



Vocal emotion decoding in the subthalamic nucleus: An intracranial ERP study in Parkinson's disease



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ABSTRACT

Using intracranial local field potential (LFP) recordings in patients with Parkinson's disease (PD) undergoing deep brain stimulation (DBS), we explored the electrophysiological activity of the subthalamic nucleus (STN) in response to emotional stimuli in the *auditory* modality. Previous studies focused on the influence of *visual* stimuli. To this end, we recorded LFPs within the STN in response to angry, happy, and neutral prosodies in 13 patients with PD who had just undergone implantation of DBS electrodes. We observed specific modulation of the *right* STN in response to anger and happiness, as opposed to neutral prosody, occurring at around 200–300 ms post-onset, and later at around 850–950 ms post-onset for anger and at around 3250–3350 ms post-onset for happiness. Taken together with previous reports of modulated STN activity in response to emotional visual stimuli, the present results appear to confirm that the STN is involved in emotion processing irrespective of stimulus valence and sensory modality.

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1. Introduction

Emotional prosody is defined as suprasegmental changes in the course of a spoken utterance, encompassing intonation, amplitude, envelope, tempo, rhythm, and voice quality (Grandjean, Banziger, & Scherer, 2006). The perception and decoding of emotional prosody has been studied through functional magnetic resonance imaging (fMRI) and patient studies, allowing researchers to delineate a distributed neural network involved in its identification and

recognition (for a recent review, see Witteman, Van Heuven, & Schiller, 2012). Accordingly, models of emotional prosody processing have long postulated the existence of multiple information processing stages related to different levels of representations (Schirmer & Kotz, 2006; Wildgruber, Ethofer, Grandjean, & Kreifelts, 2009). Following the processing of auditory information within the primary auditory regions (Bruck, Kreifelts, & Wildgruber, 2011; Wildgruber et al., 2009), including the activation of predominantly right-hemispheric primary and secondary auditory regions (for a review, see Witteman, van Ijzendoorn, van de Velde, van Heuven, & Schiller, 2011), two prosody decoding steps have been identified. The first step, related to the *representation of meaningful suprasegmental acoustic sequences*, is thought to involve projections from the superior temporal gyrus to the anterior superior temporal sulcus. These cortical structures are thought to represent the so-called temporal voice area that encompasses voice-sensitive neuronal populations (Belin & Zatorre, 2000; Grandjean et al., 2005). In the second step, emotional information

Abbreviations: AC, anterior commissure; BG, basal ganglia; CT, computed tomography; DBS, deep brain stimulation; ERP, event-related potential; f_0 , fundamental frequency; fMRI, functional magnetic resonance imaging; FWER, familywise error rate; IAPS, International Affective Picture System; LFP, local field potential; PC, posterior commissure; PD, Parkinson's disease; STN, subthalamic nucleus.

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derived at the level of the superior temporal sulcus is made available for higher-order cognitive processes mediated by the right inferior frontal gyrus (Frühholz & Grandjean, 2013) and orbitofrontal cortex (Ethofer et al., 2006; Grandjean, Sander, Lucas, Scherer, & Vuilleumier, 2008; Sander et al., 2005; Wildgruber et al., 2004). This step is thought to involve higher representation such as the *explicit evaluation of vocally expressed emotions*. In addition to this frontotemporal network, increased activity has been observed within the amygdala in response to emotional prosody (Frühholz, Ceravolo, & Grandjean, 2012; Grandjean et al., 2005; Sander et al., 2005). Furthermore, although they were not the focus of these studies, the involvement of subcortical regions (other than the amygdala) such as the thalamus (Wildgruber et al., 2004) and the basal ganglia (BG) in the processing of emotional prosody has also been reported. The involvement of the caudate and the putamen has repeatedly been observed in healthy participants by using fMRI and in brain-damaged patients by using the electroencephalographic method (Bach et al., 2008; Grandjean et al., 2005; Kotz et al., 2003; Morris, Scott, & Dolan, 1999; Paulmann & Kotz, 2008). More recently, studies exploring the effects of subthalamic nucleus (STN) deep brain stimulation (DBS) in Parkinson's disease (PD) have highlighted the involvement of the STN in the brain network subtending vocal emotions (Bruck, Wildgruber, Kreifelts, Kruger, & Wachter, 2011; Péron, Cekic, et al., 2015; Péron, Frühholz, Vérin, & Grandjean, 2013; Péron et al., 2010).

From convergent evidence in the latter literature, Péron et al. (2013) have posited that the STN would coordinate neural patterns, either synchronizing or desynchronizing the activity of the different neuronal populations responsible for specific emotion components. They claim that the STN plays “*the role of neural rhythm organizer at the cortical and subcortical levels in emotional processing, thus explaining why the BG are sensitive to both the temporal and the structural organization of events*” (Péron, Frühholz, Ceravolo, & Grandjean, 2015; Péron et al., 2013). This model suggests that the BG and, more specifically, the STN, are sensitive to rhythm *because of their intrinsic functional role of rhythm organizer, or coordinator of neural patterns*. In a more operational way, this model hypothesizes that (i) the STN is involved in all stages of emotional processing, and (ii) the STN is involved in emotion processing irrespective of stimulus valence (positive or negative) and sensory modality (e.g., visual or auditory). To date, these two hypotheses have yet to be tested at the neurophysiological level in the vocal modality.

