Cognitive dysfunction and dementia in Parkinson’s disease

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Summary. Parkinson’s disease (PD) is a slowly progressive neurodegenerative disorder mainly characterized by degeneration of dopaminergic neurons in the substantia nigra and the ventral tegmental area, in combination with a varying loss of central noradrenergic ( locus coeruleus), cholinergic (nucleus basalis of Meynert) and serotonergic (dorsal raphe nuclei) integrity, leading to a multitude of motor and non-motor behavioral disturbances.

Apart from the clinical motor hallmarks, in the early stages of disease, subtle cognitive dysfunction might be seen comprising mainly executive dysfunction, with secondary visuospatial and mnemonic disturbances. In about 20–40% of patients, these problems may eventually proceed to dementia, which constitutes an important risk factor for caregiver distress, decreased quality of life and nursing home placement. Dementia in PD is typically characterized by a progressive dysexecutive syndrome with attentional deficits and fluctuating cognition, often accompanied by psychotic symptoms. It is thought to be the result of a combination of both subcortical and cortical changes. PD-related dopaminergic deficiency in the nucleus caudatus and mesocortical areas (due to degeneration of projections from the substantia nigra and ventral tegmental area) and cholinergic deficiency in the cortex (due to degeneration of ascending projections from the nucleus basalis of Meynert), combined with additional Alzheimer-pathology and cortical Lewy bodies, may greatly contribute to dementia.

Current treatment of dementia in PD is based on compensation of the profound cholinergic deficiency. Recent studies with the cholinesterase inhibitors galantamine, donepezil and rivastigmine show promising results in improving cognition and ameliorating psychotic symptoms, which must further be confirmed in randomized controlled trials.

Keywords: Parkinson’s disease, cognition, dementia.
Introduction

Parkinson’s disease is a slowly progressive neurodegenerative disease, in which dopaminergic neurons in the substantia nigra and the ventral tegmental area degenerate, leading to dopaminergic deficiency in the striatum and mesocorticocolimbic areas. In addition to degeneration of the dopaminergic system, in PD other ascending subcortical neurotransmitter systems are affected as well: the cholinergic system (nucleus basalis of Meynert), the noradrenergic system (locus coeruleus) and serotonergic system (dorsal raphe nuclei) (Jellinger, 1999). The cardinal motor symptoms are brady(hypo-)kinesia, tremor, rigidity and postural instability. Non-motor symptoms mainly comprise autonomic disturbances, depression, cognitive dysfunction/dementia and psychotic symptoms. As a rule, these symptoms are often more important in determining the quality of life of patients and caregivers than the motor disturbances.

Dementia in PD constitutes not only an important factor for caregiver distress and nursing home placement (Aarsland, 2000, 1999), but is also associated with increased mortality (independent of severity of motor symptoms) (Levy, 2000). As these symptoms are potentially treatable, identification is of major clinical importance both for the patients and their caregivers and may enable the Parkinson’s disease patient to maintain living at home for a longer period. Additionally, postponement of nursing home placement can lead to substantial reductions in healthcare costs.

Cognitive deficits in non-demented PD patients

Cognitive impairment is often associated with PD, although deficits may be relatively subtle and not clinically apparent, or not overtly affect daily functioning. However, when compared to controls, subtle to prominent cognitive impairment is almost always found in PD patients. A wide variety of cognitive deficits has been described in non-demented PD patients, the most prominent of which is a deficit in executive function.

Executive function is a broad term used to describe a range of cognitive functions involved in the realisations of goal-directed, adaptive behaviour in response to new, challenging environmental situations, including attention, inhibition, task management, planning, monitoring and coding (Smith, 1999). A dysexecutive syndrome, resembling cognitive deficits found in frontal lobe patients (Rowe, 2002; Rogers, 1998a), is thought to be at the heart of cognitive dysfunction and dementia in PD and is usually one of the earliest cognitive symptoms found in PD (Dubois, 1997).

Besides executive dysfunction, there is considerable evidence of deficits in visuospatial function in non-demented PD, even when tests contain few motor components (Hovestadt, 1987; Boller, 1984; Bowen, 1972). Most authors, however, believe visuospatial dysfunction to be the result of the high cognitive demand that is usually required by such tasks. Indeed, with the possible exception of judgment of line orientation, it would appear that visuospatial dysfunction in PD can be readily explained by the demand of visuospatial tasks on executive functions such as planning and (shifting of) attention (Bondi, 1993; Raskin, 1992; Ogden, 1990; Ransmayr, 1987; Brown, 1986).