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Acute Changes in Mood Induced by Subthalamic Deep Brain Stimulation in Parkinson Disease Are Modulated by Psychiatric Diagnosis

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ABSTRACT

Background: Deep brain stimulation of the subthalamic nucleus (STN DBS) reduces Parkinson disease (PD) motor symptoms but has unexplained, variable effects on mood.
Objective: The study tested the hypothesis that pre-existing mood and/or anxiety disorders or increased symptom severity negatively affects mood response to STN DBS.
Methods: Thirty-eight PD participants with bilateral STN DBS and on PD medications were interviewed with Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID) and completed Beck Depression Inventory (BDI) and Spielberger State Anxiety Inventory (SSAI) self-reports. Subsequently, during OFF and optimal ON (clinical settings) STN DBS conditions and while off PD medications, motor function was assessed with the United Parkinson Disease Rating Scale (UPDRS, part III), and participants rated their mood with Visual Analogue Scales (VAS), and again completed SSAI. VAS mood variables included anxiety, apathy, valence and emotional arousal.
Results: STN DBS improved UPDRS scores and mood. Unexpectedly, PD participants diagnosed with *current* anxiety or mood disorders experienced greater STN DBS-induced improvement in mood than those diagnosed with *remitted* disorders or who were deemed as having never met threshold criteria for diagnosis. BDI and SSAI scores did not modulate mood response to STN DBS, indicating that clinical categorical diagnosis better differentiates mood response to STN DBS than self-rated symptom severity. SCID diagnosis, BDI and SSAI scores did not modulate motor response to STN DBS.
Conclusions: PD participants diagnosed with current mood or anxiety disorders are more sensitive to STN DBS-induced effects on mood, possibly indicating altered basal ganglia circuitry in this group.

Introduction

Twenty-five to 40% of individuals with Parkinson disease (PD) suffer from mood and anxiety disorders that substantially impair quality of life [1,2]. While impairments in motor behavior in PD arise primarily from basal ganglia dysfunction [3], the neurobiological underpinnings of comorbid psychiatric disorders in PD remain less clear. PD patients in the advanced stages of the disease are particularly susceptible to psychiatric symptoms [1]. Since patients treated with subthalamic nucleus deep brain stimulation (STN DBS) typically have advanced motor symptoms, they may fall within this vulnerable population. Although PD patients are frequently screened for current psychiatric disorders prior to STN DBS surgery [4], they may have recovered at the time of screening from past illness, or may develop new psychiatric symptoms after surgery as the disease progresses and treatment changes.

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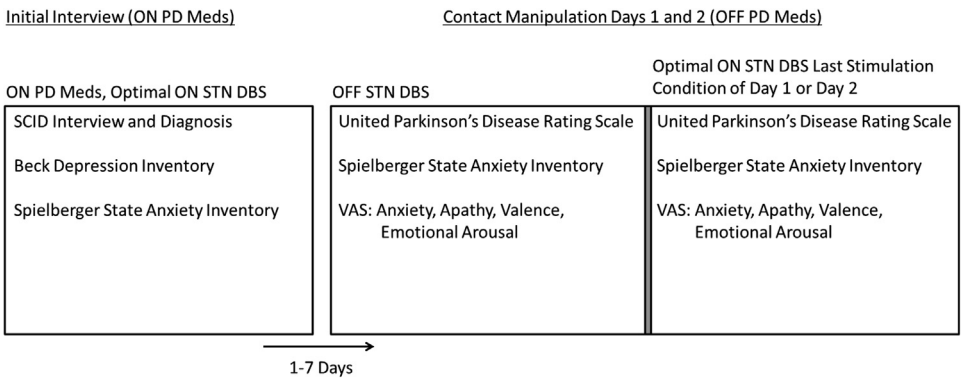

Figure 1. Experimental procedure detailing interviews, self-report questionnaires, motor assessment, and computer tasks (Visual Analogue Scales self-ratings) from which dependent variables were obtained. Participants underwent contact manipulation conditions 1–7 days after the Initial Interview. In the case of participants who underwent 2 days of stimulation conditions, OFF STN DBS dependent measure scores were obtained by averaging across both OFF conditions.

