnetic resonance imaging was performed on Philips 3.0T Achieva scanner with a 32 channel head coil.

After group analysis of the task using a general linear model (GLM), we extracted 30 coordinates corresponding to areas of peak task activation/deactivation (Figure 2). For each coordinate, we created a 10mm diameter mask in standard space and transformed that to native space to calculate mean subject-specific timecourses for each ROI. Scaled timecourses from these ROIs were subjected to exploratory factor analysis in a structural equation modeling framework[4] across all sessions and task runs (Figure 3).

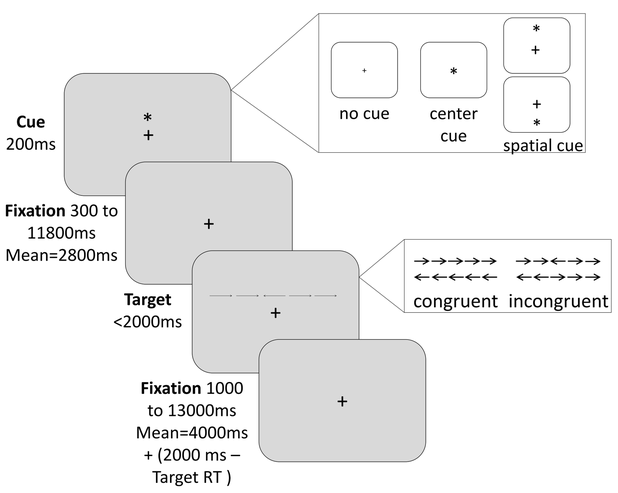
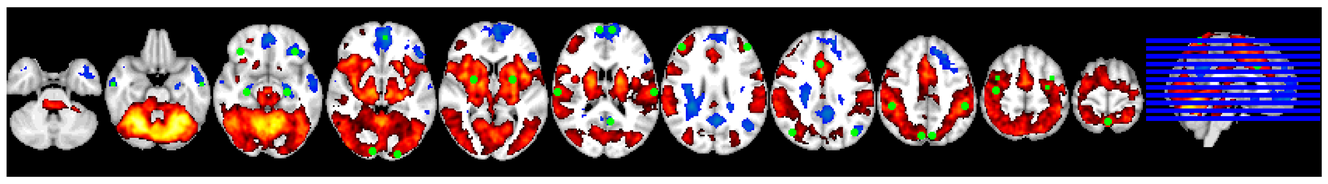
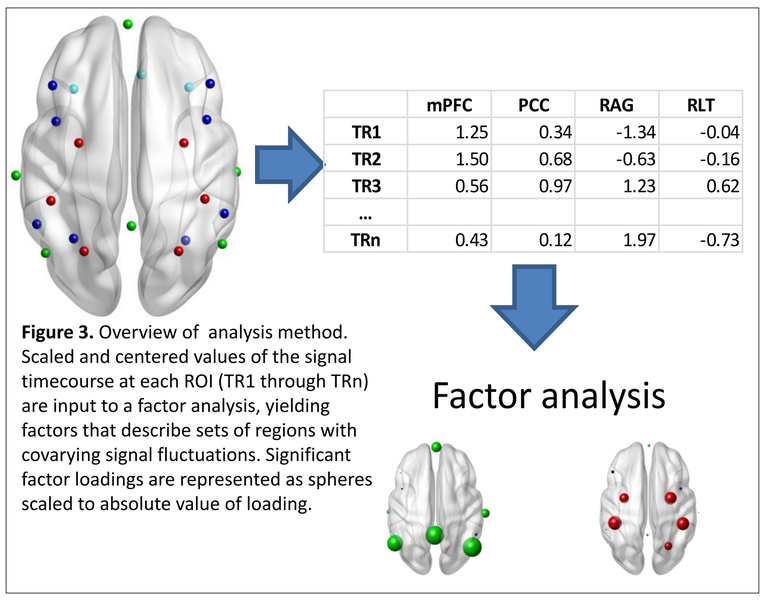


Figure 1. Schematic of attention network test (Fan, 2005). During each trial, a **cue** (no cue, center cue, or spatial cue) appeared on the screen for 200ms. This was followed by a **fixation** delay before a **target** set of five congruent or incongruent arrows appeared above or below fixation. The target arrows remained on the screen until the participant responded, or 2000ms elapsed, and was followed by **fixation** of jittered duration.

