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Subthalamic nucleus stimulation affects subjective emotional experience in Parkinson's disease patients

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ABSTRACT

A number of studies have reported impaired facial emotion recognition following subthalamic nucleus (STN) stimulation in Parkinson's disease (PD), and have related these changes to a limbic dysfunction induced by STN stimulation. The present study examined the effect of STN stimulation in PD patients on a specific component of emotion, namely the subjective experience of emotion. Thirteen post-operative PD patients, 13 pre-operative PD patients matched on clinical and neuropsychological characteristics, and 16 controls matched on age and education, were administered a validated battery of film excerpts known to primarily induce specific emotional feelings (anger, happiness, sadness, fear, disgust, and neutral), and self-rated the intensity of their emotional feelings on a discrete emotions questionnaire. The post-operative group showed a significant lower level of differentiation between the target feeling (i.e., the more likely to be reported) and non-target feelings for the film excerpts intended to induce "sadness" and "fear" respectively, as compared with the pre-operative and healthy control groups. Moreover, the post-operative group reported significantly less intense feelings of fear, anxiety and disgust for the excerpt intended to induce "fear" as compared with the pre-operative and the control groups, while no significant difference was observed between the pre-operative and control groups. Finally, the post-operative group reported significantly less intense feelings of sadness and anxiety during the excerpt intended to induce "sadness" as compared to the control group, although the differences between the pre- and post-operative groups and between the pre-operative and the control groups did not reach significance. Our study suggests that STN stimulation affects the subjective experience of emotion, thus providing a preliminary account of the modulation induced by STN stimulation of a distributed neuronal network underlying the subjective experience of emotion, although the exact contribution of the STN within such network remains to be specified.

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1. Introduction

The efficiency of subthalamic nucleus (STN) stimulation on Parkinson's disease (PD) motor symptoms is now largely confirmed (see Kleiner-Fisman et al., 2006, for a meta-analytic review). Proposed to advanced PD patients with medically intractable motor symptoms, this treatment has proven to have positive effects on all parkinsonian symptoms (Broggi et al., 2001; Kumar et al., 1998; Limousin et al., 1998) with a great stability over time (Krack et al., 2003; Visser-Vandewalle et al., 2005).

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However, a number of studies have also reported non-motor effects following STN stimulation, specifically in the cognitive, behavioural and emotional domains (for a review, see Voon, Kubu, Krack, Houeto, & Tröster, 2006). Despite discrepant findings, probably due to methodological issues, STN stimulation seems to have a relatively limited impact on cognitive functioning, with the most consistently reported finding being a reduction in verbal fluency performance (see Parsons, Rogers, Braaten, Woods, Tröster, 2006 for a meta-analysis). Conversely, evidence for behavioural changes and psychiatric symptoms after STN stimulation is largely documented (for a review see Temel et al., 2006). The most commonly reported changes include mood disorders (Dujardin, Defebvre, Krystkoviac, Blond, & Destee, 2001; Perozzo et al., 2001; Vingerhoets et al., 2002), mania and hypomania (Funkiewiez et al., 2004; Kulisevsky et al., 2002), apathy (Drapier et al., 2006; Funkiewiez et al., 2004), and episodes of aggressive behaviour, irritability, and disturbed emotional reactivity (Funkiewiez et al., 2004; Houeto et al., 2002; Sensi et al., 2004; Smeding et al., 2006).

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Reports of changes of emotional behaviour have led researchers to explore the effect of STN stimulation on emotional processing. Emotional processing during STN stimulation was examined using a mood-induction procedure - according to the authors' terminology - in which PD patients were presented with slides of happy or sad facial expressions with the instruction to adjust their emotional state to the perceived facial emotion (Schneider et al., 2003). The authors reported "more positive self-reported mood" and an "enhanced mood induction effect" in the stimulation on/medication off condition as compared to the stimulation off/medication off condition, and concluded that STN stimulation may increase emotional processing. However, no stimulation effect was observed in an emotion discrimination task requiring participants to differentiate happy, sad and neutral faces (Schneider et al., 2003). In contrast, impaired facial expression recognition has consistently been reported in subsequent studies focusing on the effect of STN stimulation on emotion recognition (Biseul et al., 2005; Drapier et al., 2008; Dujardin et al., 2004; Schroeder et al., 2004). While the details of the materials and procedure differ across studies, one important finding is that the impairment seems to selectively concern negative emotions: anger recognition is selectively impaired in Schroeder et al.'s (2004) study, recognition of all negative emotions under study (anger, disgust, sadness) are impaired in Dujardin et al.'s (2004) study, fear recognition is selectively impaired in Biseul et al.'s (2005) study, and fear and sadness are impaired in Drapier et al.'s (2008) study. Another important finding is that the impairment could not be attributed to secondary variables such as anxiety or depression, visuospatial deficit or general cognitive decline (Biseul et al., 2005; Drapier et al., 2008; Dujardin et al., 2004; Schroeder et al., 2004). Moreover, subjective feelings of fear and panic have been described during STN stimulation, either post-operatively (Okun et al., 2004) or intraoperatively (Sauleau et al., 2005). Altogether, these studies suggest that STN stimulation affects the processing of emotional information.

The interpretation for these emotional effects induced by STN stimulation lies in the basal ganglia neuroanatomical organization, in which the STN is thought to play a central role not only in the regulation of motor function but also in the regulation and/or integration of associative and limbic functions (Mallet et al., 2007; Temel, Blocland, Steinbusch, & Visser-Vandewalle, 2005). The basal ganglia are interconnected to specific motor, associative and limbic cortical regions through a series of - partially - segregated and highly topographically organized circuits (Alexander, Crutcher, & DeLong, 1990; Alexander, DeLong, & Strick, 1986; Parent & Hazrati, 1995a; see also Temel et al., 2005 for a schematic illustration of these interconnections), which underlie specific motor, oculomotor, associative and limbic functions. In primates, the anatomical and functional partitioning of the basal ganglia through the so-called cortico - basal ganglia - thalamocortical circuits has also been described at the level of the STN, which comprises a sensorimotor (dorsolateral), an associative (ventromedial) and a limbic (medial) compartment (Joel & Wiener, 1997; Parent & Hazrati, 1995b).

The STN is thus closely connected to the limbic areas of the basal ganglia, such as the ventral pallidum and ventral striatum, as well as to limbic cortical areas such as the anterior cingulate cortex and the orbitofrontal cortex (Parent & Hazrati, 1995b). As part of a large cerebral network underlying emotional processing, the anterior cingulate cortex and orbitofrontal cortex are known to play a major role in several aspects of emotional processing (Hornak et al., 2003; Phan, Wager, Taylor, & Liberzon, 2002) including the recognition of emotions from faces and voices (e.g., Adolphs, 2002; Wildgruber, Ackermann, Kreifelts, & Ethofer, 2006), and exposure to emotional procody (e.g., Quadflieg, Mohr, Mentzel, Miltner, & Straube, 2008; Sander, Grandjean, Pourtois, et al., 2005). It has been hypothesized that the impaired recognition of facial emotions observed in PD patients following STN stimulation is a result of a

limbic dysfunction induced by deep brain stimulation (e.g., Biseul et al., 2005; Drapier et al., 2008; Dujardin et al., 2004; Schroeder et al., 2004; Temel et al., 2006). Providing support for this hypothesis, PET studies in PD patients reported activity changes in non-motor areas that are part of the associative and limbic circuits during STN stimulation (Hilker et al., 2004; Schroeder et al., 2002, 2003), and a study using local field potentials recordings found a "limbic" activation of the STN in response to emotionally arousing versus neutral pictures, demonstrating a role of this structure in the processing and/or the transmission of visual emotional information (Kühn et al., 2005). Furthermore, it has been observed in a neuroimaging study that STN stimulation interferes with the normal functioning of cortical regions involved in the recognition of facial expressions (Geday, Ostergaard, & Gjedde, 2006). Finally, a recent PET study conducted in our group demonstrated a significant correlation between impaired fear recognition induced by STN stimulation in PD patients and a decrease in glucose metabolism in the right orbitofrontal cortex (Le Jeune et al., 2008).

The convergence of anatomical, clinical and neuroimaging data strongly support the hypothesis that the STN is involved in a distributed network underlying emotional processing. Whereas previous studies focused on the influence of STN stimulation on the recognition of emotional facial expressions, the present study examined the effects of STN stimulation on one specific aspect of emotion, namely the subjective experience of emotion.

