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# The role of the motor system in action naming in patients with neurodegenerative extrapyramidal syndromes

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## ABSTRACT

Previous studies of patients with brain damage have suggested a close relationship between aphasia and movement disorders. Neurodegenerative extrapyramidal syndromes associated with cognitive impairment provide an interesting model for studying the neural substrates of cognitive and motor symptoms.

In this review, we focused on studies investigating language production abilities in patients with Parkinson's disease (PD), Corticobasal Syndrome (CBS) and Progressive Supranuclear Palsy (PSP). According to some reports, these patients exhibit a reduction in performance in both action and object naming or verb production compared to healthy individuals. Furthermore, a disproportional impairment of action naming compared to object naming was systematically observed in patients with these disorders.

The study of these clinical conditions offers the unique opportunity to examine the close link between linguistic features and motor characteristics of action. This particular pattern of language impairment may contribute to the debate on embodiment theory and on the involvement of the basal ganglia in language and in integrating language and movement.

From a translational perspective, we suggest that language ability assessments are useful in the clinical work-up, along with neuropsychological and motor evaluations. Specific protocols should be developed in the near future to better characterize language deficits and to permit an early cognitive diagnosis. Moreover, the link between language deficits and motor impairment opens a new issue for treatment approaches. Treatment of one of these two symptoms may ameliorate the other, and treating both may produce a greater improvement in patients' global clinical conditions.

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## 1. Introduction

Parkinson's disease (PD), Corticobasal Syndrome (CBS) and Progressive Supranuclear Palsy (PSP) are well recognised neurodegenerative extrapyramidal syndromes that are often associated with cognitive impairment (Armstrong et al., 2013; Burrell, Hodges, & Rowe, 2014; Davis & Racette, 2016).

PD is the second most prevalent neurodegenerative disease, exceeded only by Alzheimer's disease (AD) (Mayeux, 2003). Clinically, PD is characterized by resting tremor, rigidity, bradykinesia, gait impairment, and postural instability. The primary clinical feature of patients with PD is motor impairment, but cognitive impairment, mood disorders and sleep disturbances often occur over the disease course (Chaudhuri & Schapira, 2009; Kalia & Lang, 2015; Lees, Hardy, & Revesz, 2009; Litvan et al., 2012; Padovani, Costanzi, Gilberti, & Borroni, 2006). Indeed, although distinctive motor symptoms have been described in patients with PD for centuries, cognitive impairment has only recently been recognized as a central feature (Davis & Racette, 2016). In patients with advanced PD, the prevalence of dementia is more than 80% (Hely, Reid, Adena, Halliday, & Morris, 2008) and approximately 30% of patients with PD experience mild cognitive impairment (Litvan et al., 2011). A number of risk factors associated with the development of cognitive impairment have been suggested, such as age, disease duration, a rigid-akinetic phenotype, neuro-vegetative symptoms and Rapid eye movement (REM) sleep behavioural disorders (Anang et al., 2014; Vasconcellos & Pereira, 2015). The pattern of cognitive impairment is related to the more affected side. Patients with predominantly right-side motor symptoms more frequently show problems in language-related tasks and verbal memory, whereas patients with predominantly left-side motor symptoms exhibit worse performances in spatial attention, visuospatial-orienting memory and mental imagery. Notably, difficulties in executive functions and attention have been shown to be unrelated to motor symptom laterality (Verreyt, Nys, Santens, & Vingerhoets, 2011). Indeed, dementia conversion in patients with PD is predicted by performances on fronto-executive tasks (Olde Dubbelink et al., 2014). Accordingly, progression to dementia is associated with more severe cortical thinning in frontal and temporo-parietal cortices (Mak et al., 2015).

In patients with CBS and PSP, cognitive impairment represents an early feature, which is mainly defined by deficits in frontal functions. CBS is a neuropathologically heterogeneous disorder, and different pathological hallmarks are recognised at autopsy (Shelley, Hodges, Kipps, Xuereb, & Bak, 2009). Indeed, we refer to CBS according to the clinical syndrome, which is characterized by varying combinations of stiffness, clumsiness, dystonia, orobuccal and limb apraxia, alien limb phenomenon, cortical sensory loss, visual or sensory hemineglect, myoclonus and language deficits (Armstrong et al., 2013). CBS is associated with a pattern of brain atrophy that involves prefrontal and parietal areas, as well as atrophy of other cortical and subcortical structures involved in action organization and motor control (Armstrong et al., 2013; Borroni et al., 2008; Whitwell et al., 2010). The clinical picture of CBS has recently been shown to be caused by different

pathological conditions, namely corticobasal degeneration with extensive neuronal and glial tau-positive cytoplasmic inclusions, Alzheimer's disease (AD) pathology and, in some cases, TDP-43 pathology (Boeve et al., 1999). More recently, revised clinical criteria have attempted to predict corticobasal degeneration based on the clinical characteristics. In addition to the proper CBS clinical characteristics described above, the new criteria have introduced CBS with the agrammatic variant of the primary progressive aphasia phenotype when prominent language disturbances are present (Armstrong et al., 2013). Indeed, asymmetric fronto-parietal atrophy is a hallmark of CBS, and language disturbances are usually observed in patients with left-sided atrophy (Borroni et al., 2008). Patients with CBS and the agrammatic variant of the primary progressive aphasia phenotype show grammatical simplification, with relatively well-preserved single word comprehension, errors in speech production (apraxia of speech) and effortful, halting speech (Armstrong et al., 2013).

PSP is the second most common cause of neurodegenerative extrapyramidal syndrome after PD. The classical PSP syndrome is widely recognized by neurologists, and most frequently presents as a symmetric, akinetic-rigid syndrome, vertical supranuclear gaze palsy, prominent postural instability and falls (Stamelou et al., 2010). However, several variants in the clinical presentation of pathologically confirmed PSP have been recently described, complicating the early differential diagnosis (Stamelou et al., 2010). Thus, a subgroup of patients with PSP exhibits a predominantly frontal presentation at onset that resembles frontotemporal dementia and then progresses into typical PSP over the course of the disease (Donker Kaat et al., 2007).

Despite the differences in cortical involvement, PD, CBS and PSP are characterised by basal ganglia atrophy (Draganski & Bhatia, 2010). In addition to regulating motor control, the basal ganglia are crucial elements in language functions, further supporting the hypothesis that language abilities change in these patients (Leisman, Braun-Benjamin, & Melillo, 2014). Thus, studies of language abilities in patients with neurodegenerative extrapyramidal syndromes are critical for characterising the core deficits, defining intervention approaches and obtaining additional information regarding the association between motor abilities and linguistic processing of actions.

These premises prompted the present review, which is aimed at evaluating one of the often neglected aspects of cognitive impairment in patients with PD, CBS and PSP, namely language profiles and naming abilities. The ability to recognise patients with language disturbances and their relationships with motor impairment is essential for providing possible interventions and predicting prognostic outcomes.

## 2. Background: noun and verb processing

Words belong to different grammatical classes, and the two most basic word classes are nouns and verbs. All languages distinguish between nouns and verbs with syntactic and morphological implications (Druks, 2002). Grammatical classes are considered an organizational principle of lexical knowledge (Caramazza & Hillis, 1991; Laudanna & Voghera,

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