Figure 2. Location of ROIs obtained from task analysis (green dots) superimposed on task activation map.





	mPFC	PCC	RAG	RLT
TR1	1.25	0.34	-1.34	-0.04
TR2	1.50	0.68	-0.63	-0.16
TR3	0.56	0.97	1.23	0.62
...				
TRn	0.43	0.12	1.97	-0.73

Figure 3. Overview of analysis method. Scaled and centered values of the signal timecourse at each ROI (TR1 through TRn) are input to a factor analysis, yielding factors that describe sets of regions with covarying signal fluctuations. Significant factor loadings are represented as spheres scaled to absolute value of loading.

Scaled timecourses from these ROIs were subjected to exploratory factor analysis in a structural equation modeling framework across all sessions and task runs, yielding a well-fitting solution with nine intrinsic networks (Figure 4) that satisfied conditions for measurement invariance, meaning that the overall structure of the networks is the same in PD and controls. The factor solution yields a score for each network for each 2.4 second TR.

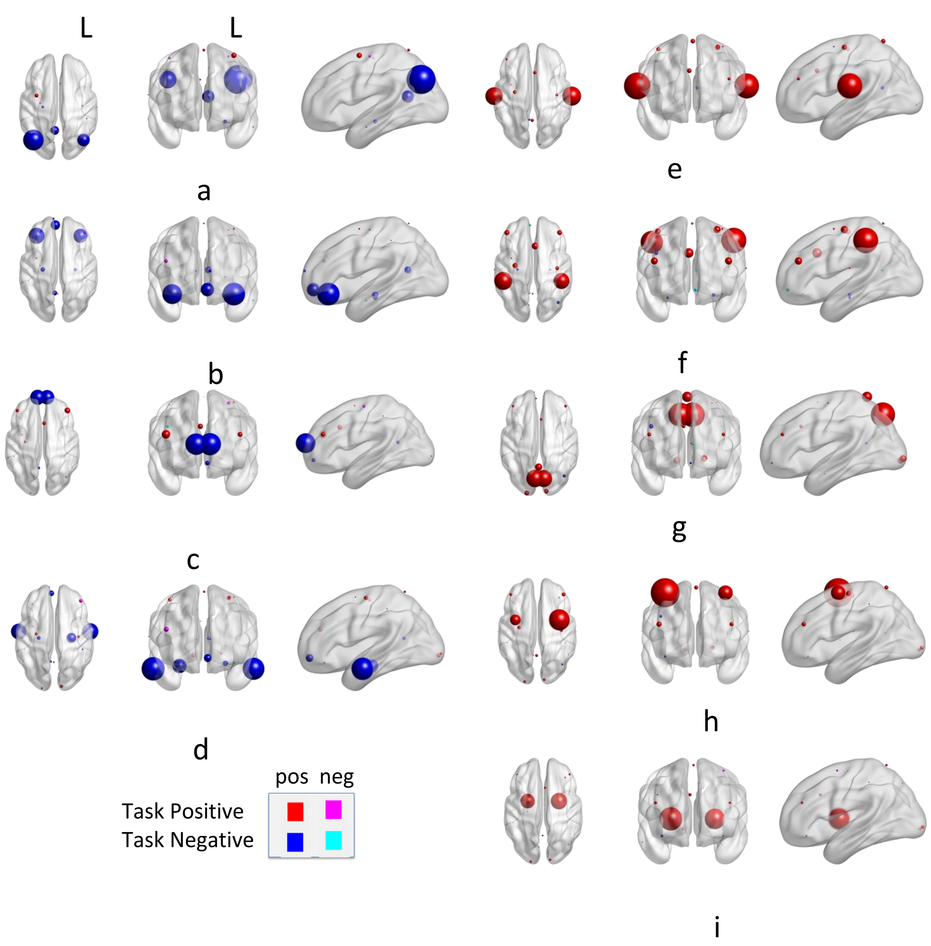


Figure 4. Representation of factors representing dynamic patterns of BOLD fluctuations from 9 factor model with loading matrix invariance, intercept invariance, and factor covariance matrix invariance (CFI=.950, RMSEA=.028). Networks are color-coded for positive and negative loadings in task positive and task negative networks as shown in key. Diameter of sphere is linearly scaled to absolute value of loading. Only spheres from loadings significant at p < .05 are displayed.

We merged behavioral task data from correct trials (97.2%) with factor scores, to examine group differences in activation at each TR before and after task onset.

Results

Behaviorally, PD subjects were significantly slower to respond (Table 1). GLM analysis showed no differences between the groups in fronto-parietal task control networks.