Emotion is considered a complex phenomenon that consists of several components (e.g., cognitive, physiological, motor/ expressive) serving more or less dissociable functions, and the term "emotion" refers to those episodes during which all or most of the various components synchronize to produce a response to a situation or a stimulus event evaluated as highly relevant for the organism (Sander, Grandjean, & Scherer, 2005; Scherer, 2004). The feeling, or subjective emotional experience, is one of the components of emotion, which has a peculiar status though, since it emerges through the integration and synchronization of the other components (Grandjean, Sander, & Scherer, 2008; Scherer, 2004). Thus the feeling component itself is a complex "multifaceted" component with the verbally reported feelings capturing only partially what is effectively consciously experienced (Grandjean et al., 2008; Scherer, 2004). Although there is at present little evidence for the neuroanatomical mechanisms underlying subjective feeling, a number of neuroimaging studies suggest that the orbitofrontal and anterior cingulate circuits involved in the recognition of emotions from faces are also involved in the subjective experience of emotion (Decety & Chaminade, 2003; Takahashi et al., 2004; Taylor, Phan, Decker, & Liberzon, 2003; see also Phan et al., 2002, for a meta-analysis). Moreover, the important work conducted by Rolls and colleagues emphasized the key role of the orbitofrontal cortex in the emergence of the affective value and associated subjective emotional experience of stimuli or events (for a detailed review see Rolls & Grabenhorst, 2008). On the basis of recent findings showing anatomical connections between regions involved in emotional processing such as the orbitofrontal cortex and the amygdala (Ghashghaei, Hilgetag, & Barbas, 2007) and neuronal synchronization of different cerebral regions during the processing of emotional stimuli (Luo, Holroyd, Jones, Hendler, & Blair, 2007), it has been proposed that different more or less distant neuronal populations work in conjunction and in synchrony in the emergence of subjective feeling (Grandjean et al., 2008). A recent publication of our group clearly demonstrates an influence of the STN on distant brain regions known to be involved in emotional processing, namely, the orbitofrontal cortex, and indirectly, possibly via the orbitofrontal cortex, the amygdala (Le Jeune et al., 2008). Because of the intimate STN connections with cerebral areas involved in various aspects of emotional processing, STN may participate to the synchronization process underlying the emergence of feeling, and hence STN

Demographic and clinical characteristics of the participating groups.

Variable	Healthy controls Mean (SD)	Pre-operative Mean (SD)	Post-operative Mean (SD)	<i>p</i> -Value
Age (years)	56.6 (5.3)	55.2 (6.8)	58.1 (8.7)	0.66 [†]
Education (years)	9.8 (2.2)	12(3.5)	9.8 (2.5)	0.10 [†]
Disease duration (years)	N/A	11.7 (5.7)	13.1 (3.6)	0.20††
Equivalent dopa dose (mg/day)	N/A	1062.6 (598.5)	1060.8 (445.7)	0.96††
UPDRS motor score (part III) ^a	N/A	8.4 (4.6)	8.4 (5.5)	0.78††
Hoehn and Yahr score ^a	N/A	1.1 (0.8)	1.3 (1.1)	0.47 ^{††}

Note. N/A = Not applicable.

^a Values obtained in the on-drug condition for both PD groups and with the stimulator turned on in the post-operative group.

[†] Kruskal–Wallis test.

†† Mann-Whitney test.

stimulation is likely to affect the subjective experience of emotion. By using a validated emotion induction procedure based on film excerpts (Schaefer, Nils, Sanchez, & Philippot, in revision), the aim of the present study was to explore the extent to which STN stimulation affects the subjective experience of emotion in PD patients in order to provide support to the hypothesis of a STN influence on a distributed neuronal network contributing to the emergence of feeling.

2. Methods

2.1. Participants

Two groups of individuals with idiopathic PD participated in the study. Idiopathic PD was defined on the basis of the United Kingdom Parkinson's disease Brain Bank criteria (Gibb & Lees, 1988). The first group included 13 patients (7 males and 6 females) with advanced PD and candidates for STN deep brain stimulation (preoperative group). The second group included 13 consecutive patients (10 males and 3 females) who underwent bilateral surgical implantation of stimulating electrodes into the STN (post-operative group) for the treatment of severe motor fluctuations and/or dyskinesias (24.80 ± 16.3 months post-operatively). All PD patients were receiving their anti-parkinsonian medication during the assessment. A group of 16 healthy controls (7 males and 9 females) also participated in the study. They had no history of neurological disease or psychiatric disorder, and none of them presented signs of global cognitive deterioration as documented by the Mini Mental State Examination (MMSE, Folstein, Folstein, & McHugh, 1975) (mean score = 29.6, SD=0.5). The study was approved by the Ethical Committee of Rennes University Hospital and all participants gave their informed consent prior to their inclusion in the study. Participants' demographic and clinical characteristics are summarized in Table 1. There were no significant statistical differences between the three groups regarding age (H=0.83, p=0.66) and education (H=4.52, p=0.10). Similarly, there were no significant differences between the two patient groups regarding duration of the disease (U = 59.50, p = 0.20), total levodopa-equivalent dose (U = 83.00, p = 0.96), and motor condition in the on-drug state as assessed by the Unified Parkinson's Disease Rating Scale-part III (UPDRS, Fahn & Elton, 1987), and the Hoehn and Yahr scale (Hoehn & Yahr, 1967) (U = 73.00, p = 0.78, and U = 71.00, p = 0.47, respectively), motor condition under which the testing has been conducted for both patient groups. It is worthy to note that the PD patients presented suitable clinical characteristics for the purpose of the study. First, both PD patient groups were relatively early-onset PD patients thus corresponding to "a 'pure or predominant dopaminergic' form of the disease" (Blin et al., 1991, p. 782). Second, because the involvement of dopamine as a key neurotransmitter in emotional processing is largely documented (for a review see for example Salgado-Pineda, Delaveau, Blin, & Nieoullon, 2005), it was mandatory that the total levodopa-equivalent dose did not differ between the two groups of PD patients.

2.2. Materials and procedure

2.2.1. Emotion elicitation procedure

Emotion elicitation using film excerpts is an effective method for eliciting intense and specific target emotions (Gross & Levenson, 1995; Philippot, 1993; Rottenberg, Ray, & Gross, 2007), and has been found to be the most powerful method to elicit emotion in the laboratory as compared to a variety of other elicitation techniques (see Westermann, Spies, Stahl, & Hesse, 1996, for a meta-analysis). Because of their dynamic and multimodal nature, film stimuli also provide an emotional context with a relatively high degree of ecological validity, as compared, for example, to static emotional slides (Rottenberg et al., 2007).

Two series of 6 film excerpts each were used to elicit different emotional feelings: happiness, anger, fear, sadness, disgust and neutral. The film excerpts were selected from a large validated battery of film excerpts on the basis of their degree of discreteness (Schaefer et al., in revision; http://nemo.psp.ucl.ac.be/emotion/FilmStimuli/),

that is the degree to which each film excerpt is more likely to primarily induce a specific subjective feeling although mixed feelings are not excluded. The selected excerpts were randomly allocated to series A and B as following: happiness (A: *Les trois frères*, B: *The dinner game*), anger (A: *Schindler's* list, B: *Sleepers*), fear (A: *The Blair Witch Project*, B: *The Shining*), sadness (A: *City of angels*, B: *Dangerous mind*), disgust (A: *Trainspotting*, B: *Seven*) and neutral (A: *French weather forecast*, B: *Belgium weather forecast*). The film excerpts duration ranged from 1 to 4 min and all excerpts were in French. Presentation of series A and B was counterbalanced across participants. For each participant, the order of presentation of the six excerpts within a series was determined randomly. Participants were comfortably seated and the light in the room was dimmed. Before each excerpt participants went through a relaxation procedure for about 3 min. They were instructed to carefully watch to the whole excerpt. The film excerpts were displayed on a 22" color screen.

2.2.2. Evaluation of the subjective experience of emotion

After each relaxation and each excerpt presentation, participants were asked to report the intensity of their emotional feelings, i.e., the evaluation of their subjective emotional experience, on a short questionnaire. The questionnaire used is the French translation of the Differential Emotions Scale (DES: Izard, Dougherty, Bloxom, & Kotsch, 1974; French translation by Philippot, 1993) consisting of 10 emotional categories to be rated on a 5-point Lickert-type scale (from 1="not at all" to 5 "very much"): (1) interested, concentrated, alert: (2) joyful, happy, amused: (3) sad, downhearted, blue; (4) angry, irritated, mad; (5) fearful, scared, afraid; (6) anxious, tense, nervous; (7) disgusted, turned off, repulsed; (8) disdainful, scornful, contemptuous; (9) surprised, amazed, astonished; (10) warmhearted, gleeful, elated. The DES has two main advantages for the purpose of the present study: (i) it has shown to successfully discriminate among discrete emotional states in previous studies (Philippot, 1993; Schaefer et al., in revision, 2003), and (ii) because the range of emotional categories assessed by the DES is greater than the range of emotional feelings supposedly induced by the film excerpts (i.e., happiness, anger, fear, sadness and disgust), it does not specifically turn participants' attention to the target emotional feelings when filling out the questionnaire.

2.2.3. Neuropsychological assessment

In addition to the procedure assessing emotional experience, the two groups of PD patients were administered a set of neuropsychological tasks assessing cognitive efficiency and executive functioning. Performances of the two patient groups on the neuropsychological tests are presented in Table 2. Cognitive efficiency was assessed using the Mattis Dementia Rating Scale (MDRS, Mattis, 1988) and executive

Table 2

Performances of the two PD patient groups on the neuropsychological tests.

