

PARKINSONISM WITH COGNITIVE IMPAIRMENT

LUIGI RAMPOLLO*, IGNAZIO VECCHIO**, MICHELE MALAGUARNERA***, LIBORIO RAMPOLLO*

*"G.F. Ingrassia" Department, Neurosciences Unit, University of Catania, Azienda Policlinico Vittorio Emanuele, **Department of Medical and Pediatric Sciences, ***Department of Biological Chemistry, Medical Chemistry and Molecular Biology, University of Catania

[*Parkinsonismi con compromissione cognitiva*]

ABSTRACT

Many extrapyramidal disorders can develop complications or be associated with cognitive impairment. This paper lists the main forms of parkinsonism with cognitive impairment and discusses the salient features

Key words: Parkinson, amyotrophic lateral sclerosis, Huntington's disease, multiple system atrophy, corticobasal degeneration

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Clinical varieties

Many diseases with impairment of the extrapyramidal system may develop complications or be associated with cognitive impairment, different timing of onset and with different degrees of severity of clinical expression⁽¹⁾.

The most common occurrences are Parkinson's disease (PD), Lewy body dementia (LBD), multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and Huntington's disease (HD). At times, there is an initial presentation of cognitive impairment subsequently complicated with severe extrapyramidal involvement, as in some variants of Alzheimer's disease

In some cases, in association with the extrapyramidal impairment, rather than a actual deterioration of cognitive functions, a similar yet reversible condition known as pseudodementia has been observed. Its features are more like those of depression than of a real dementia, as is sometimes observed in some types *Parkinson's disease* where the timing of the depressive condition is associated with the disease, as its manifestation may occur in

simultaneous association with the onset. At times it may complicate the course, or even precede the onset by several years, as noted already in 1924, when the possibility that depression could occur long before the Parkinson's disease was described for the first time. This occurrence then fueled the inference by which certain antidepressants could cause Parkinson's disease: post hoc, ergo propter hoc. This type of association, either simultaneous or deferred, is not surprising when you consider all the many neurotransmitter and neuropathological alterations that characterize PD⁽²⁻⁵⁾.

The appearance of true cognitive impairment in PD is observed only in advanced stages of the disease and has already been described by Charcot: the frequency of this association stands at around 15% and the incidence increases with age, exceeding 50% at over 80 years of age. Such cases are characterized by NMR evidence of the alterations of the white matter of the brain that are not observed in patients with PD without dementia⁽⁶⁾.

A cognitive deterioration may occur in both forms of *multisystem atrophy* (MSA-C and MSA-P), and to a lesser degree in the Shy-Drager variant. Moreover, in most of these cases it is possible to

observe alterations of perception such as hallucinations, as well as characteristic signs and symptoms that include emotional incontinence and some cortical and language dysfunctions, but they never reach the actual conditions of dementia, even in advanced stages of neurological deterioration⁽⁷⁾.

The *Steele-Richardson-Olszewski syndrome (PSP)* is associated with cognitive impairment, subcortical dementia and frontal lobe disorder, and more pronounced attention disorders compared to PD and MSA, as well as with the usual neurological disorders typical of the disease, such as the limitation of gaze especially vertically, with a tendency to early falls and the hyperextension of the trunk, early cognitive impairment with at least two of the following features: apathy, thinking disorder, reduced verbal fluency, imitation behavior, and frontal release signs.

The neuropathological substrate of the significant cognitive impairment is represented by a neurofibrillary degeneration in the frontal association cortex, associated with the typical morpho-volumetric alterations of the midbrain⁽⁸⁻¹⁰⁾.

Corticobasal degeneration is frequently confused, especially in the early stage of disease, with other extrapyramidal diseases, including PD.

The cognitive disorder, consisting of apraxia, speech disorders and dementia, may accompany, precede or follow the movement disorders. The significant neuropsychological impairment consists in unilateral ideomotor apraxia (alien hand syndrome) by which an upper limb is no longer integrated in the body scheme and cannot be used without visual control, as reported by a patient aware of this limitation. It is associated with reduced verbal fluency, sometimes slurred speech, distractibility, in some cases visual field constriction (one patient referred the tendency to hit obstacles ignored in the same half of the visual field when driving), frontal release signs, lack of awareness of the disease: the convergence of different cognitive impairments greatly hampers the description of each taken individually⁽¹¹⁾.

Huntington's disease is an autosomal dominant disease caused by abnormal triplet replication (cytosine-adenosine-guanine), with over 37 repeat units, in the short arm of chromosome 4, and characterized by a variable atrophy of the caudate nucleus, relentless progression of motor and cognitive symptoms consisting of visual-spatial disorders and qualitative and quantitative alterations of mood and ideation, with an extremely variable age of

onset (phenomenon of anticipation), antisocial behaviors and at times depression, with a high frequency of suicide⁽¹²⁾.

Lewy body dementia is characterized by a simultaneous onset and development of extrapyramidal and cognitive impairment, with a propensity for episodes of mental confusion. Often clinically confused with Alzheimer's disease, it is distinguished by the presence of cortical neuronal inclusions called Lewy bodies, but without the light halo found in PD, and by the absence of neurofibrillary tangles and senile plaques. It is clinically characterized by a possible coexistence of orthostatic hypotension (cell depletion in the mid-lateral column of the spinal cord), episodes of confusion, visual and auditory hallucinations with possible paranoid states, behavioral fluctuations and extreme sensitivity to treatment with neuroleptics, which may also cause the onset of neuroleptic malignant syndrome.

The association of Parkinson's disease, dementia and ALS and frontotemporal dementia with parkinsonism are also worth mentioning⁽¹³⁾.

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Request reprints from:
Prof. LIBORIO RAMPELLO
Direttore U.O.C. di Neurofisiopatologia
Padiglione 2 (Neurologia)
Policlinico dell'Università di Catania
V. Santa Sofia 78
95100 Catania
(Italy)