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Electrophysiological registration of phonological perception in the subthalamic nucleus of patients with Parkinson's Disease

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ABSTRACT

Phonological processing is usually associated with the activation of cortical areas, especially in the left cerebral hemisphere. This study examined if phonologically elicited evoked potentials can be recorded directly from the subthalamic nucleus in patients with Parkinson's Disease (PD). Seven PD patients who had undergone implantation of deep brain electrodes for the stimulation of the subthalamic nucleus were included. Local field potentials were recorded in a pre-attentive auditory phonological task, an attentive auditory phonological discrimination task, and a word recognition task. Auditory evoked potentials related to phonological, but not lexical processing, could be demonstrated in the subthalamic nucleus for all three tasks. Only minor changes were found after levodopa administration.

This study demonstrates that the subthalamic nucleus is involved in early phonological perception, which puts the subthalamic nucleus in a position to modify phonological perception in a larger cortico-subcortical network.

1. Introduction

Phonological perception and production have traditionally been correlated with activity within cortical areas. Production of the more automatic and overused aspects of syllabification involves diffuse and bilateral processing while less automatic and more online syllable production involves a network of unilateral left hemispheric structures, especially the inferior frontal and temporal lobes (Hartsuiker, Bastiaanse, Postma, & Wijnen, 2003). Phonological perception is similarly associated with left hemisphere activation whereby phoneme discrimination is supported by the sublexical route, projecting from the posterior superior temporal gyrus via the inferior parietal cortex to the motor cortex and inferior frontal gyrus (Hickok & Poeppel, 2004, 2007; Saur et al., 2008) and word recognition is supported by the lexico-semantic route, projecting from the anterior parts of the superior temporal gyrus and sulcus to the inferior frontal gyrus (DeWitt & Rauschecker, 2012). Neurobiological research of serial order in language confirms this neuroanatomical network description and adds that different mechanisms underlie the processing of phoneme sequences within syllables and words on the one hand and the processing of word and morpheme sequences in sentences on the other hand. These mechanisms are described as synfire chains, consisting of sets of connected neurons, in which each synfire chain defines a precise spatiotemporal pattern of neuronal activity. The synfire chains may overlap and cross with other chains while keeping separate the spatiotemporal activity patterns they organize (Pulvermüller & Shtyrov, 2009).

Cortical neuron ensembles are strongly connected to subcortical neurons and their activity seems to be regulated by subcortical neurons during language tasks (Pulvermüller, 2003). This was elegantly shown in a neuroimaging study of the postsynaptic dopaminergic receptors in the striatum by means of 11C-raclopride, which demonstrated that both a more accurate and a fast phonological processing are accompanied by a reduced dopamine requirement in the caudate nucleus and putamen respectively (Tettamanti et al., 2005).

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In addition to a functional neuroanatomical and biological approach, the assumption of a subcortical involvement in phonological tasks is also corroborated by findings from ontogenetic research as well as from clinical observations. Ontogenetic evidence for a subcortical involvement in primary sound processing is based on the similarity in the underlying neural mechanisms in human and bird vowel perception/production (Beckers, Nelson, & Suthers, 2004; Ohms, Escudero, Lammers, & ten Cate, 2012). Moreover, the basal ganglia were shown to play a crucial role in the development and maturation of language, in particular in phonological rule processing (De Diego-Balaguer et al., 2008; Janowsky & Nass, 1987; Rektorova, Aarsland, Chaudhuri, & Strafella, 2012). In clinical pathology the subcortical involvement in phonological processing has repeatedly been objectified in syndromes such as Parkinson's Disease (PD) (Murdoch, 2009).

In PD a number of auditory perceptual changes have been reported. The auditory phonological processing disturbances in PD have been described as perception changes in loudness (Ho, Bradshaw, & Iansek, 2000), a reduced ability to discriminate changes in frequency and amplitude (Pekkonen, 2000; Troche, Troche, Berkowitz, Grossman, & Reilly, 2012), impairments in word recognition (Gräber, Hertrich, Daum, Spieker, & Ackermann, 2002), insensitivity to emotional prosody conveyed by tone of voice (Pell, 1996; Pell, Cheang, & Leonard, 2006; Pell & Leonard, 2003) and inability to detect syntactically relevant prosodic markers such as segmental stress patterns that mark nouns and verbs (Kotz, Schwartze, & Schmidt-Kassow, 2009). Two mechanisms underlying these perceptual deficits can be proposed:

1. The fact that the prodromal stage of Parkinson's Disease is accompanied by lewy body pathology affecting the auditory interneurons in the brainstem (Braak & Braak, 2000). As consonants are brief and rapidly changing aspects of speech, the perception of which is regulated by the brainstem, lower level auditory deficits as a consequence of lewy body pathology can lead to difficulties in the perception of consonants. It is however unclear to what extent such lower level auditory deficits influence higher level linguistic processes (Tallal, 1980).
2. The hypothesis of the frontostriatal dysfunction as a consequence of dopaminergic denervation, disrupting the ability to discriminate tones (Burton & Small, 2006; Pekkonen, Jousmäki, Reinikainen, & Partanen, 1995). The functional reorganization mechanism underlying this disruption is described as an increased connectivity between the right putamen and the right supramarginal gyrus, correlated with more variability of pitch, and an enhanced connectivity between the right posterior superior temporal gyrus and the right inferior parietal lobule, correlated with increased speech loudness (Rektorova et al., 2012).

