Dynamic Functional Connectivity in Parkinson Disease

Tara Madhyastha[1,3], Mary K. Askren[1,3], Elliot Collins[3], Thomas Grabowski[1,2,3]

[1]Department of Radiology, [2]Department of Neurology, [3]Integrated Brain Imaging Center at the University of Washington

Introduction

Correlations among low-frequency spontaneous fluctuations in the blood oxygen level-dependent (BOLD) signal reflect the connectivity of intrinsic large-scale networks in the brain. We hypothesize that the coherence of fluctuations in connectivity within networks at rest is a sensitive indicator of the ability to recruit cognitive resources, and should predict overall task performance. Similarly, the coherence of fluctuations in connectivity during task should predict ongoing task performance.

Parkinson's disease (PD) includes both motor and cognitive symptoms spanning memory and attentional domains and is characterized by systematic deficits in dopaminergic, noradrenergic, serotonergic and cholinergic ascending systems. We hypothesize that these deficits make it difficult for PD subjects to dynamically change network configurations.

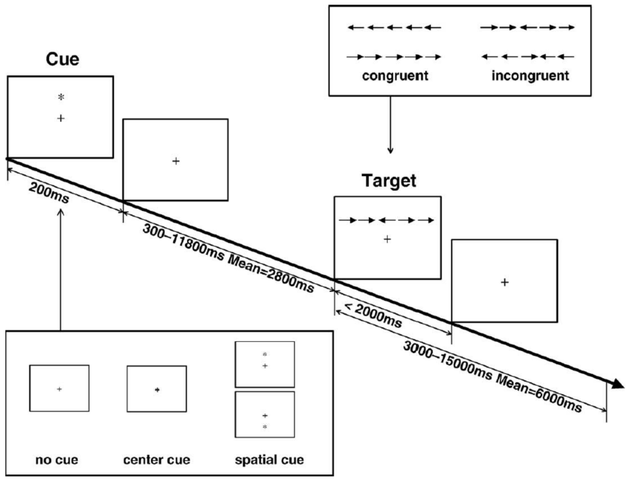
Methods

We examine resting state and Attention Network Task data from 25 medicated early-stage PD patients (M_{age}=66) and 21 healthy controls (M_{age}=62). Subjects were scanned twice, 1-2 weeks apart. We extracted time-varying signals from pre-identified nodes in the default mode network (DMN) and dorsal attention network (DAN). We computed pairwise correlations within overlapping (slide=2.4s) sliding windows (40.8s) for each network, and subjected these correlations from both resting state sessions across groups to a factor analysis, extracting 4 factors for each network as in prior work. Analysis for task-based data was analogous (using data from a single task run from session 2). We extracted factors based on Kaiser criterion (5 factors in DAN), and used factor scores to predict trial to trial response time.

Alerting:
Center Cue - No Cue
Norepinephrine

Orienting:
Spatial Cue - Center Cue
Acetylcholine

Executive:
Incongruent - Congruent
Dopamine

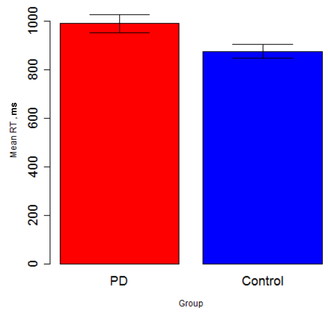


Attention Network Task

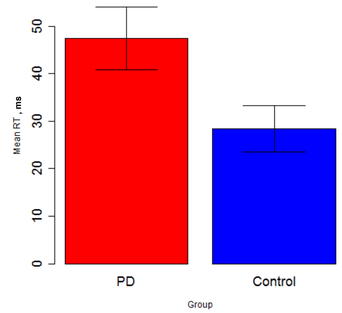
Fan et al, The activation of attentional networks, Neuroimage 2005

Results

Behavioral Differences in Alerting



Response latency without cue

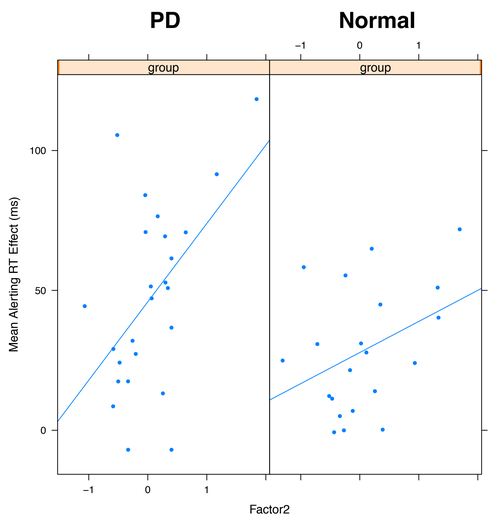


Alerting (Center cue – no cue)