Variable	Pre-operative Mean (SD)	Post-operative Mean (SD)	<i>p</i> -Value [†]
MDRS	141.23 (1.58)	140.08 (2.21)	0.20
Stroop interference	3.98 (6.05)	2.78 (7.67)	0.48
TMT B-A	56.38 (32.51)	63.54 (39.22)	0.50
MCST cat.	6(0)	5.75 (0.45)	0.06
MCST pers.	0.85(1.21)	1.25 (1.35)	0.31
Letter fluency	24.36 (6.59)	19.58 (6.66)	0.10
Category fluency	33.91 (7.79)	26.08 (11.67)	0.04
STAI-Trait	40.92 (7.66)	39.44 (8.51)	0.66
STAI-State	32.53 (10.38)	37.37 (11.99)	0.35

Note. MDRS = Mattis Dementia Rating Scale; TMT B-A = time difference between completion of parts B and A on the Trail-Making test; MCST cat. = number of categories achieved on the Modified Card Sorting Test; MCST pers. = number of perseverative errors on the Modified Card Sorting Test; STAI-Trait = score on the Trait subscale of the State-Trait Anxiety Inventory; STAI-State = score on the State subscale of the State -Trait Anxiety Inventory.

† Mann-Whitney test.

functioning was assessed using a series of tests including the Trail-Making test (TMT, Reitan, 1958), the Modified Card Sorting Test (MCST, Nelson, 1976), the Stroop test (Stroop, 1935), as well as phonemic (letter P) and semantic (animal category) verbal fluency tasks. The dependant measures were the total score on the MDRS, the time difference between completion of parts B and A for the TMT, the number of categories correctly completed and number of perseveration errors for the MCST, the interference index for the Stroop test, and the number of words produced (minus repetitions and intrusions) for a period of 2 min for the verbal fluency tasks. The Strate-Trait Anxiety Inventory (STAI-Y, Spielberger, Gorsuch, Luschene, Vagg, & Jacobs, 1993) was used to assess anxiety.

2.3. Surgical procedure and electrode location

The 13 PD patients with STN stimulation (i.e., the post-operative group) all underwent the same surgical procedure which is briefly described below.

Quadripolar deep brain stimulation electrodes (Medtronic, Minneapolis, MN, USA) were implanted bilaterally in the STN in two successive operating sessions. The overall methodology was similar to that previously described in Benabid et al. (2000). The location of the two selected electrode contacts (one on the left side and one on the right side) was determined using the stereotactic coordinates provided by the ventriculography done at the onset of the surgical procedure. The mean coordinates of the selected contacts were similar to those reported in our previous work (Le Jeune et al., 2008).

2.4. Data analysis

Because of the restricted sample sizes, comparisons of the three independent groups were performed using the non-parametric Kruskal–Wallis statistic. When the Kruskal–Wallis test yielded to a significant difference, pairwise Mann–Whitney tests were carried out to determine which group differed from one another. Moreover, comparisons of the two PD patients groups on clinical and neuropsychological variables were conducted using Mann–Whitney tests. Finally, analyses of the matrices of response patterns were performed using chi–square statistic (χ^2). All the analyses used an alpha level of 0.05.

3. Results

3.1. Neuropsychological assessment

Performances of the pre- and post-operative groups on the neuropsychological tests are presented in Table 2. Cognitive efficiency as assessed by the Mattis Dementia Rating Scale was not significantly different between the two groups of patients. Similarly, there was no significant differences between the pre- and post-operative groups on the executive tests except for the semantic fluency task (p = 0.04). Finally, anxiety scores were within the normal range for the two PD patient groups and there was no significant difference between them on these scores.

3.2. Evaluation of the subjective experience of emotion

3.2.1. Relaxation sessions

Ratings from each emotional category of the questionnaire were averaged across the six relaxation sessions for each participant and compared between the three groups (see Table 3).

The Kruskal–Wallis test revealed no significant difference in the ratings between the three groups except for the DES item

Table 3

Mean self-rated emotional intensity scores across the relaxation sessions in each group.

joyful, happy, amused (H = 7.5, p = 0.024). Pairwise Mann–Whitney tests indicated that the difference was due to controls who rated themselves as happier than the pre-operative patients (U = 42.5, p = 0.007), with the post-operative participants being in an intermediate position since they did not differ significantly from either the pre-operative patients (U = 70.5, p = 0.47), or the controls (U = 65, p = 0.09).

3.2.2. Emotional film excerpts

Analyses were conducted for each film excerpt separately. Although we were more particularly interested in the ratings on the 5 emotional categories of the questionnaire that corresponded to the 5 emotional feelings under study, that is, DES items 2 (joyful, happy, amused), 3 (sad, downhearted, blue), 4 (angry, irritated, mad), 5 (fearful, scared, afraid) and 7 (disgusted, turned off, repulsed) targeting respectively the feeling of happiness, sadness, anger, fear, and disgust, ratings on the whole set of emotional categories were nevertheless examined. Moreover, for each film excerpt, ratings on the target emotional category (i.e., the category that corresponded to the subjective feeling the more likely to be reported for a given excerpt) were considered independently of the ratings on the nontarget emotional categories, except for the neutral film for which no such distinction was made. For instance, for the film intended to induce a feeling of disgust, the target emotional category was DES item 7 (disgusted, turned off, repulsed), and the non-target emotional categories were the nine remaining items of the questionnaire.

A first series of analyses has been conducted within the healthy control group and examined whether there were gender differences in the reactivity to the film excerpts. For each film excerpt the average ratings on the non-target emotional categories were compared to the ratings on the target emotional category and no significant differences was found between men and women for any of the 6 film clips.

A second series of analyses examined for each film excerpt whether the three groups differed in the intensity with which the target feeling (i.e., the more likely to be reported) was reported in comparison with the non-target feelings, thus providing information regarding their ability to differentiate the target emotional feeling from the non-target emotional feelings. Ratings on the nontarget emotional categories were averaged for each film excerpt and difference scores between ratings on the target emotional category and the average ratings on the non-target emotional categories were computed for each participant and compared across the three groups. Mean difference scores for each film excerpt and each group are presented in Table 4. No significant differences were found between the three groups for the film excerpts intended to induce a feeling of happiness, anger and disgust (see Table 4), suggesting that the intensity with which the target feeling was reported in comparison with the non-target feelings did not significantly differ across the three groups. In contrast, for the film excerpts intended to induce a feeling of sadness on the one hand, and a feeling of fear on

DES item	Healthy controls Mean (<i>SD</i>)	Pre-operative Mean (SD)	Post-operative Mean (SD)	$p ext{-Value}^\dagger$
(1) Interested, concentrated, alert	4.08 (0.74)	3.58 (0.95)	4.02 (0.85)	0.31
(2) Joyful, happy, amused	2.63 (0.88)	1.72 (0.64)	2.02 (0.94)	0.02
(3) Sad, downhearted, blue	1.20 (0.27)	1.28 (0.50)	1.26 (0.49)	0.98
(4) Angry, irritated, mad	1.15 (0.27)	1.26 (0.55)	1.34 (0.56)	0.81
(5) Fearful, scared, afraid	1.13 (0.22)	1.11 (0.18)	1.23 (0.38)	0.80
(6) Anxious, tense, nervous	1.27 (0.27)	1.33 (0.62)	1.45 (0.53)	0.44
(7) Disgusted, turned off, repulsed	1.22 (0.44)	1.17 (0.37)	1.26 (0.52)	0.91
(8) Disdainful, scornful, contemptuous	1.10 (0.21)	1.07 (0.19)	1.16 (0.30)	0.59
(9) Surprised, amazed, astonished	1.48 (0.53)	1.20 (0.33)	1.47 (0.50)	0.23
(10) Warmhearted, gleeful, elated	2.53 (1.05)	1.81 (0.66)	2.53 (1.23)	0.14

† Kruskal–Wallis test.

Table 4

Mean difference scores between ratings on the target emotional category and average ratings on the non-target emotional categories for each film excerpt in each group.

Film excerpt	Healthy controls Mean (SD)	Pre-operative Mean (SD)	Post-operative Mean (SD)	p-Value
Happiness	2.33 (0.99)	2.60 (1.04)	2.14 (0.80)	0.10
Anger	0.90 (1.24)	1.14 (1.25)	1.10 (1.03)	0.97
Sadness	1.48 (1.10)	1.27 (1.05)	0.31 (1.07)	0.02
Fear	1.13 (1.15)	1.19 (0.37)	0.11 (0.97)	0.01
Disgust	1.36 (1.22)	1.17 (1.31)	0.83 (1.61)	0.60

† Kruskal-Wallis test.

the other hand, significant group effects were found (respectively p = 0.02 and p = 0.01, see Table 4). Post hoc pairwise Mann–Whitney tests revealed that the differences were due to significant lower level of differentiation between the target emotional feeling and the non-target emotional feelings in the post-operative group as compared with both the healthy control group (U = 44.5, p = 0.009, for the film excerpt intended to induce a feeling of sadness; U = 50, p = 0.02 for the film excerpt intended to induce a feeling of fear) and the pre-operative group (U = 42.5, p = 0.03, for the film excerpt intended to induce a feeling of fear) and the pre-operative group (U = 42.5, p = 0.03, for the film excerpt intended to induce a feeling of fear), while the healthy control group and the pre-operative group did not differ significantly from one another (U = 86.5, p = 0.44, for the film excerpt intended to induce a feeling of sadness; U = 102, p = 0.93 for the film excerpt intended to induce a feeling of fear).