Most likely a combination of the frontostriatal and brainstem theories contributes to the auditory speech processing problems in people with Parkinson's Disease.

Whether the STN plays a dominant role in phonological processing or rather fulfills a role as a relay nucleus in the complex phonological network is not known. Direct local field potentials (LFP) registration in the STN could be a reliable method to obtain information about phonological activity in this nucleus. From an ethical perspective this method can only be used in people who undergo deep brain stimulation (DBS) in the context of neuronal pathology, e.g. PD. In an advanced stage of PD, STN deep brain stimulation is established as an effective surgical treatment for the characteristic motor symptoms such as bradykinesia (Limousin et al., 1995; Weaver et al., 2009). DBS stimulation of the dorsolateral sensorimotor area in the STN is assumed to result in the best motor outcome (Richardson, Ostrem, & Starr, 2009). DBS of the STN can induce speech and language changes, which have often been explained by current spread to nonmotor parts of the STN or adjacent tracts, such as the corticospinal tract (Saint-Cyr, Trépanier, Kumar, Lozano, & Lang, 2000; Woods, Fields, & Tröster, 2002). Most likely these effects are dependent on electrode location and modification of stimulation settings (Tripoliti et al., 2008). The most reported language side effects of STN DBS are phonemic and verbal fluency changes (Parsons, Rogers, Braaten, Woods, & Tröster, 2006), with the stimulation of the ventral contacts in the STN being more frequently associated with decreased letter fluency than category fluency performance (Mikos et al., 2011). Anyway, in contrast to DBS of the STN, stimulation of the pedunculopontine nucleus does not affect phonology and lexical semantics (Zanini et al., 2009), which supports the hypothesis of separate subcortical phonological networks in which the STN plays a crucial role.

The impact of dopaminergic administration on verbal performance in people with Parkinson's Disease is variable (Morrison et al., 2004; Schroeder et al., 2003). Levodopa-induced speech and language changes have to be interpreted with respect to hemisphere-related language dominance theory, handedness versus lateralization of the Parkinsonian symptoms and the fluctuations between hypo- and hyper-dopaminergic states. In hypodopaminergic conditions the neuronal activity within the cortico-subcortical circuits is hypersynchronized. During hyperdopaminergic states, which can be induced by dopaminergic treatment, asynchronous neuronal activity is enhanced. Both conditions can induce defect signaling and lead to behaviorally dysfunctional outcome in motor and cognitive functions (Costa, 2007). Alternatively the dopaminergic effects can be explained as a change in speed of information processing, which may subsequently affect language function (Angwin, Chenery, Copland, Murdoch, & Silburn, 2007). With the aim of better understanding the perceptual phonological function of the STN, the present study focuses on a direct recording of local field potentials in the STN during several phonological paradigms. The STN local field potential activity was recorded in seven patients with advanced PD who had undergone electrode implantation for DBS in the STN. In order to investigate the influences of levodopa on phonological perception in the STN, five of the seven patients were studied in both medication off- and on-conditions.

2. Materials and methods

2.1. Subjects

Seven patients (3 men, 4 women) with a clinical diagnosis of probable idiopathic PD were included in this study. Their ages varied between 47 and 69 years with a mean of 59 years. All patients had been treated with levodopa for a long time, some in combination with other medications. Due to motor fluctuations with identifiable off and on periods DBS was considered. All patients were extensively examined preoperatively. This examination included neurological assessment (UPDRS) (Fahn, Elton, & Committee, 1987) in on and off stages with video-monitoring, neuropsychological testing, psychiatric evaluation, cerebral MRI, DAT scan and flow-SPECT, as well as neurolinguistic testing. None of the patients had unstable medical diseases other than Parkinson's Disease. Cognitive dysfunction exceeding the well-known deficits of Parkinson's Disease and major psychiatric problems were absent in all. Pre-operative neurolinguistic testing demonstrated the presence of hypokinetic dysarthria in all participants. The presence of aphasic symptomatology was excluded in all patients.

All participants were right-handed, as verified with the Dutch Handedness Inventory (Van Strien, 2012). Two of the seven