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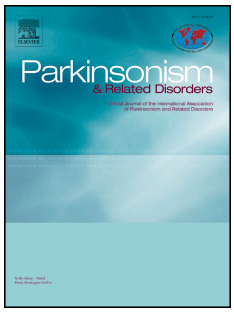

Subtype definition of vascular parkinsonism

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Subtype definition of vascular parkinsonism

To the Editor,

We thank Dr. Levin for expressing interest in our work. Dr. Levin applies a traditional clinico-anatomic perspective to interpret our proposed criteria, pointing out that our criteria do not exclusively require that vascular lesions be located within specific topographic regions, such as the nigrostriatal and striato-thalamo-cortical pathways. At the same time, Dr. Levin notes the often observed clinical scenario in which patients with extensive and confluent vascular lesions on brain MRI scans may be fully asymptomatic motor-wise despite the fact that some of these lesions may be located in regions of critical motor circuitry. This scenario shows that factors other than the geographic location of vascular lesions in the brain may play a role in the pathogenesis of vascular parkinsonism (VaP).

Post-mortem studies have shown that the presence of parkinsonian signs in elderly subjects who do not have Lewy body pathology is best explained by the presence of brain vascular lesions and nigral dopaminergic cell loss [1, 2]. We recently showed that the presence of mild parkinsonian signs in elderly patients with vascular brain lesions was dependent on specific genetic determinants of dopamine metabolism, in particular polymorphisms of the catechol-O-methyl transferase (COMT) enzyme [3]. These *ex vivo* and *in vivo* observations emphasize an important interaction effect between the presence of cerebrovascular lesions and the functional integrity of the dopaminergic system as it relates to the presence of parkinsonian motor symptoms in elderly subjects in the absence of Parkinson's disease (PD). In other words, the combination of age-related declines and/or genetic changes in dopaminergic system functions and the presence of vascular lesions may be a more important determinant of parkinsonism than the strategic location of vascular lesions alone. This multi-system interaction model may provide an explanation for the clinical observation that extensive leucoaraiosis can be fully asymptomatic in some individuals.

Dr. Levin warns about over-diagnosis of VaP using our criteria. The threshold for the emergence of motor symptoms in PD is at least 50% loss of dopaminergic nerve