This second set of analyses revealed that for the film excerpts intended to induce a feeling of sadness on the one hand, and a feeling of fear on the other hand, the intensity with which the target feeling was reported in comparison with the non-target feelings was significantly lower in the post-operative group as compared with both the pre-operative and healthy control groups.

A third series of analyses examined whether the three groups differed in the kind of subjective emotional feelings reported in the course of each film excerpt and was thus conducted on each DES item separately. Difference intensity scores between the ratings reported after a given film excerpt and the ratings reported after the preceding relaxation period, were computed for each relaxation-excerpt pair. This was done in order to minimize the influence of a given excerpt on the reported subjective feelings induced by the following excerpt, influence that may potentially remain despite the period of relaxation between them. Mean difference intensity scores on the ten emotional categories of the DES for each film excerpt and each group are presented in Table 5. As can be seen from Table 5, no significant difference was observed between the three groups for the film excerpts intended to induce a feeling of happiness, a feeling of disgust and a neutral state, either on the target or on the non-target emotional categories, suggesting that, in this sample, STN stimulation does not significantly affect the subjective experience of happiness and disgust.

For the film excerpt intended to induce a feeling of fear, as can be seen from Table 5, a significant group effect was found for the target emotional feeling of fear (DES item 5, p = 0.001), as well as for the feelings of anxiety (DES item 6, p = 0.001) and disgust (DES item 7, p = 0.02). A significant group effect was also observed for the non-target emotional feeling of happiness (DES item 2, p = 0.02). As far as the target feeling of fear is concerned, post hoc pairwise Mann–Whitney tests revealed that the difference was due to a significant lower difference intensity score of fear (i.e., a lower decrease of self-rated feeling of fear between the period of film excerpt and the previous relaxation period) in the post-operative group as compared with both the healthy control group (U=34, p=0.002) and the pre-operative group (U=23, p=0.001), while the healthy control group and the pre-operative group did not differ significantly from one another (U = 83, p = 0.33). Interestingly, post hoc pairwise Mann-Whitney tests revealed the same pattern of differences for the group effects concerning the feelings of anxiety and disgust. The differences were due to significant lower difference intensity scores of anxiety and disgust in the post-operative group as compared with both the healthy control group (U = 35.5, p=0.002 for the feeling of anxiety; U=49, p=0.01 for the feeling of disgust) and the pre-operative group (U=24.5, p=0.001 for the feeling of anxiety; U = 41.5, p = 0.02 for the feeling of disgust), while the healthy control group and the pre-operative group did not differ significantly from one another (U=88, p=0.46 for the feeling of anxiety; U = 97.5, p = 0.77 for the feeling of disgust). Thus the post-operative group reported significantly less intense feelings of fear, anxiety and disgust after the film excerpt intended to induce a feeling of fear (in comparison with the preceding relaxation period) than both the pre-operative group and the healthy control group, while these latter two groups did not significantly differ from one another. Concerning the significant group effect observed for the non-target emotional feeling of happiness, post hoc pairwise Mann-Whitney tests revealed that the difference was due to a significant lower difference intensity score of happiness (i.e., a lower decrease of self-rated feeling of happiness between the period of film excerpt and the previous relaxation period) in both the pre-operative group (U=56, p=0.03) and the post-operative group (U = 54, p = 0.02) as compared with the healthy control group, while the pre- and post-operative groups did not differ significantly from one another (U = 84, p = 0.98).

As can be seen in Table 5, for the film excerpt intended to induce a feeling of sadness, a significant group effect was found for the target emotional feeling of sadness (DES item 3, p = 0.01), as well as for the non-target emotional feeling of happiness (DES item 2, p = 0.03), and a tendency for the emotional feeling of anxiety (DES item 6, p = 0.07) could be noted. Post hoc pairwise Mann–Whitney tests revealed that, for the target emotional feeling of sadness, the difference was due to a significant lower difference intensity score of sadness (i.e., a lower decrease of self-rated feeling of sadness between the period of film excerpt and the previous relaxation period) in the post-operative group as compared with the healthy control group (U=40, p=0.004), while the pre-operative group was in an intermediate position since it did not differ significantly from either the post-operative group (U=52, p=0.09), or the healthy controls (U = 75, p = 0.19). Thus the self-reported feeling of sadness after the film excerpt intended to induce a feeling of sadness (in comparison with the preceding relaxation period) was significantly less intense in the post-operative group than in the healthy control group. Interestingly, post hoc pairwise Mann-Whitney tests revealed the same pattern of differences for DES item 6 for which a tendency toward a group effect was observed, that is, a significant lower difference intensity score of anxiety (i.e., a lower decrease of self-rated feeling of anxiety between the period of film excerpt and the previous relaxation period) in the post-operative group as compared with the healthy control group (U = 55, p = 0.02), while the pre-operative group was in an intermediate position since it did not differ significantly from either the post-operative group (U=67, p=0.34), or the healthy controls (U = 75.5, p = 0.16). Thus, the self-reported feeling of anxiety after the film excerpt intended to induce a feeling of sadness (in comparison with the preceding relaxation period) was significantly less intense in the post-operative group than in the healthy control group. Concerning the significant group effect found for the non-target emotional feeling of happiness, similarly to what was observed for the film excerpt intended to induce a feeling of fear, post hoc pairwise Mann-Whitney tests revealed that the difference was due to a significant lower difference intensity score of happiness (i.e., a lower decrease of self-rated feeling of happiness between the period of film excerpt and the previous relaxation period) in both the pre-operative group (U = 58.5, p = 0.03) and the

Table 5

Mean difference intensity scores between the ratings reported after the film excerpt and the ratings reported after the preceding relaxation session for each relaxation-film excerpt pair in each group.