PD patients with STN DBS provide a unique opportunity to investigate the neural underpinnings of mood and anxiety disorders in PD. The STN may have substantial functional heterogeneity, given its convergent inputs from and projections to motor, limbic and associative cortical regions [5–8]. Growing evidence demonstrates that STN DBS, a therapy aimed at decreasing motor impairment and dopaminergic medication use in PD, also can alter mood [9,10]. Some studies have found reduced depression, apathy and psychiatric symptoms with stimulators turned ON relative to OFF [11–13]. By contrast, case studies demonstrate that some patients experience adverse changes in mood-related behavior with STN DBS, including fits of laughter [14], hypomania [15], and severe transient depression [16,17]. Case reports [17] and other studies [18,19], although not designed to experimentally test whether past psychiatric disorders affect acute alterations in mood induced by STN DBS, highlight the importance of considering the effects of past and current psychiatric disorders on the mood response to STN DBS, which can be quite variable across PD patients.

Here, we test whether past and present psychiatric history modulate the acute effects of STN DBS on mood using a double-blind OFF/clinically optimal ON STN DBS experimental design and well-validated measures of acute mood and behavioral change. In addition, PD participants refrained from dopaminergic medication overnight to reduce confounding the effects of STN DBS on mood [12–14]. Based on past findings from our laboratory [11], we predicted that STN DBS would induce beneficial acute effects on mood in PD participants without past or current mood or anxiety symptomatology. By contrast, we hypothesized that STN DBS would acutely cause adverse alterations in mood in participants with remitted or current mood and anxiety symptoms based on evidence that pre-existing psychiatric conditions may render PD patients more susceptible to adverse mood alterations induced by STN DBS [17–19].

Materials and methods

Participants

Thirty-eight participants with PD and bilateral STN DBS were recruited from the Washington University in St. Louis Movement Disorders Center. Six of these participants previously participated in a different study that measured mood response to STN DBS [11]. Participants were informed of all relevant risks and provided signed consent forms in accordance with the Declaration of Helsinki; the study was approved by the Washington University in St. Louis Human Research Protection Office. Subjects were included based on clinically definite diagnosis of PD [20–22], previously implanted bilateral STN-DBS electrodes and an absence of neurological deficits including dementia, head injury or stroke. Details regarding the specific surgical technique used to implant DBS electrodes and the programming paradigm can be found elsewhere [23]. Soletra or Activa (Medtronic Inc.) pulse generators were used in all participants. DBS implants were previously optimized for motor benefit using monopolar stimulation prior to recruitment into the study.

Localization of STN DBS electrode contacts

Pre-operative clinical MRIs were obtained with a Siemens Vision 1.5T scanner. MRIs were aligned to post-operative computed tomography (CT) images and atlas registration was performed using a validated method [24]. The atlas location of each electrode contact was visualized by overlaying the fused MRI-CT image (resliced to match the Mai atlas [25]) on Mai atlas slices where contact coordinates were plotted [24].

Behavioral protocol

The experimental procedure is diagrammed in Fig. 1 and described below.

Initial Interview

Prior to contact manipulation days, subjects were evaluated with their clinically-determined optimal STN DBS stimulation settings while on anti-parkinsonian medications (optimal ON DBS, on medications) (see Fig. 1). Presence of current or remitted mood or anxiety disorders was determined by administration of the Structural Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I/NP [26]) by a movement disorders-trained neuropsychiatrist (KJB), except that the DSM-IV-TR causation criteria were ignored as suggested by a consensus panel [27], e.g. Major Depressive Disorder was diagnosed rather than Mood Disorder Due to Parkinson Disease. Current depressive and anxiety symptoms were further assessed by 2 self-report questionnaires: the Beck Depression Inventory-II (BDI-II [28]) and the Spielberger State-Trait Anxiety Inventory (SSAI [29]).

For some analyses (described below), the SCID was used to separate groups of participants based on the presence of a threshold-level (as defined by the SCID and as determined by the interviewing psychiatrist) current (threshold criteria met during the last month) or remitted mood or anxiety disorder. The union of these two groups includes all subjects who were diagnosed with past and/or current mood and/or anxiety disorders during the Initial Interview. Due to low numbers of participants who were