Speech production in Parkinson's disease: neuroimaging findings

Serge Pinto
Laboratoire Parole et Langage, CNRS UMR6057, Aix-en-Provence
serge.pinto@lpl.univ-aix.fr

Introduction

Dysarthric speech is one of the frequent signs of Parkinson's disease (PD), which appears generally in the later stage of the disease. The description of Parkinsonian dysarthria is classically a ″monotony of pitch, monotony of loudness, reduced stress, short phrases, variable rate, short rushes of speech, and imprecise consonants″ (Darley *et al.*, 1975). These characteristics have been attributed to the weakness and slowness of movement (referred respectively as hypokinesia and bradykinesia), rigidity and tremor at rest. Any or all components of speech production may be affected, including alterations of the respiratory, phonatory and articulatory systems. The progressive dopaminergic cell loss of the nigro-striatal pathway, projecting from the substantia nigra pars compacta to the striatum, is the main cerebral lesion and notably, the origin of the motor loop dysfunction involving the basal ganglia (Alexander *et al.*, 1990). This denervation leads to the appearance of Parkinsonian motor symptoms among which is the alteration of speech.

Cerebral activations associated with motor tasks in Parkinson's disease

Recent findings revealed that dysfunctions observed during motor speech tasks do not parallel those associated with limb movements.

Upper limb movements - During the execution of a manual, freely chosen, unilateral motor task, underactivation (*i.e* a reduction of regional cerebral blood flow) was found in the supplementary motor area (SMA), dorsolateral prefrontal (DLPFC) and anterior cingulate cortices of PD patients compared to normal subjects (Playford *et al.*, 1992). These cerebral areas are respectively the main output projections of the basal ganglia to the motor, associative and limbic loops. Conversely, the primary motor (M1), parietal and lateral premotor cortices were normally activated. Studies have demonstrated an overactivation involving, among others, the lateral cerebellum-parietal-premotor cortex circuitry (Samuel *et al.*, 1997), as potentially a compensation for the decreased activation of the basal ganglia motor loop. M1 cortex, both ipsi- and contralateral to the limb movement, may also be overactivated in PD even in early stages of the disease (Sabatini *et al.*, 2000). These abnormal activation patterns depend obviously on the nature of the task: during an externally-cued, sequential and repetitive motor task, the SMA is normally activated in PD while the M1 cortex and the cerebellum are underactivated (Turner *et al.*, 2003). All these data together represent the commonly accepted background that characterises PD cerebral dysfunctions associated with (proximal) limb movements.

Speech movements - Liotti *et al.* (2003) showed that abnormalities of brain activation associated with PD speech were essentially represented by an overactivation of orofacial M1 cortex, inferior lateral premotor cortex and SMA. Another study showed that in PD, there is 1/ a lack of activation in the right orofacial M1 cortex and bilateral cerebellar hemispheres, 2/ an abnormal increased of haemodynamic response in the right superior premotor cortex and bilateral dorsolateral prefrontal cortex (DLPFC), and 3/ an overactivation of the SMA (Pinto *et al.*, 2004a). The authors suggested that Parkinsonian dysarthria is associated with an altered recruitment of the principal brain motor regions (orofacial M1 cortex, cerebellum), and an increased involvement of premotor and prefrontal cortices (DLPFC, SMA, superior premotor cortex). This would represent either a compensatory phenomenon or the inherent activation pattern underlying brain dysfunctions of PD dysarthria. In both studies, the activation patterns dids not parallel those associated with hand motor tasks and may explain the frequent therapeutical challenge encountered by the clinician who has to deal with the heterogenous

responses of limb and speech movements to pharmacological and surgical therapies. Furthermore, evolution of the disease along time is concomitant with aggravation of dysarthria, which suggests that it is also linked to the increasing severity of cerebral non-dopaminergic lesions. Thus, PD dysarthria physiopathology cannot be restricted to the alteration of the motor basal ganglia loop: the cerebellum-M1 cortex circuitry may also play a key-role in the appearance of dysarthric spech in PD.

Towards a better understanding of PD dysarthria physiopathology: what should we learn from the deep brain stimulation experience

Improvement of individual speech parameters (Dromey *et al.*, 2000 ; Gentil *et al.*, 2001 ; Pinto *et al.*, 2003) following stimulation of the subthalamic nucleus (STN), which is recognised as one of the most efficient surgical treatment for Parkinsonian signs, is often not sufficient to achieve substantial improvement of speech intelligibility (Rousseaux *et al.*, 2004 ; Törnqvist *et al.*, 2005). Motor control of the overall anatomo-functional system underlying speech production, *i.e.* the pneumo-laryngo-articulatory coordination, does not seem to be sensitive to the modification of neuronal activity within the basal ganglia and subthalamic areas induced by the surgical procedure. Apart from the interpretation we already addressed in terms of implication of the cerebello-cortical circuitry involvement, the current spread towards fibres of the cortico-bulbar tract, which innervates essentially the orofacial musculature, has to be also taken into account. This concept also includes other neighbouring structures that should not be concerned by the chronic electrical stimulation around the STN: thalamus, cerebello-thalamic fibres or even substantia nigra *pars reticulata*, Inadequate stimulation parameters or localisation represent issues that have to be dealt with to ensure the optimal stimulation adjustment (Pinto *et al.*, 2005).

Conclusions

So far, only two positron emission tomography (PET) studies are available in regards to the cerebral activations associated with Parkinsonian dysarthria. Even if important issues have been addressed, it is still difficult to conclude on the cerebral changes related to PD dysarthria, still precluding PD dysarthria management by the clinician and its acceptance by the patient. In this context, neuroimaging is a useful and promising technique able to further our knowledge regarding dysarthria, particular and highly disabling sign among PD motor signs.

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