Film excerpt and DES item	Healthy controls Mean (SD)	Pre-operative Mean (SD)	Post-operative Mean (SD)	$p ext{-Value}^\dagger$
Happiness				
(1) Interested, concentrated, alert	0.31 (1.30)	0.23 (1.59)	0.08 (1.19)	0.93
(2) Joyful, happy, amused	1.63 (1.45)	2.62 (1.71)	2.00 (1.29)	0.10
(3) Sad, downhearted, blue	-0.06(0.68)	-0.23 (1.16)	0.15 (0.90)	0.99
(4) Angry, irritated, mad	0.00(0.96)	-0.31 (1.03)	0.00(0.71)	0.97
(5) Fearful, scared, afraid	-0.19 (0.40)	-0.23 (0.83)	-0.15 (0.37)	0.76
(6) Anxious, tense, nervous	-0.25(0.58)	-0.54 (1.05)	-0.15 (0.90)	0.86
(7) Disgusted, turned off, repulsed	0.19 (0.83)	-0.23(0.60)	-0.15 (0.55)	0.39
(8) Disdainful, scornful, contemptuous	0.25 (0.58)	0.00 (0.00)	0.00(0.71)	0.37
(9) Surprised, amazed, astonished (10) Warmhearted, gleeful, elated	-0.19 (0.98) 0.75 (1.00)	0.00 (0.91) 1.00 (1.47)	-0.15 (0.69) 0.85 (1.46)	0.79 0.82
Anger	0.10 (0.00)	0.01 (1.00)		0.07
(1) Interested, concentrated, alert	0.13 (0.88)	0.31 (1.03)	0.08 (0.86)	0.97
(2) Joyful, happy, amused	-1.88(1.20)	-0.46 (1.20)	-1.08(1.19)	0.02
(3) Sad, downnearted, blue	2.25 (1.44)	1.69 (1.32) 2 54 (1.20)	1.85 (1.77)	0.57
(4) Angry, Irritated, mad (5) Foarful scared afraid	2.75 (1.57) 2.12 (1.26)	2.34 (1.20)	2.40 (1.00)	0.75
(5) Fedilul, Scaleu, allalu	2.15 (1.50)	1.40 (1.32)	1.34 (1.39)	0.55
(7) Disgusted turned off repulsed	1.94(1.12)	2.60 (1.14)	2.46 (1.45)	0.25
(7) Disgusted, turned on, repuised	2.01 (1.42)	2.05 (1.44)	1.60 (1.70)	0.75
(0) Surprised amazed astonished	2.00 (2.10)	1.77 (1.50)	1.09 (1.70)	0.72
(10) Warmhearted gleeful elated	-1.13(1.71) -1.94(1.48)	-0.77(0.60)	-1.46(1.20)	0.98
Sadness	101(110)	0.17 (0.00)	(127)	
(1) Interested, concentrated, alert	0.38 (0.62)	0.62 (1.12)	0.54 (0.97)	0.90
(2) Joyful, happy, amused	-1.56 (1.36)	-0.54 (0.88)	-0.15 (1.40)	0.03
(3) Sad, downhearted, blue	2.38 (1.20)	1.85 (1.14)	0.85 (1.34)	0.01
(4) Angry, irritated, mad	0.94 (1.00)	0.54 (0.88)	0.46(1.13)	0.41
(5) Fearful, scared, afraid	1.06 (0.77)	0.69 (0.95)	0.69 (1.18)	0.17
(6) Anxious, tense, nervous	1.44 (1.03)	0.92 (0.95)	0.54 (0.88)	0.07
(7) Disgusted, turned off, repulsed	0.63 (1.02)	0.31 (0.63)	0.23 (1.01)	0.51
(8) Disdainful, scornful, contemptuous	0.13 (0.50)	0.23 (0.44)	0.15 (0.90)	0.87
(9) Surprised, amazed, astonished	0.88 (1.41)	0.38 (0.65)	0.23 (0.44)	0.21
(10) Warmhearted, gleeful, elated	-1.19 (1.42)	-0.54 (1.13)	-0.54 (1.61)	0.44
Fear				
(1) Interested, concentrated, alert	0.19 (0.83)	0.00 (1.68)	-0.15 (0.69)	0.51
(2) Joyful, happy, amused	-1.56 (1.26)	-0.46 (1.13)	-0.54(0.88)	0.02
(3) Sad, downhearted, blue	1.56 (1.50)	0.85 (0.99)	0.92 (1.32)	0.38
(4) Angry, irritated, mad	1.38 (1.26)	1.38 (1.26)	1.00 (1.35)	0.55
(5) Fearful, scared, afraid	2.63 (1.31)	2.46 (0.78)	0.92 (1.04)	0.001
(6) Anxious, tense, nervous	2.37 (1.45)	2.15 (1.14)	0.62 (0.87)	0.001
(7) Disgusted, turned off, repulsed	1.75 (1.39)	1.54 (1.27)	0.31 (1.18)	0.02
(8) Disdainful, scornful, contemptuous	0.75 (0.86)	1.08 (1.44)	0.31 (0.86)	0.16
(9) Surprised, amazed, astonished	1.56 (1.41)	0.85 (1.46)	1.00(1.08)	0.38
(10) Warmhearted, gleeful, elated	-1.69 (1.62)	-0.77(1.03)	-1.08(1.19)	0.12
(1) Interested concentrated alert	0.00(0.89)	-0.31(1.18)	-0.08(166)	0.75
(2) Joyful happy amused	0.13 (1.75)	-0.23(1.01)	-0.08(1.00)	0.75
(2) Sod downbearted blue	0.15(1.75)	0.54 (0.66)	0.85(1.34)	0.75
(4) Angry irritated mad	0.06(0.68)	0.46 (0.52)	0.63(1.54)	0.55
(5) Fearful scared afraid	0.88 (1.36)	100(115)	0.69(1.03)	0.23
(6) Anxious tense nervous	100(137)	0.54 (0.66)	0.46(1.26)	0.26
(7) Disgusted, turned off, repulsed	2.25 (1.48)	2.00 (1.29)	1.85 (1.72)	0.77
(8) Disdainful scornful contemptuous	0.75(0.93)	0.85(1.07)	0.15(0.69)	0.09
(9) Surprised, amazed, astonished	1.50 (1.32)	1.15 (1.28)	1.00 (1.47)	0.65
(10) Warmhearted, gleeful, elated	-0.63 (1.41)	-0.15 (1.57)	-0.77 (2.00)	0.53
Neutral				
(1) Interested, concentrated, alert	-0.31 (0.87)	-0.31 (1.55)	-0.15 (1.52)	0.61
(2) Joyful, happy, amused	-0.56(1.55)	0.31 (0.85)	-0.38 (1.12)	0.17
(3) Sad, downhearted, blue	0.25 (0.86)	-0.15 (0.99)	0.31 (0.75)	0.64
(4) Angry, irritated, mad	-0.06 (0.77)	-0.23 (1.23)	0.31 (1.18)	0.73
(5) Fearful, scared, afraid	-0.06 (0.25)	-0.15 (0.99)	0.00(0.81)	0.91
(6) Anxious, tense, nervous	-0.25 (0.58)	-0.31 (0.95)	-0.23 (0.93)	0.94
(7) Disgusted, turned off, repulsed	0.00(1.41)	-0.31 (0.85)	0.31 (1.11)	0.35
(8) Disdainful, scornful, contemptuous	-0.19 (0.54)	-0.15 (0.90)	0.15 (0.55)	0.30
(9) Surprised, amazed, astonished	-0.19 (1.38)	-0.23 (1.01)	0.31 (1.25)	0.48
(10) Warmhearted, gleeful, elated	-0.25 (2.02)	-0.08 (1.01)	-0.31 (1.60)	0.92

Note. The target item for each emotional film excerpt is presented in bold. Positive values indicate a more intense self-reported feeling after the film excerpt than after the

preceding relaxation session.

[†] Kruskal–Wallis test.

post-operative group (U = 53, p = 0.02) as compared with the healthy control group, while the pre- and post-operative groups did not differ significantly from one another (U = 78.5, p = 0.73).

Finally, for the film excerpt intended to induce a feeling of anger, no significant group effect was observed for the target emotional feeling of anger (DES item 4, see Table 5), however a group effect was found for the non-target emotional feeling of happiness (DES item 2, p = 0.02), and a tendency for the closely-related emotional feeling of joyfulness was also observed (DES item 10, p = 0.07). Quite similarly to what was observed for the film excerpt intended to induce a feeling of fear and for the one intended to induce a feeling of sadness, post hoc pairwise Mann-Whitney tests revealed that the difference was due to a significant lower difference intensity score of happiness (i.e., a lower decrease of self-rated feeling of happiness between the period of film excerpt and the previous relaxation period) in the pre-operative group as compared with the healthy control group (U = 41, p = 0.004), while the post-operative group was in an intermediate position since it did not differ significantly from either the pre-operative group (U = 70.5, p = 0.45), or the healthy controls (U=67, p=0.09). We point out here, without giving further details, that it was the same pattern of differences that was observed for the emotional feeling of joyfulness (DES item 10) for which only a tendency was found.

To summarize, these analyses suggest that STN stimulation affects (1) the feeling of fear and feelings likely to come with such as anxiety and disgust in a situation intended to induce a feeling of fear, and (2) the feeling of sadness and feelings likely to come with such as anxiety in a situation intended to induce a feeling of sadness, even though the difference between the pre- and post-operative group did not reach significance in such a situation.

A fourth series of analyses examined the patterns of response of the three participating groups in order to address the following question: to what extent did the three groups categorized in a similar fashion the different emotional categories? The analysis of a matrix containing for each group the number of cases where one and only one emotional category was ranked first (i.e., number of straight or unmixed categorizations) and the number of cases where 2 emotional categories or more were ranked first equal (i.e., number of mixed categorizations), indicated that globally, that is independently of the kind of emotional excerpt, the distribution of unmixed versus mixed categorizations did not significantly differ across the three groups ($\chi^2(2) = 0.11$, p > 0.95). Note that DES item 1 (interested, concentrated, alert) was excluded from the categorization analyses because this item - which does not refer to a peculiar emotional feeling - generally received a high score and could thus influence the analyses (the three groups of participants globally described themselves as "highly concentrated" and there were no significant differences in their self-reported level of concentration, see Tables 3 and 5). When considering the categorizations for each film excerpt separately, the analyses indicated that the distribution of unmixed versus mixed categorizations did not significantly differ across the three groups for the film excerpts intended to induce "happiness", "anger", "fear", "disgust" and a neutral state (all ps > 0.30). However, for the film excerpt intended to induce "sadness", the distribution of unmixed versus mixed categorizations did significantly differ across the three groups ($\chi^2(2) = 7.55$, p = 0.02). Pairwise comparisons indicated that the difference was due to a significantly higher number of mixed categorizations in the post-operative group as compared with the healthy control group ($\chi^2(1) = 7.53$, p = 0.006), while the pre-operative group was in an intermediate position since it did not significantly differ from either the post-operative group ($\chi^2(1) = 1.42$, p = 0.23), or the healthy controls ($\chi^2(1) = 2.52$, p = 0.11). Thus, the excerpt intended to primarily induce a feeling of sadness induced significantly more blended feelings in the post-operative patients than in the healthy controls which where more straightforward in their categorizations. This result is in line with the lack of differentiation between target and non-target emotional feelings previously observed in the post-operative group as compared with the pre-operative and healthy control groups for the film excerpt inducing "sadness", and is also consistent with the observation that post-operative patients reported a significantly less intense feeling of sadness for the film excerpt inducing "sadness" than the healthy controls.

A last set of analyses examined the variability in the ratings of each DES item across the three groups in order to determine whether differences in the use of the 5-point Lickert-type scale could account for the significant group effects observed. We computed within-participant standard deviations across the 10 DES items for each film excerpt and then averaged these across all film excerpts for each participant. The mean standard deviation for healthy controls was 1.36, compared with 1.20 and 1.27 for the preand post-operative groups respectively. No significant group effect was found in the variability of the ratings (H = 3.33, p = 0.19), indicating that the ratings made by any one group were not more extreme than those made by the other two, and thus suggesting the three groups did not differ in their use of (or ability to use) the scale.

4. Discussion

The purpose of the present study was to examine the effect of STN stimulation on the subjective experience of emotion by comparing the ratings of a pre-operative, a post-operative and a healthy control group in an emotion eliciting procedure using film excerpts.

