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LETTER TO THE EDITOR

The cerebellum in Parkinson's disease and parkinsonism in cerebellar disorders

José Luiz Pedroso, Pedro Braga-Neto, Paulo Victor Sgobbi de Souza and Orlando G. P. Barsottini

Department of Neurology, Ataxia Unit – Universidade Federal de São Paulo, São Paulo, Brazil

Correspondence to: Jose Luiz Pedroso, MD
Rua Botucatu,
740. 04.023-900,
São Paulo,
SP, Brazil
E-mail: jlpedroso.neuro@gmail.com

Sir, We have read with great interest the article by Wu and Hallett (2013) entitled 'The cerebellum in Parkinson's disease'. These authors reviewed related anatomical, clinical and neurophysiological findings, and discuss the possible roles of the cerebellum in the pathophysiology of Parkinson's disease. They pointed out that Parkinson's disease is associated with pathological and structural changes in the cerebellum, and also stated that functional neuroimaging has demonstrated increased activation of the cerebellum in Parkinson's disease. Furthermore, tremor and cerebellar involvement is discussed in Parkinson's disease, and a primary dysfunction in the cerebello-thalamo-cortical circuit, particularly the vermis/paravermis region, is thought to be responsible for the occurrence of resting tremor. Another assumption is that functional or structural changes in the cerebellum may contribute to non-motor symptoms in Parkinson's disease. The authors propose that the major role of the cerebellum in Parkinson's disease includes pathological and compensatory effects, and that pathological changes in the cerebellum might be induced by dopaminergic degeneration (Wu and Hallet, 2013).

Spinocerebellar ataxias (SCA) are defined as a group of autosomal dominant ataxic disorders caused by degeneration of the cerebellum and its afferent and efferent connections (Schöls *et al*., 2004). Besides ataxia, SCA have a wide range of neurological symptoms including extrapyramidal signs, such as parkinsonism. The most common SCA worldwide is spinocerebellar ataxia type 3 (SCA3) or Machado-Joseph disease (Pedroso *et al*., 2012). Interestingly, a specific phenotype of SCA3 classically described in patients of African origin, is comprised by pure parkinsonism without ataxia. Also, parkinsonism, especially the akinetic-rigid syndrome, has been described in patients with SCA, particularly SCA2, SCA3 and SCA17, and is a common condition in Asian patients (Schöls *et al*., 2000; Schmitz-Hübsch *et al*., 2008). In a Brazilian series of 104 patients with Machado-Joseph disease, parkinsonism was seen in eight cases and there was no relationship with CAG repeat size or age of symptom onset. It should be noted that levodopa is an effective treatment in this group of patients with SCA3 (Teive *et al*., 2012). But what is the reason for the presence of parkinsonism in SCA?

Considering pathological studies in SCA3, atrophy of the pons, basal ganglia, midbrain, medulla oblongata, multiple cranial nerve nuclei, thalamus, and the frontal, parietal, temporal, occipital and limbic lobes have been observed (Rub *et al*., 2008). Of note, degeneration of the substantia nigra is not an unusual pathological finding (Fig. 1). As for neuroimaging features, hyperechogenicity of the substantia nigra has been observed through transcranial sonography in patients with SCA3, similarly to Parkinson's disease, although no correlation between echogenicity and parkinsonian features has been found (Pedroso *et al*., 2011). In addition, single-photon emission computed tomography (SPECT) with ^{99m}Tc-TRODAT-1, a dopamine transporter (DAT) radiotracer restricted to the striatum, discloses significant reductions of dopamine transporter density in the caudate and putamen of patients with SCA3, as well as in Parkinson's disease (Braga-Neto *et al*., 2012). Anatomical and biochemical findings have previously suggested the existence of connections between the cerebellum and basal ganglia and more recent studies have shown that the cerebellum influences glutamatergic and dopaminergic striatal activity (Delis *et al*., 2013). This is in line with Wu and Hallett (2013), when they presumed that pathological changes in the cerebellum might be induced by dopaminergic degeneration; perhaps

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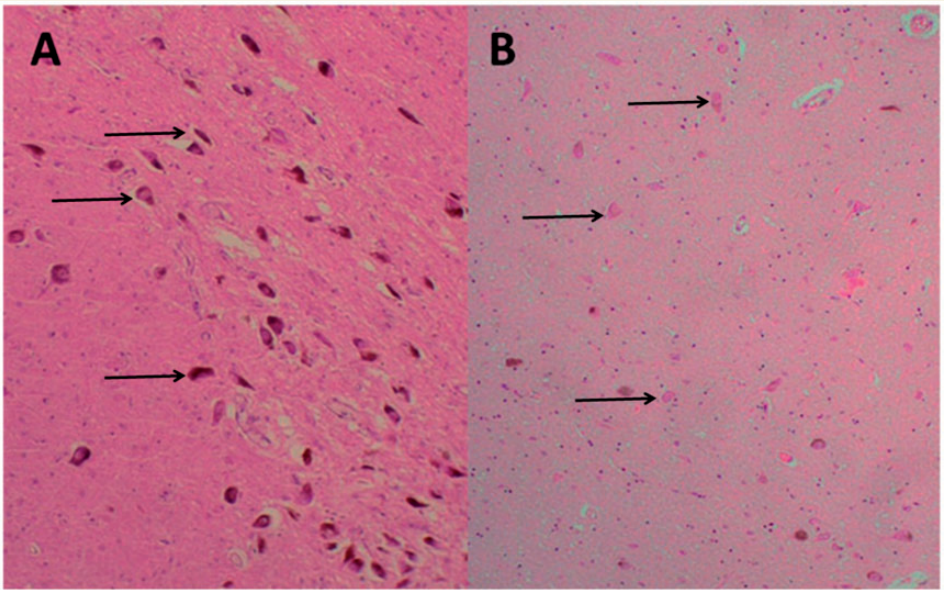

Figure 1 (**A**) Pathological study of a previous healthy subject with normal dopaminergic neurons in the substantia nigra. (**B**) Patient with SCA3 in advanced stage, with degeneration of the substantia nigra in the midbrain. This patient had parkinsonism characterized by bradykinesia and postural instability. Note thinner and sparse cells of the substantia nigra in (**B**), when compared with (**A**).

parkinsonism in primary cerebellar disorders is related to cerebello-thalamo-cortical circuit involvement and basal ganglia impairment.

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