Brain Activation in Parkinson's Disease during a Functional Magnetic Resonance Imaging Set Shifting Task: Preliminary Findings

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Objective

To investigate differences in the functional brain patterns for set shifting in patients with Parkinson's disease (PD) and age-matched controls using event-related functional magnetic resonance imaging (fMRI).

Introduction

Cognitive impairment is a common non-motor manifestation of Parkinson's disease (PD). Cognitive deficits include difficulties in set shifting, monitoring behavior and manipulating information and can lead to a significant reduction in quality of life for patients and caregivers.

Functional magnetic resonance imaging (fMRI) is an established method to probe brain activity during task performance of subjects inside a magnetic resonance scanner. Temporal signal variations originating from changes of blood flow to the area of neural activation are analyzed to identify regions in the brain activated during this task. Intergroup comparison can be performed by transforming the activation maps into a standard space (Talairach space) in combination with ANOVA analysis.

Methods

1. Subjects

6 PD patients and 6 healthy controls (HC)

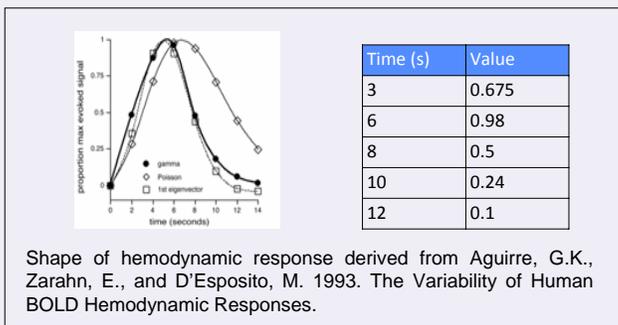| Table 1: Demographics		
	PD	HC
Gender	67/33	50/50
Age	67.5 (4.3)	62.7 (7.2)
Education	12.8 (2.9)	15.7 (2.3)
H&Y off	2.0 to 3.0	NA

2. fMRI Task

In a visual stimulus, large numbers 1-2 composed of small numbers 3-9 were presented and subjects were asked to switch back and forth between sets by responding to the large number or to the small number. The paradigm was presented visually and contained a total of 256 stimuli with 50 switches occurring randomly. Consecutive axial gradient EPI images (256 phases, 64x64,FOV=220mm, slice thickness 3 mm, duration: 12 min 48 sec) were acquired during task performance. Total number of images for this task was in the order of 12,000.

Large number one composed of small numbers three

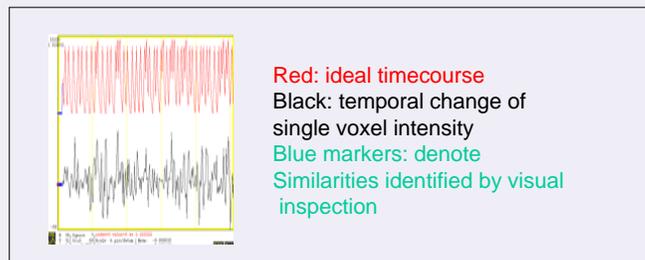Small numbers one composing large number three
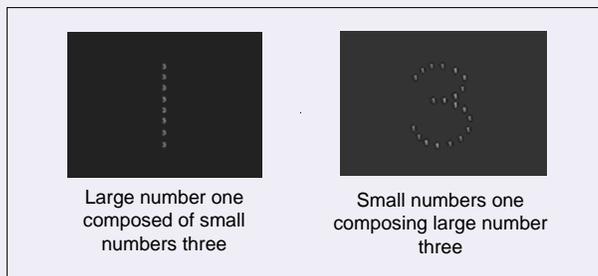
3. Data Analysis

Within the software package AFNI (NIH) the voxel-based timeseries correlated with an ideal response function. fMRI maps were transformed into Talairach space and were segmented into 123 brain areas. Maximum and average correlation coefficients (CC) were calculated for each area using Matlab (Mathworks Inc.). Student t-test was employed to identify statistically significant (p< 0.1) differences in activation.
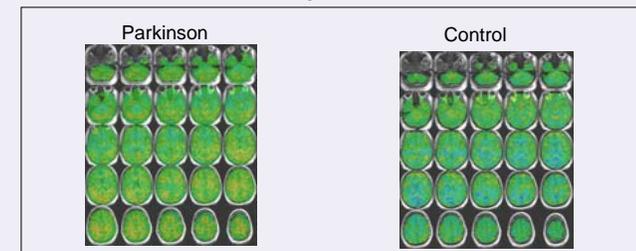

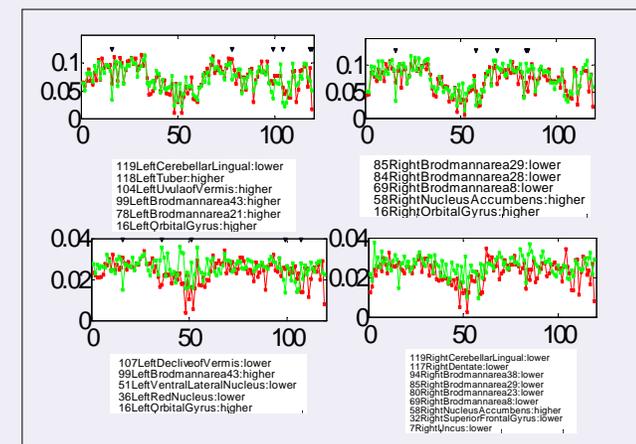| Time (s)	Value
3	0.675
6	0.98
8	0.5
10	0.24
12	0.1

Shape of hemodynamic response derived from Aguirre, G.K., Zarahn, E., and D'Esposito, M. 1993. The Variability of Human BOLD Hemodynamic Responses.

Results

1. Single Voxel Timecourse

Red: ideal timecourse
Black: temporal change of single voxel intensity
Blue markers: denote Similarities identified by visual inspection

Results

2. Functional Activation Maps

Parkinson   Control

3. Inter-Group Comparison

119LeftCerebellarLingual:lower
118LeftTuber:higher
104LeftUvulaofVermis:higher
99LeftBrodmannarea43:higher
78LeftBrodmannarea21:higher
16LeftOrbitalGyrus:higher

85RightBrodmannarea29:lower
84RightBrodmannarea28:lower
69RightBrodmannarea8:lower
58RightNucleusAccumbens:higher
16RightOrbitalGyrus:higher

107LeftDecliveofVermis:lower
99LeftBrodmannarea43:higher
51LeftVentralLateralNucleus:lower
36LeftRedNucleus:lower
16LeftOrbitalGyrus:higher

119RightCerebellarLingual:lower
117RightDentate:lower
94RightBrodmannarea38:lower
85RightBrodmannarea29:lower
80RightBrodmannarea23:lower
69RightBrodmannarea8:lower
58RightNucleusAccumbens:higher
32RightSuperiorFrontalGyrus:lower
7RightUncus:lower

Discussion

In this preliminary study, event-related fMRI of a set-switching task demonstrated promising findings. The PD patients demonstrated functional differences during the performance on the task in frontal, temporal, and cerebellar cortex, in addition to areas involved in reward and the planning of movements. Our preliminary findings suggest that fMRI is capable of measuring functional differences in PD patients and age-matched controls during the performance of a set-shifting task.