The results indicated that the group of patients with STN stimulation significantly differed from the pre-operative group and the healthy control group in showing a significant lower level of differentiation between the target feeling (i.e., the more likely to be reported) and non-target feelings for the film excerpts intended to induce a feeling of sadness on the one hand, and a feeling of fear on the other hand. This result was further supported by the analyses in which group differences on each individual DES item of each film excerpt were examined. These analyses indicated that the post-operative group reported a significantly less intense feeling of fear during the film excerpt intended to induce fear as compared with the pre-operative and the control groups, while no significant difference was observed between the pre-operative and control groups. The post-operative group not only differed significantly from the two other groups for the less intense reported feeling of fear but more generally for the less intense mixed feelings that may be induced by a film excerpt intended to induce primarily a feeling of fear as it is the case here for the feelings of anxiety and disgust. Moreover, the post-operative group reported a less intense feeling of sadness, as well as a less intense feeling of anxiety, during the film excerpt intended to primarily induce a feeling of sadness as compared to the control group, although the difference between the pre- and post-operative groups on the one hand, and between the pre-operative and the control groups on the other hand did not reach significance. Consistent with this result and with the observation of a lack of differentiation between target and non-target feelings, the analysis of the patterns of categorization indicated that the post-operative patients were less straightforward and reported more blended feelings than the healthy controls for the excerpt intended to primarily induce a feeling of sadness. Concerning the group differences that were observed for the self-reported feeling of happiness in three different film excerpts (those intended to induce a feeling of fear, a feeling of sadness, and a feeling of anger), they may be interpreted as a result of the significantly higher intensity score of happiness in the healthy controls during the relaxation sessions as compared with the pre-operative group (see Section 3.2.1 Relaxation sessions and Table 3), and to a lesser extent, with the post-operative group even though the difference did not reach significance. Finally, the analyses indicated that the significant group effects observed could not be explained by differences in the use of the 5-point Lickert-type scale since the variability in the ratings was of the same magnitude across the three groups.

To summarize, in a situation supposedly inducing primarily a feeling of fear, a blend of feelings may also be induced and what the present data indicate is that STN stimulation affects not only the feeling of fear but a combination of feelings likely to be induced in such a situation (here feelings of fear, of anxiety and of disgust). Similarly, in a situation supposedly inducing primarily a feeling of sadness, a mixture of feelings may also be induced, and the present data suggest that STN stimulation possibly affects not only the feeling of sadness but a combination of feelings likely to be induced in such a situation (here feelings of sadness and of anxiety), even though this latter result must be interpreted with caution since the difference between the pre- and post-operative groups did not reach significance. In contrast, our results suggest that STN stimulation does not significantly affect the mixed feelings likely to be induced in situations supposedly inducing primarily a feeling of happiness, a feeling of anger, a feeling of disgust, or a neutral state, at least in this sample.

It is noteworthy that there were no significant differences between the three groups regarding age and education and that there were no significant differences between the two PD patient groups regarding disease duration, total levodopa equivalent dose and severity of motor symptoms thus indicating that neither demographical variables nor clinical characteristics could account for the observed effects. In the same way, although the pre- and postoperative groups differed significantly on the semantic fluency test, which is a consistently reported result in the STN stimulation literature (e.g., Dujardin et al., 2004; see the meta-analysis of Parsons et al., 2006), the absence of significant differences between the preand post-operative groups regarding neuropsychological performances and anxiety scores suggests that the group effects observed on subjective emotional experience could not be attributed to differences in general cognitive efficiency, executive functioning, or level of anxiety.

There are a number of limitations that need to be addressed before discussing further the results. First, because the study did not include a measure of participants' mood, the possibility of a confounding effect of mood differences influencing the self-reported feelings cannot be excluded. However, the clinical follow-up of the post-operative patients indicated that there were free of mood disorders, and both the pre- and post-operative groups were within the normal range as for the level of anxiety. Second, it is important to stress that the surgical procedure might have been a traumatic experience that affected the post-operative patients' life in terms of emotional processing, and especially their appraisal of a new threatening and negative event or situation. Although the current study cannot disprove the possibility that the experience of the surgery might have negatively influenced the self-reported feelings in the post-operative group, the fact that these patients were included in the study two years in average after surgery may have however alleviated this potential bias. The only way to exclude such a bias would have been to include another surgical PD patients group in the study stimulated in a different cerebral target than the STN. Another limitation comes from our study design since one could argue that the inclusion of a "stimulation on" versus "stimulation off" condition would have enabled us to draw stronger conclusions as to the stimulation effect. However, it was essential that the patients were in a satisfactory motor condition during the assessment, that is, in their best "on" state (on-drug state and onstimulation) in order to avoid any methodological bias such as a negative impact on the self-reported feelings. We suggest that a within-subject design in which the same patient group is followed longitudinally pre- and post-operatively would be the best way to avoid most of the possible confounding factors and to provide a

stronger account for the stimulation effect. Finally, the fact that we studied parkinsonian brains means that we can make only limited speculations about a possible role of the STN in subjective emotional experience in normal brains. Because to our knowledge, no study has explored the effect of PD disease on the processes underlying the emergence of feeling, the possibility that these processes are disrupted in PD patients cannot be discarded.

The present results are in line with previous studies demonstrating impaired facial expression recognition after STN stimulation in PD patients, and more specifically, impaired recognition of negative emotions (Biseul et al., 2005; Drapier et al., 2008; Dujardin et al., 2004; Schroeder et al., 2004). Interestingly, the present findings globally reproduced the data obtained in a recent work of our group in which a cohort of 17 PD patients followed longitudinally 3 months before and 3 months after STN stimulation showed a specific impairment of recognition of facial expressions of fear and sadness (Drapier et al., 2008). Therefore, the present study along with those quoted above, suggests that STN stimulation does not only affect the recognition of facial emotions but also the subjective experience of emotion with a probable differential effect on negative feelings.

However, the present findings contradict the view that STN stimulation increases emotional processing as suggested in Schneider et al.'s (2003) study. In a "stimulation on" versus "stimulation off" study design, these authors found no stimulation effect in a task of recognition of facial expressions (happy, sad and neutral faces) but reported a stimulation effect in a mood-induction procedure in the sense of a more positive self-reported mood leading to the conclusion that STN stimulation facilitates emotional processing. Several factors may have contributed to the divergence of result with those reported here such as differences in the design and objective of the induction procedure used. The mood-induction procedure used by Schneider et al. (2003) consisted in the presentation of slides of happy or sad facial expressions with the instruction for the PD patients to adjust their emotional state to the perceived emotion whereas the procedure used here was not designed to lead individuals to explicitly adopt a specific mood (i.e., positive or negative) but rather to collect their emotional feelings as they were spontaneously elicited by the presentation of a variety of multimodal and dynamic emotional stimuli (film excerpts). Another possible explanation is that because post-operative patients have difficulties to recognize and/or subjectively experience sadness as a number of studies suggest including ours, they may also have difficulties to adjust their emotional state to facial expressions of sadness leading to a bias toward a more positive self-reported mood. Although interpretations for the discrepant results are speculative and deserve further investigation, the present findings are nevertheless in line with a number of studies demonstrating that STN stimulation affects emotional processing and provide support to the hypothesis according to which the STN is involved in the processing of the subjective experience of emotion.

Subjective feeling is thought to rely on the integration of the different component of emotional processes (Scherer, 2004) implemented in regions distributed in the brain that need to interact and synchronize for the subjective feeling to emerge (Grandjean et al., 2008). Among the cerebral areas well known to be involved in emotional processing, the orbitofrontal cortex is considered to play a critical role in the emergence of the affective value and associated subjective emotional experience of stimuli or events (Rolls & Grabenhorst, 2008). Originally considered to be dedicated to the processing of fearful stimuli or events, the amygdala is more generally seen as a "relevance detector" also involved in the processing of the affective value of stimuli or events (Rolls & Grabenhorst, 2008; Sander, Grandjean, & Scherer, 2005). Interconnections between the orbitofrontal cortex and the amygdala have been evidenced in the monkeys (Ghashghaei et al., 2007) and recent results of our group

clearly demonstrated an influence of the STN on the activity of these two regions (Le Jeune et al., 2008). These data together with the results obtained in the present study thus suggest that the STN, through its connections with these cerebral areas – either direct or indirect – modulates the integration process underlying the emergence of subjective emotional experience.

In this context, impairments in subjective emotional experience observed in the present study may be the result of a dysfunction - or perhaps even a desynchronization - induced by STN stimulation within a largely distributed neuronal network underlying the emergence of subjective feeling, although it remains to be specified whether or not the STN itself is part of such network. In addition, the mechanisms by which STN stimulation interferes with the functioning of cerebral areas underlying the subjective experience of emotion are not yet fully understood. Given the small size of the STN, the stimulating current flow may not be restricted to the targeted sensorimotor STN compartment and may also affect other STN compartments, in particular the limbic one, and possibly the closely connected basal ganglia limbic areas as well as afferent or efferent connections to subcortical and cortical limbic regions, as supported by several neuroimaging studies (Hilker et al., 2004; Le Jeune et al., 2008; Schroeder et al., 2002, 2003). Moreover, although STN stimulation may have an orthodromic effect through a physiological plausible way, it is not excluded that STN stimulation may also have an antidromic effect in an implausible physiological way. Another possible explanation, which does not exclude the previous ones, is that the functional partitioning of the STN is not absolute with probable interactions between subterritories (Joel & Wiener, 1997; Mallet et al., 2007), and as some authors suggest, the STN acts as an integrator, combining the motor, cognitive and emotional components of behaviour which may explain why stimulation of this core structure has effects on motor but also on limbic and/or on associative functions (Mallet et al., 2007).

