

Introduction

Depression and anxiety are among the most prominent non-motor symptoms in Parkinson's disease (PD) and the pathophysiology underlying these symptoms remains largely unknown.

We used permanent prefrontal cortex implants to investigate neural correlates of these symptoms and to develop a novel neurostimulation therapy for these mood symptoms of PD.

This study focused on the orbito-frontal cortex (OFC), part of the cortico-striatal-thalamic circuit that has been implicated in major depression in previous non-invasive studies.

Methods

Subjects: 2 PD patients with motor fluctuations and moderate anxiety and depression have been implanted with bilateral DBS STN DBS leads and a permanent 4-contact ECoG strip with at least 2 contacts covering the right OFC (fig. 1). The ECoG and right STN lead were attached to the Activa® PC+S (investigational device, Medtronic).

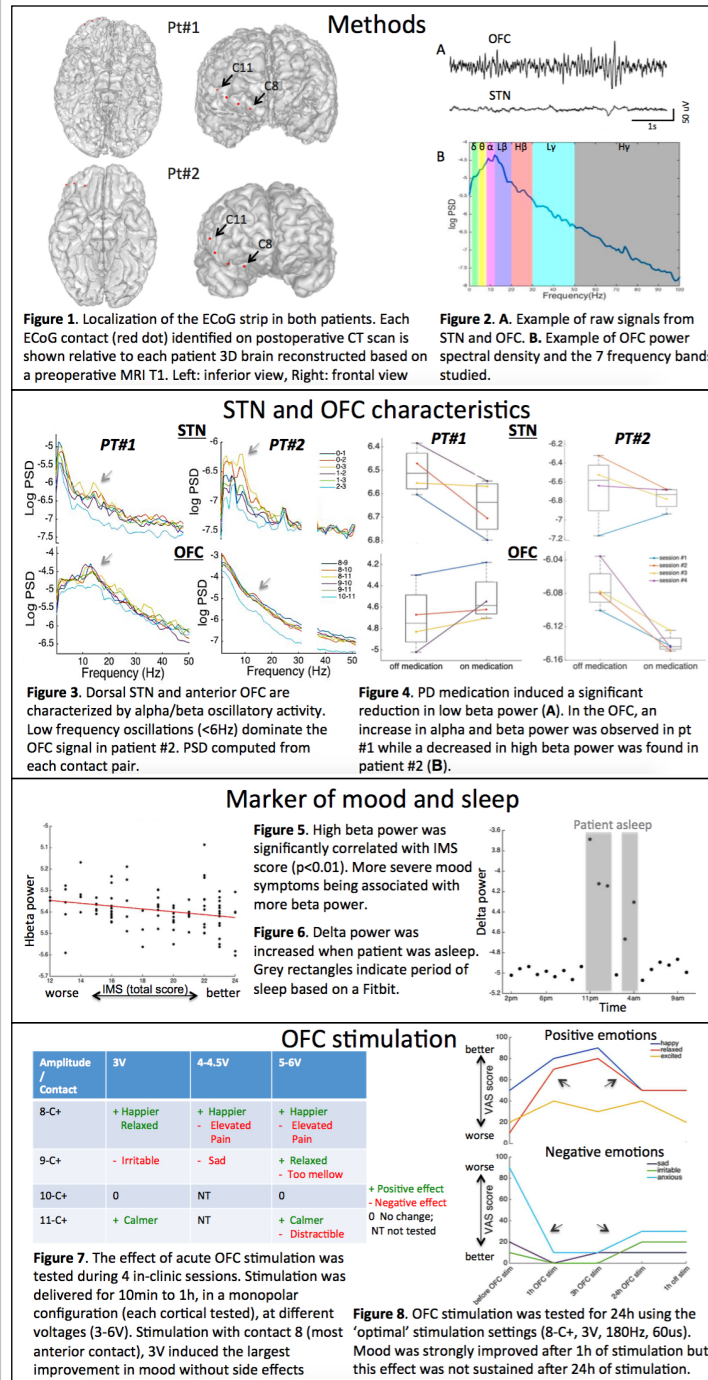
Recordings: 30s to 1min of cortical and STN potentials were recorded either on or off PD medication, during the presence of minimal and more severe anxiety or depression. Signals were sampled at 422 Hz, stored internally and downloaded noninvasively by radiotelemetry (fig. 2A).

Symptoms assessment: Anxiety and depression were assessed with the 'Immediate mood scale' (IMS), a 12-item valid tool to assess momentary mood symptoms (Positscience, Score=[-36 36]), and using visual analogue scales.

ECoG localization: was confirmed by merging a preoperative MRI to an intra-operative CT scan as well as postoperative CT scan taken 2-3months after surgery (Fig. 1)

Cortical stimulation: The effect of acute (10min-24hr) OFC stimulation was also studied in both patients

Analyses: Power spectral density (PSD) was computed for each recording and average across multiple frequency bands: d:2-5Hz; ?: 5-8Hz; a: 8-13Hz; β: 13-30Hz; low β: 13-20Hz; high β: 20-30Hz; low ?: 30-50Hz and high ?: 50-100Hz (fig.2B). Correlations between each frequency band, mood symptoms and circadian rhythm were studied.



Patient #	Gender	Age (years)	Disease Duration (years)	Baseline UPDRS III (off/on med)	BDI	BAI/PAS	DBS target	cortical target
1	F	53	6	39 / 19	21	16/20	STN	OFC
2	F	68	11	41/21	12	34/28	STN	OFC/IFG

Table 1: Patients demographic. F:Female; BDI: Beck's Depression Inventory; BAI: Beck's Anxiety Inventory; PAS: Parkinson's anxiety scale; OFC: orbito-frontal cortex; IFG: Inferior frontal gyrus.

Results

We found that:

- 1) OFC potentials are characterized by oscillatory activity especially in the alpha/beta band although delta/theta wave dominate the posterior OFC (pt#2)
- 2) Dopaminergic medication reduced STN beta power but did not consistently affect OFC signals; An increase in alpha/beta power was found in pt#1 while a decrease in High beta and low gamma power was found in pt#2 .
- 3) The severity of depression and anxiety was significantly correlated with the OFC beta power (p<0.01).
- 4) Sleep was associated with an increase in delta oscillations
- 5) Acute OFC stimulation (3V, 80-100us, 100-180Hz) was associated with a reduction of anxiety and depression severity without inducing side effects.
- 6) The effect of OFC stimulation was maximal after a few hours and was not sustained after 24h of stimulation, suggesting the importance of developing closed loop stimulation paradigms.

Conclusions

These preliminary results suggest that OFC beta oscillations may be associated with anxiety and depression in PD, and indicate a potential therapeutic effect of OFC stimulation.

Acknowledgments

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