Studies featuring intracranial recordings of local field potentials (LFPs) in the STN in response to emotional stimuli have investigated the impact on the STN's electrophysiological activity of processing *visual* stimuli that induce affective states. These studies have consistently reported event-related desynchronization of alpha activity within the STN between 1000 and 2000 ms post-onset in response to emotional stimuli in the form of both pleasant and unpleasant images drawn from the International Affective Picture System (IAPS) (Brucke et al., 2007; Huebl et al., 2011; Kühn et al., 2005). This effect has been shown to be correlated with strength of *valence* (both positive and negative), but not *arousal* (Brucke et al., 2007). Furthermore, in the presence of depressed mood, this effect is reduced for positive emotions, but enhanced for negative emotions (Huebl et al., 2011), supporting the idea that the bias toward negative emotions in depression has an electrophysiological signature in this region (Péron et al., 2011). Taken together, these results confirm the STN's functional role in emotion processing. However, the use of *visual* (emotional) material introduces several confounding factors. First, the pictures used in studies exploring the visual modality (see, for example, Benedetti et al., 2004; Kühn et al., 2005) are often not controlled for low-level physical features (brightness, contrast, spatial frequency, etc.). This is methodologically problematic, particularly for the analysis of

neural oscillations in response to emotional stimuli, as these features are known to influence emotional perception and related brain activities (Delplanque, N'Diaye, Scherer, & Grandjean, 2007). Moreover, the emotional effects reported in the visual domain could be explained either by deficits in visual exploration related to oculomotor abnormalities (Fawcett, Dostrovsky, Lozano, & Hutchison, 2005), or by specific oculomotor patterns generated during the visual exploration of visual emotional stimuli (Van Reekum et al., 2007).

For all these reasons, previous research has left several questions unanswered, and it has yet to be determined whether the STN's electrophysiological changes in response to emotional stimuli are modality-specific or supramodal, as suggested by behavioral studies exploring the emotional effects of STN DBS in PD (see Péron et al., 2013 for an exhaustive review). To the best of our knowledge, the only study in the *auditory* modality was recently performed by Eitan et al. (2013). They reported microelectrode recordings in the STN of 17 PD patients in response to emotional prosody stimuli (onomatopoeias from the Montreal Affective database, Belin, Fillion-Bilodeau, & Gosselin, 2008). The authors reported ventral STN activity in response to emotional versus neutral auditory material, with increases of oscillations observed solely in the *right* STN; this difference has not been demonstrated in the *left* STN. However, similar to studies of the facial modality, this study did not control for low-level physical features known to have an impact on emotional prosody (e.g., fundamental frequency [f_0], energy). Moreover, as mentioned earlier, the authors used single-unit recordings, and to the best of our knowledge, no previous study investigated LFPs in response to emotional auditory stimuli. The latter type of signal presents the advantage, as compared to single-unit recordings, to reflect the averaged dendrosomatic activity of synaptic signals of large neuronal population (Buzsáki, Anastassiou, & Koch, 2012).

In this context, the aim of the present study was thus to examine the influence of the processing of (both positive and negative) emotional prosody stimuli on event-related potentials (ERPs) in the STN, controlling for low-level physical features crucial for emotional prosody decoding. To this end, we explored the electrophysiological activity (LFPs) of the STN in response to angry, happy, and neutral prosodies, but also to acoustically matched nonhuman synthesized stimuli, in 13 PD patients.

The operational hypotheses are mainly based on Péron and colleagues' recent model of the STN's functional role in emotional (prosody) processing (2013), together with previous results from studies featuring intracranial recordings in the STN in response to emotional stimuli (Brucke et al., 2007; Huebl et al., 2011; Kühn et al., 2005). Péron and colleagues' model (2013) suggested that the STN would be involved in all stages of emotional processing, irrespective of stimulus valence (positive or negative) and sensory modality. Accordingly, in the present study we expected to observe STN modulation for both positive and negative emotional prosody stimuli.

Moreover, this model hypothesizes that the STN would participate in the acquisition and expression of sequential, repetitive, motor, and cognitive behaviors, as well as emotional behaviors, elicited by external or internal triggers, recruiting and synchronizing the activity of the cortical and subcortical structures required for the relevant process, depending on the nature of the environmental cues and how the individual appraised such characteristics. As a consequence, “*several different [STN] temporal dynamics [are speculated]: (i) sustained, synchronized activity, leading to the creation of a new functional neural pattern; (ii) early, transient synchronized activity, resulting in the activation of an overlearned/innate pattern; and (iii) later, transient synchronized activity as part of a mechanism that inhibits the overlearned pattern (involving the prefrontal regions)*” (Péron et al., 2013, p. 370). Given that we do not explore

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