Our study is the first to suggest that STN stimulation affects the subjective experience of emotion, especially the feeling of fear and blended feelings likely to be induced in a "fearful" situation such as anxiety and disgust, and possibly, the feeling of sadness and blended feelings likely to be induced in a situation of "sadness" such as anxiety, thus providing a preliminary account of the modulation induced by stimulation of a largely distributed neuronal network of cerebral areas underlying the subjective experience of emotion, although the exact nature of the STN contribution within such network remains to be specified. The present results and specifically the differential impact of STN stimulation on the subjective experience of negative emotions need to be confirmed with a larger sample of PD patients with STN stimulation and - as previously suggested - in a within-subject design. In addition, it would be important to control (i) for the natural course of the disease by including a group of non-stimulated matched PD patients assessed twice within the same interval as the group of PD patients with STN stimulation, and also (ii) for the effect of the surgery by including a group of matched PD patients stimulated in a different cerebral target than the STN, as noted above. Finally, it would be interesting to examine the neural correlates of the changes in subjective emotional experience observed after STN stimulation using functional neuroimaging. Because the ability to appropriately perceive, interpret, express and feel emotions is essential for the regulation of interpersonal relationships and social adaptation, further research is needed to fully understand the impact of STN stimulation in the processing of non-motor information.

References

Adolphs, R. (2002). Recognizing emotion from facial expressions: Psychological and neurological mechanisms. *Behavioral and Cognitive Neuroscience Reviews*, 1, 21–62.

- Alexander, G. E., Crutcher, M. D., & DeLong, M. R. (1990). Basal gangliathalamocortical circuits: Parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. *Progress in Brain Research*, 85, 119–146.
- Alexander, G. E., Delong, M. R., & Strick, P. L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience*, 9, 357–381.
- Benabid, A. L., Krack, P. P., Benazzouz, A., Limousin, P., Koudsie, A., & Pollak, P. (2000). Deep brain stimulation in the subthalamic nucleus for Parkinson's disease: Methodologic aspects and clinical criteria. *Neurology*, 55, S40–S44.
- Biseul, I., Sauleau, P., Haegelen, C., Trebon, P., Drapier, D., Raoul, S., et al. (2005). Fear recognition is impaired by subthalamic nucleus stimulation in Parkinson's disease. *Neuropsychologia*, 43, 1054–1059.
- Blin, J., Dubois, B., Bonnet, A. M., Vidailhet, M., Brandabur, M., & Agid, Y. (1991). Does ageing aggravate Parkinsonian disability? *Journal of Neurology, Neurosurgery, and Psychiatry*, 54, 780–782.
- Broggi, G., Franzini, A., Ferroli, P., Servello, D., D'Incerti, L., Genitrini, S., et al. (2001). Surgical Neurology, 56, 89–96.
- Decety, J., & Chaminade, T. (2003). Neural correlates of feeling sympathy. Neuropsychologia, 41, 127–138.
- Drapier, D., Drapier, S., Sauleau, P., Haegelen, C., Raoul, S., Biseul, I., et al. (2006). Does subthalamic nucleus stimulation induce apathy in Parkinson's disease? *Journal* of Neurology, 253, 1083–1091.
- Drapier, D., Péron, J., Leray, E., Sauleau, P., Biseul, I., Drapier, S., et al. (2008). Emotion recognition impairment and apathy after subthalamic nucleus stimulation in Parkinson's disease have separate neural substrates. *Neuropsychologia*, 46, 2796–2801.
- Dujardin, K., Blairy, S., Defebvre, L., Krystkoviac, P., Hess, U., Blond, S., et al. (2004). Subthalamic nucleus stimulation induces deficits in decoding emotional facial expression in Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychi*atry, 75, 202–208.
- Dujardin, K., Defebvre, L., Krystkoviac, P., Blond, S., & Destee, A. (2001). Influence of chronic bilateral stimulation of the subthalamic nucleus on cognitive function in Parkinson's disease. *Journal of Neurology*, 248, 603–611.
- Fahn, S., & Elton, R. (1987). UPDRS developement committee. Unified Parkinson's Disease Rating Scale. Recent Developement in Parkinson's Disease, 2,153–163.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini Mental State": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.
- Funkiewiez, A., Ardouin, C., Caputo, E., Krack, P., Fraix, V., Klinger, H., et al. (2004). Long term effects of bilateral subthalamic nucleus stimulation on cognitive function, mood, and behavior in Parkinson's disease. *Journal of Neurology, Neurosurgery* and Psychiatry, 75, 834–839.
- Ghashghaei, H. T., Hilgetag, C. C., & Barbas, H. (2007). Sequence of information processing for emotion based on the anatomic dialogue between prefrontal cortex and amygdala. *NeuroImage*, 34, 905–923.
 Geday, J., Ostergaard, K., & Gjedde, A. (2006). Stimulation of subthalamic
- Geday, J., Ostergaard, K., & Gjedde, A. (2006). Stimulation of subthalamic nucleus inhibits emotional activation of fusiform gyrus. *NeuroImage*, 33, 706–714.
- Gibb, W. R. G., & Lees, A. J. (1988). The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry*, 51, 745–752.
- Grandjean, D., Sander, D., & Scherer, K. R. (2008). Conscious emotional experience emerges as a function of multilevel, appraisal-driven response synchronization. *Consciousness and Cognition*, 17, 484–495.
- Gross, J. J., & Levenson, R. W. (1995). Emotion elicitation using films. Cognition and Emotion, 9, 87–108.
- Hilker, R., Voges, J., Weisenbach, S., Kalbe, E., Burghaus, L., Ghaemi, M., et al. (2004). Subthalamic nucleus stimulation restores glucose metabolism in associative and limbic cortices and in cerebellum: Evidence from a FDG-PET study in advanced Parkinson's disease. Journal of Cerebral Blood Flow and Metabolism, 24, 7–16.
- Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: Onset, progression, and mortality. *Neurology*, 17, 427–442.
- Hornak, J., Bramham, J., Rolls, E. T., Morris, R. G., O'Doherty, J., Bullock, P. R., et al. (2003). Changes in emotion after circumscribed surgical lesions of the orbitofrontal and cingulated cortices. *Brain*, 126, 1691–1712.
- Houeto, J. L., Mesnage, V., Mallet, L., Pillon, B., Gargiulo, M., Tezenas du Moncel, S., et al. (2002). Behavioural disorders, Parkinson's disease and subthalamic stimulation. *Journal of Neurology Neurosurgery and Psychiatry*, 72, 701–707.
- Izard, C. E., Dougherty, F. E., Bloxom, B. M., & Kotsch, N. E. (1974). The differential Emotions Scale: A method of measuring the meaning of subjective experience of discrete emotions. Nashville: Vanderbilt University, Department of Psychology.
- Joel, D., & Wiener, I. (1997). The connections of the primate subthalamic nucleus: Indirect pathways and the open-interconnected scheme of basal gangliathalamocortical circuitry. *Brain Research Reviews*, 23, 62–78.
- Kleiner-Fisman, G., Herzog, J., Fisman, D. N., Tamma, F., Lyons, K. E., Pahwa, R., et al. (2006). Subthalamic nucleus deep brain stimulation: Summary and metaanalysis of outcomes. *Movement Disorders*, 21, S290–S304.
- Kulisevsky, J., Berthier, M. L., Gironell, A., Pascual-Sedano, B., Molet, J., & Pares, P. (2002). Mania following deep brain stimulation for Parkinson's disease. *Neurology*, 59, 1421–1424.
- Krack, P., Batir, A., Van Blercom, N., Chabardes, S., Fraix, V., Ardouin, C., et al. (2003). Five-Year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *New England Journal of Medicine*, 349, 1925–1934.
- Kühn, A. A., Hariz, M. I., Silberstein, P., Tisch, S., Kupsch, A., Schneider, G. H., et al. (2005). Activation of the subthalamic region during emotional processing in Parkinson disease. *Neurology*, 65, 707–713.

