Impulsivity and resting state functional connectivity of the supplementary motor area in Parkinson's disease

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BACKGROUND

- Impulse control disorders (ICD) in Parkinson's disease (PD) often relate to medication use and alterations within the reward pathways including the ventral striatum and pre-frontal cortex.
  - Sweet craving has previously been described as a form of ICD in PD (Shahed 2006)
- The pathophysiology of ICDs in PD is likely related to dopamine receptor stimulation in the reward systems of the nucleus accumbens (nAcc) and dorsomedial frontal lobes (Okai 2011, Muresano 2012).
- The nAcc projects directly to the spinal cord, to several nuclei of the basal ganglia, and possesses reciprocal connections with motor and supplementary motor areas, which place it in an ideal position for goal-directed response control (Bari and Robbins, 2013).
- The supplementary motor area (SMA) relates to response inhibition, and dysfunction may lead to increased impulsivity.
- Atrophy in pre-frontal regions including the SMA in PD is recognized, but a previous study found that the contribution of cortical atrophy to ICD was marginal (Biundo et al, 2011).

- **OBJECTIVE:** To assess the resting state functional connectivity (RSFC) between the SMA and striatal areas that control movement and reward-related impulse control in PD.

METHODS

- We studied SMA resting state functional connectivity (RSFC) in PD patients and age- and sex-matched controls (Table 1).
- Subjects were scanned for 5 minutes at rest in a Siemens 3T Trio MRI while 3x3x3 mm voxel BOLD data was collected.
- Functional images were pre-processed using SPM8 (The Wellcome Trust, UK).
- Regions of interest (SMA, the reward circuit-related areas of the striatum and habenula, amygdala, prefrontal cortex and anterior cingulate cortex were delineated using AFNI (NIH, Bethesda, MD).
- RSFC was calculated using CONN (Martinos Center, Boston, MA).
- SMA RSFC in PD patients and controls were compared.
- In PD patients, connectivity to striatal regions was correlated to subscores on the Barratt Impulsivity Scale (BIS) and the sweet craving questionnaire (Shahed 2006).

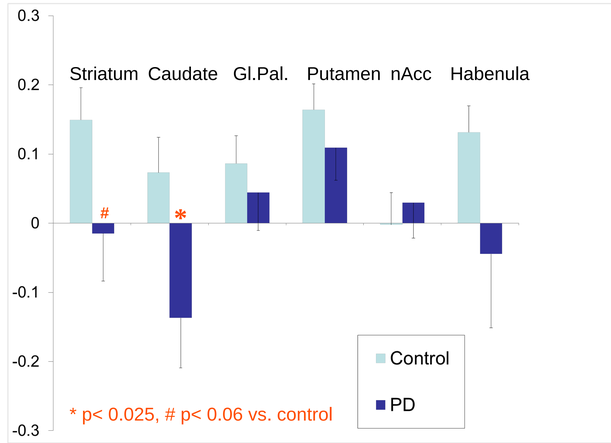
RESULTS

Table 1: Subject characteristics

	PD patients	Controls
N	10 (3F)	16 (6F)
Mean age (yrs)	65	60
Mean PD duration (yrs)	7.19±5.63 years	--
Mean LEDD	612.5±252.68	--
Mean BIS		--
Attentional	14.5±2.41	--
Motor	19.5±2.69	--
Planning	23±5.34	--
Mean score on SCQ	3.1±1.57	--

LEDD = levodopa equivalent dosing;
BIS = Barratt Impulsivity Scale
SCQ = sweet craving questionnaire

Figure 1: RSFC between the SMA and reward system

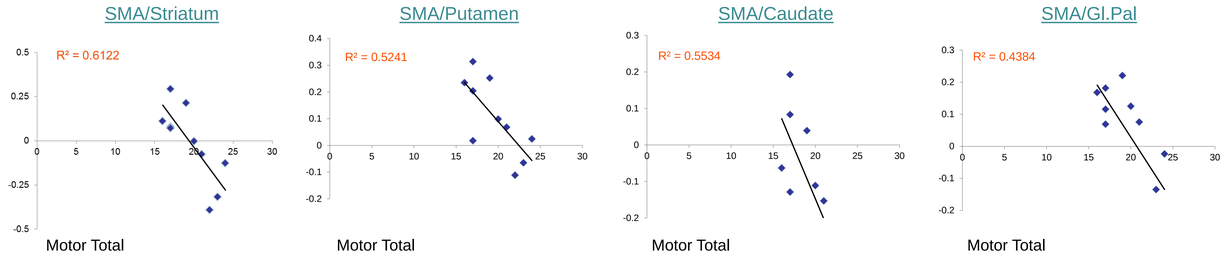


- Striatum = caudate, globus pallidus and putamen combined
- Gl.Pal = globus pallidus, nAcc = nucleus accumbens

- No statistically significant differences in connectivity to amygdala, prefrontal cortex, anterior cingulate cortex, and habenula (Figure1).

Table 2: RSFC of the SMA in PD patients

	Motor	Non-planning	Attention	Sweet craving
SMA/striatum	R2 = 0.61 p=0.007	R2 = 0.19 p =0.2	R2 = .28 p=0.1	R2 = 0.34 P=0.08
SMA/putamen	R2 = 0.52 P=0.017	R2 = 0.41 P=0.05	R2 = 0.18 P=0. 23	R2 = 0.24 P = 0.15
SMA/caudate	R2 = 0.55 P=0.015	R2 = 0.06 P=0.48	R2 = 0.28 P=0. 12	R2 = 0.43 P=0.03
SMA/globus pallidus	R2 = 0.44 P=0.037	R2 = 0.14 P=0.29	R2 = 0.31 P = 0.1	R2 = 0.10 P=0.37
SMA/accumbens	R2 = 0.06 P=0.47	R2 = 0.08 P=0. 43	R2 = 0.46 P=0.03	R2 =0.24 P=0.24
SMA/habenula	R2 = 0.23 P= 0.16	R2 = 0.017 P=0. 72	R2 = 0.28 P=0. 11	R2 = 0.03 P = 0.6



DISCUSSION

- Subscales of the BIS assess various components of impulsivity:
  - Attentional Impulsiveness assesses task-focus, intrusive thoughts, and racing thoughts [inability to focus attention or concentrate].
  - Motor Impulsiveness assesses tendency to act on the spur of the moment and consistency of lifestyle [acting without thinking].
  - Non-planning Impulsiveness assesses careful thinking and planning and enjoyment of challenging mental tasks [lack of concern for the future or consequences of one's actions].

- This preliminary data implicates SMA/striatal, SMA/putamen, SMA/caudate and SMA/pallidal RSFC in symptoms of impulsiveness in PD.
  - In this small sample, SMA RSFC to the striatum and globus pallidus in PD correlates most consistently with the BIS motor subscale, indicating that the SMA contributes to this aspect of impulsive behavior, and possibly to ICD in PD.
  - Scores on the sweet craving questionnaire also negatively correlated with SMA/striatal RSFC, supporting the role of impaired impulse control on this behavior in PD (Shahed 2006).
  - Altered SMA perfusion and connectivity have been previously implicated in the severity of pathologic gambling in PD (Cilia 2011).

CONCLUSIONS

- These preliminary findings indicate that further investigation into the functional connectivity of SMA in PD patients with and without ICD is warranted.

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