doi:10.1093/brain/awt100 Brain 2013: 136; 1–2 | e249

BRAIN
A JOURNAL OF NEUROLOGY

LETTER TO THE EDITOR

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

Tao Wu[1] and Mark Hallett[2]

1 Department of Neurobiology, Key Laboratory on Neurodegenerative Disorders of Ministry of Education, Beijing Institute of Geriatrics, Xuanwu Hospital, Capital Medical University, Beijing, 100053, China
2 Human Motor Control Section, Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA

Correspondence to: Tao Wu, MD
Department of Neurobiology,
Key Laboratory on Neurodegenerative Disorders of Ministry of Education,
Beijing Institute of Geriatrics, Xuanwu Hospital,
Capital Medical University,
Beijing, 100053, China
E-mail: wutao69@gmail.com

Sir,

We thank Pedroso *et al*. (2013) for their interest in our paper (Wu and Hallett, 2013), in which we discussed the role of the cerebellum in Parkinson's disease; other types of parkinsonism were not included. Such parkinsonian disorders often contain overt pathological changes in both basal ganglia and cerebellar systems. The origin of these changes is generally thought to be primary in both locations, but it is conceivable that the primary pathology is in one location and secondary in the other. It is important to recognize that genetic mutations can cause different phenotypes and that the nomenclature should not be taken literally. The spinocerebellar ataxias (SCAs) can present as a parkinsonism, as Pedroso *et al*. (2013) have described for SCA3. Therefore because it is an 'ataxia' does not mean that the cerebellum is the only site of primary pathology.

In another SCA example, our group investigated patients with SCA2. In both patients with familial Parkinson's disease and asymptomatic carriers with SCA2 mutations, a striatal dopaminergic deficit has been demonstrated (Kim *et al*., 2007; Wang *et al*., 2009). In patients with SCA2 without parkinsonism symptoms, Varrone *et al*. (2004) found striatal dopamine transporter loss, and the striatal dopamine transporter density correlated with the severity of cerebellar ataxia; in addition, a transcranial brain parenchyma sonography study found hyperechogenicity in the substantia nigra (Mijajlović *et al*., 2008). In a recent functional MRI study in a family with SCA2 mutation, including asymptomatic carriers and mutation carriers with parkinsonian symptoms (Wu *et al*., 2013), we found that whereas both the asymptomatic carriers and patients had decreased connectivity within the basal ganglia-thalamus-cortical motor loop compared with the control subjects, the asymptomatic carriers had increased connectivity of other large-scale brain networks, including the cortico-cerebellar circuits, presumably to compensate for the dysfunction of the basal ganglia to maintain brain function in the early stage of dopaminergic deficits. The simultaneous effects of progressive disruption of basal ganglia motor circuits and failure of compensatory cerebellar mechanisms as dopaminergic dysfunction progresses may contribute to the onset of clinical symptoms. This could indicate that the basal ganglia damage was primary and increased stress on the cerebellar for compensation led to the cerebellar damage. If so, this would be in a direction similar to what we described in Parkinson's disease.

Now that it is clear that there are strong reciprocal connections between basal ganglia and cerebellum, it allows for pathological influences to go both ways, and Predroso *et al*.'s (2013) speculation that 'parkinsonism in primary cerebellar disorders [is] related to cerebello-thalamo-cortical circuit involvement and [consequent] basal ganglia impairment' is possible. However, our knowledge regarding neurodegeneration remains limited and whether any entity is due to a multifocal process or spread from one primary locus (Luk *et al*., 2012) is one of the exciting topics in neuroscience at present.

Received March 7, 2013. Accepted March 25, 2013. Advance Access publication June 4, 2013

Funding

This work was supported by grants from the National Science Foundation of China (grant numbers 30870693, 81071012, and 81271429).

References

Kim JM, Hong S, Kim GP, Choi YJ, Kim YK, Park SS, et al. Importance of low-range CAG expansion and CAA interruption in SCA2 Parkinsonism. Arch Neurol 2007; 64: 1510–8.

Luk KC, Kehm V, Carroll J, Zhang B, O'Brien P, Trojanowski JQ, et al. Pathological α-synuclein transmission initiates Parkinson-like neurodegeneration in nontransgenic mice. Science 2012; 338: 949–53.

Mijajlović M, Dragasević N, Stefanova E, Petrović I, Svetel M, Kostić VS. Transcranial sonography in spinocerebellar ataxia type 2. J Neurol 2008; 255: 1164–7.

Pedroso JL, Braga-Neto P, de Souza PV, Barsottini OG. The cerebellum in Parkinson's disease and the otherwise: parkinsonism in cerebellar disorders. 2013, in press.

Varrone A, Salvatore E, De Michele G, Barone P, Sansone V, Pellecchia MT, et al. Reduced striatal [123 I]FP-CIT binding in SCA2 patients without parkinsonism. Ann Neurol 2004; 55: 426–30.

Wang JL, Xiao B, Cui XX, Guo JF, Lei LF, Song XW, et al. Analysis of SCA2 and SCA3/MJD repeats in Parkinson's disease in mainland China: genetic, clinical, and positron emission tomography findings. Mov Disord 2009; 24: 2007–11.

Wu T, Hallett M. The cerebellum in Parkinson's disease. Brain 2013; 136: 696–709.

Wu T, Wang C, Wang J, Hallett M, Zang Y, Wu X, et al. Preclinical and clinical neural network changes in SCA2 Parkinsonism. Parkinsonism Relat D 2013; 19: 158–64.