- Kumar, R., Lozano, A. M., Kim, Y. J., Hutchison, W. D., Sime, E., Halket, E., et al. (1998). Double-blind evaluation of subthalamic nucleus deep brain stimulation in advanced Parkinson's disease. *Neurology*, *51*, 850–855.
- Le Jeune, F., Péron, J., Biseul, I., Fournier, S., Sauleau, P., Drapier, S., et al. (2008). Subthalamic nucleus stimulation affects orbitofrontal cortex in facial emotion recognition: A PET study. *Brain*, 131, 1599–1608.
- Limousin, P., Krack, P., Pollak, P., Benazzouz, A., Ardouin, C., Hoffman, D., et al. (1998). Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. New England Journal of Medicine, 339, 1105–1111.
- Luo, Q., Holroyd, T., Jones, M., Hendler, T., & Blair, J. (2007). Neural dynamics for facial threat processing as revealed by gamma band synchronisation using MEG. *NeuroImage*, 34, 839–847.
- Mallet, L., Schüpbach, M., N'Diaye, K., Remy, P., Bardinet, E., Czernecki, V., et al. (2007). Stimulation of subterritories of the subthalamic nucleus reveals its role in the integration of the emotional and motor aspects of behaviour. In *Proceedings of the National Academy of Sciences, Vol. 104* (pp. 10661–10666).
- Mattis, S. (1988). Dementia rating scale. Odessa, FL: Psychological Assessment Resources Inc.
- Nelson, H. E. (1976). A modified card sorting test sensitive to frontal lobe defects. *Cortex*, 12, 313–324.
- Okun, M. S., Raju, D. V., Walter, B. L., Juncos, J. L., DeLong, M. R., Heilman, K., et al. (2004). Pseudobulbar crying induced by stimulation in the region of the subthalamic nucleus. *Journal of Neurology, Neurosurgery, and Psychiatry*, 75, 921–923.
- Parent, A., & Hazrati, L. N. (1995a). Functional anatomy of the basal ganglia. I. The cortico-basal ganglia-thalamo-cortical loop. *Brain Research Revue*, 20, 91–127.
- Parent, A., & Hazrati, L. N. (1995b). Functional anatomy of the basal ganglia. II. The place of subthalamic nucleus and external pallidum in basal ganglia circuitry. *Brain Research Revue*, 20, 128–154.
- Parsons, T. D., Rogers, S. A., Braaten, A. J., Woods, S. P., & Tröster, A. I. (2006). Cognitive sequelae of subthalamic nucleus deep brain stimulation in Parkinson's disease: A meta-analysis. *The Lancet Neurology*, 5, 578–588.
- Perozzo, P., Rizzone, M., Bergamasco, B., Castelli, L., Lanotte, M., Tavella, A., et al. (2001). Deep brain stimulation of the subthalamic nucleus: Behavioral modifications and familiar relations. *Neurological Sciences*, 22, 81–82.
- Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage*, 16, 331-348.
- Philippot, P. (1993). Inducing and assessing differentiated emotion-feeling states in the laboratory. *Cognition and Emotion*, 7, 171–193.
- Quadflieg, S., Mohr, A., Mentzel, H.-J., Miltner, W. H. R., & Straube, T. (2008). Modulation of the neural network involved in the processing of anger prosody: The role of task-relevance and social phobia. *Biological Psychology*, 78, 129–137.
- Reitan, R. M. (1958). Validity of the Trail-Making Test as an indication of organic brain damage. Perceptual and Motor Skills, 8, 271–276.
- Rolls, E. T., & Grabenhorst, F. (2008). The orbitofrontal cortex and beyond: From affect to decision-making. *Progress in Neurobiology*, doi:10.1016/j.pneurobio. 2008.09.001
- Rottenberg, J., Ray, R. R., & Gross, J. J. (2007). Emotion elicitation using films. In J. A. Coan & J. J. B. Allen (Eds.), Handbook of emotional elicitation and assessment (pp. 9–28). New York: Oxford University Press.
- Salgado-Pineda, P., Delaveau, P., Blin, O., & Nieoullon, A. (2005). Dopaminergic contribution to the regulation of emotional perception. *Clinical Neuropharmacology*, 28, 228–237.
- Sander, D., Grandjean, D., Pourtois, G., Schwartz, S., Seghier, M. L., Scherer, K. R., et al. (2005). Emotion and attention interactions in social cognition: Brain regions involved in processing anger prosody. *NeuroImage*, 28, 848–858.
- Sander, D., Grandjean, D., & Scherer, K. R. (2005). A systems approach to appraisal mechanisms in emotion. Neural Networks, 18, 317–352.
- Sauleau, P., Raoul, S., Lallement, F., Rivier, I., Drapier, S., Lajat, Y., et al. (2005). Motor and non motor effects during intraoperative subthalamic stimulation for Parkinson's disease. *Journal of Neurology*, 252, 457–464.

- Schaefer, A., Collette, F., Philippot, P., Van der Linden, M., Laureys, S., Delfiore, G., et al. (2003). Neural correlates of "hot" and "cold" emotional processing: A multilevel approach to the functional anatomy of emotions. *NeuroImage*, *18*, 938–949.
- Schaefer, A., Nils, F., Sanchez, X., & Philippot, P. (in revision). *Multi-criteria assessment of emotional films*.
- Scherer, K. R. (2004). Feelings integrate the central representation of appraisal-driven response organization in emotion. In A. S. R. Manstead, N. H. Frijda, & A. H. Fischer (Eds.), *Feelings and emotions. The Amsterdam symposium* (pp. 136–157). Cambridge: Cambridge University Press.
- Schneider, F., Habel, U., Volkmann, J., Regel, S., Kornischka, J., Sturm, V., et al. (2003). Deep brain stimulation of the subthalamic nucleus enhances emotional processing in Parkinson's disease. Archives of General Psychiatry, 60, 296–302.
- Schroeder, U., Kuehler, A., Haslinger, B., Erhard, P., Tronnier, V., Lange, K., et al. (2002). Subthalamic nucleus stimulation affects striato-anterior cingulate cortex circuit in a response conflict task: A PET study. *Brain*, 125, 1995–2004.
- Schroeder, U., Kuehler, A., Hennenlotter, A., Haslinger, B., Tronnier, V., Pfister, R., et al. (2004). Facial expression recognition and subthalamic nucleus stimulation. *Journal of Neurology, Neurosurgery and Psychiatry*, 75, 648–650.
- Schroeder, U., Kuehler, A., Lange, K. W., Haslinger, B., Tronnier, V., Krause, M., et al. (2003). Subthalamic nucleus stimulation affects a frontotemporal network: A PET study. Annals of Neurology, 54, 445–450.
- Sensi, M., Eleopra, R., Cavallo, M. A., Sette, E., Milani, P., Quatrale, R., et al. (2004). Explosive-aggressive behavior related to bilateral subthalamic stimulation. Parkinsonism and Related Disorders, 4, 247–251.
- Smeding, H. M. M., Speelman, J. D., Koning-Haanstra, M., Schuurman, P. R., Nijssen, P., van Laar, T., et al. (2006). Neuropsychological effects of bilateral STN stimulation in Parkinson's disease: A controlled study. *Neurology*, 66, 1830–1836.
- Spielberger, C. D., Gorsuch, R. L., Luschene, R. E., Vagg, P. R., & Jacobs, G. A. (1993). Manuel de l'inventaire d'anxiété Etat-Trait Forme Y (STAI-Y). Paris: ECPA.
- Stroop, J. R. (1935). Studies of interference in serial verbal reactions. Journal of Experimental Psychology, 18, 643–662.
- Takahashi, H., Koeda, M., Oda, K., Matsuda, T., Matsushima, E., Matsuura, M., et al. (2004). An firm study of differential neural response to affective pictures in schizophrenia. *NeuroImage*, 22, 1247–1254.
- Taylor, S. F., Phan, K. L., Decker, L. R., & Liberzon, I. (2003). Subjective rating of emotionally salient stimuli modulates neural activity. *NeuroImage*, 18, 650–659.
- Temel, Y., Blokland, A., Steinbusch, H. W. M., & Visser-Vanderwalle, V. (2005). The functional role of the subthalamic nucleus in cognitive and limbic circuits. *Progress in Neurobiology*, 76, 393–413.
- Temel, Y., Kessels, A., Tan, S., Topdag, A., Boon, P., & Visser-Vandewalle, V. (2006). Behavioural changes after bilateral subthalamic stimulation in advanced Parkinson disease: A systematic review. *Parkinsonism and Related Disorders*, 12, 265–272.
- Vingerhoets, F. J., Villemure, J. G., Temperli, P., Pollo, C., Pralong, E., & Ghika, J. (2002). Subthalamic DBS replaces levodopa in Parkinson's disease: Two-year follow-up. *Neurology*, 58, 396–401.
- Visser-Vandewalle, V., van der Linden, C., Temel, Y., Celik, H., Ackermans, L., Spincemaille, G., et al. (2005). Long-term effects of bilateral subthalamic nucleus stimulation in advanced Parkinson disease: A four year follow-up study. *Parkin*sonism and Related Disorders, 11, 157–165.
- Voon, V., Kubu, C., Krack, P., Houeto, J.-L., & Tröster, A. I. (2006). Deep brain stimulation: Neuropsychological and neuropsychiatric issues. *Movement Disorders*, 21, S305–S326.
- Westermann, R., Spies, K., Stahl, G., & Hesse, F. W. (1996). Relative effectiveness and validity of mood induction procedures: A meta-analysis. *European Journal* of Social Psychology, 26, 557–580.
- Wildgruber, D., Ackermann, H., Kreifelts, B., & Ethofer, T. (2006). Cerebral processing of linguistic and emotional prosody: fMRI studies. *Progress in Brain Research*, 156, 249–268.