Group	Flanker type		Cue type		
	Congruent	Incongruent	Center	Spatial	No Cue
Mean response latencies (ms) and standard deviations					
PD	869(167)	1003(205)	942(177)	876(188)	989(193)
Controls	771(116)	887(136)	846(125)	766(122)	874(130)
Difference (PD –Controls)	97	115	95	109	115
p	0.024	0.027	0.038	0.022	0.021
Mean accuracy					
PD	97.7	96.4	96.6	97.7	96.9
Controls	98.8	98.0	98.3	98.3	98.5
Difference (PD–Controls)	-1.03	-1.53	-1.63	-0.66	-1.54
p	0.268	0.090	0.024	0.463	0.110

Table 1. ANT task behavioral summary statistics, computed over two sessions.

However, analysis of network expression from 0-3 TRs after the onset of a target or a cue showed significant differences between controls and PD in several attentional networks (Figure 4).

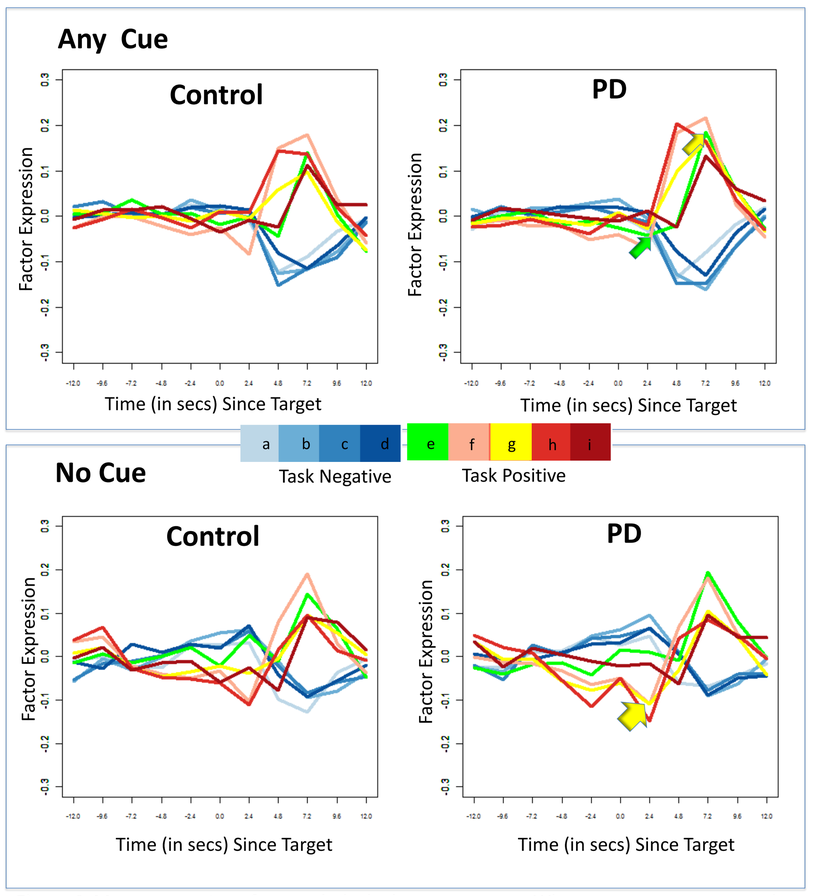


Figure 4. Mean expression of networks locked to target onset. When any cue was presented, expression of the MSP network (**g**) was higher in PD than in controls at 3TR after the target, and the expression of a central opercular network (**e**) was lower 1TR after the target in PD than in controls. When no cue was given, PD subjects had lower expression than controls of the MSP network (**g**) at 1TR after the target.

Conclusions

- We demonstrate a novel method for quantifying the level of network expression during task and equating it across fMRI task runs at multiple sessions.
- The modulation of intrinsic networks during presentation of cue and target shows significant differences.
- Coordinated activity in the MSP network in PD subjects is significantly lower pre-target when there is no cue and higher post-target when there is a cue. This may reflect compensatory regulation of intrinsic networks during task that is an early indicator of disruption of ascending control systems.

Acknowledgements: NIH 1RC4NS073008-01 and P50NS062684.

References

1.Barone, P. Neurotransmission in Parkinson's disease: beyond dopamine. Eur. J. Neurol. 17, 364–376 (2010).
2. Mattila, P. M. et al. Choline acetytransferase activity and striatal dopamine receptors in Parkinson's disease in relation to cognitive impairment. Acta Neuropathol. 102, 160–166 (2001).
3. Fan, J., McCandliss, B. D., Fossella, J., Flombaum, J. I. & Posner, M. I. The activation of attentional networks. NeuroImage 26, 471–479 (2005).
4. Asparouhov, T. & Muthén, B. Exploratory Structural Equation Modeling. Structural Equation Modeling: A Multidisciplinary Journal 16, 397–438 (2009).