- PD have higher response latency without cue
- PD have larger Alerting effect (difference between center cue and no cue)

Dynamics of Resting State Connectivity Predict Alerting RT Effect

- A factor score for DAN factor 2 computed in a scan at rest predicts alerting response time effect on a task that comes afterwards
- Replicable across sessions ~ 1 week apart



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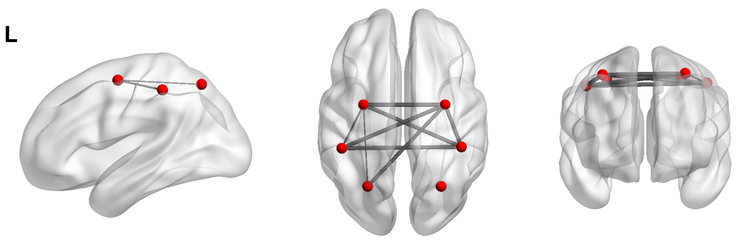

Dynamics of Task Connectivity Predict Trial-to-trial Response Latency

- Dynamic factor (DAN Factor 2) remains significant after controlling for cue type, flanker type, previous cue type, previous flanker type, and diagnostic group
- At a given level of this factor, controls have lower response latency than PD

Fixed Effects	Value	Std.Error	DF	t-value	p-value
(Intercept)	831.873	36.477	1462	22.806	0.000
Factor2	32.449	8.416	1462	3.855	0.000
Control	-56.006	51.927	44	-1.079	0.287
PrevCueTypeNoCue	10.988	11.475	1462	0.958	0.338
PrevCueTypeSpatialCue	17.926	11.799	1462	1.519	0.129
PrevFlankerTypeIncongruent	-6.019	9.433	1462	-0.638	0.524
CueTypeNoCue	79.246	15.628	1462	5.071	0.000
CueTypeSpatialCue	-56.916	15.936	1462	-3.572	0.000
FlankerTypeIncongruent	116.078	9.476	1462	12.250	0.000
Factor2 X Control	-31.068	11.590	1462	-2.681	0.007
Control X CueTypeNoCue	-35.194	22.951	1462	-1.533	0.125
Control X CueTypeSpatialCue	-18.257	23.488	1462	-0.777	0.437

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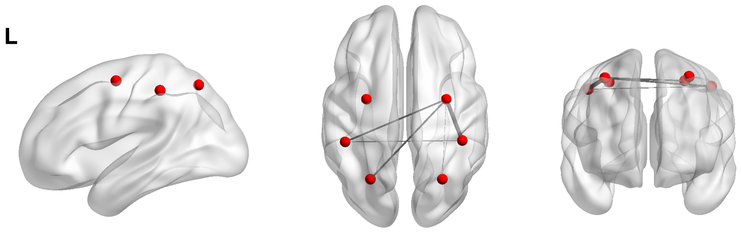

- DAN Factor 2 at task is very similar to DAN Factor 2 at rest, with weaker loadings on remaining links

Intrinsic Dynamics of Task Connectivity Predict Trial-to-trial Response Latency

- We obtain the same pattern of results after repeating our task analysis on the residuals after modeling task effects.

Fixed Effects	Value	Std.Error	DF	t-value	p-value
(Intercept)	834.144	36.403	1462	22.914	0.000
Factor2	26.708	8.051	1462	3.317	0.001
Control	-57.942	51.813	44	-1.118	0.270
PrevCueTypeNoCue	11.258	11.492	1462	0.980	0.327
PrevCueTypeSpatialCue	18.527	11.820	1462	1.567	0.117
PrevFlankerTypeIncongruent	-6.307	9.443	1462	-0.668	0.504
CueTypeNoCue	82.819	15.641	1462	5.295	0.000
CueTypeSpatialCue	-52.962	15.981	1462	-3.314	0.001
FlankerTypeIncongruent	114.561	9.461	1462	12.109	0.000
Factor2 X Control	-27.174	12.626	1462	-2.152	0.032
Control X CueTypeNoCue	-38.555	22.971	1462	-1.678	0.093
Control X CueTypeSpatialCue	-22.109	23.527	1462	-0.940	0.348

Conclusions

- Intrinsic dynamics of cortical network activity are related to task performance
  - Rest predicting task
  - Predict trial-by-trial performance
- We have developed a statistical framework in which to identify and quantify the dynamics of intrinsic fluctuations
- We can observe selective changes in dynamics with PD, suggesting the utility of this framework in studying neurodegenerative disease

Acknowledgements

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