

MATTERS ARISING

Motor response to apomorphine and levodopa in asymmetric Parkinson's disease

The study of the motor response to levodopa in patients with asymmetric parkinsonism is of relevance to the changes in response to pharmacological treatment that evolve with disease progression and to the mechanism of action of levodopa. Pathological and neuroimaging studies show that asymmetry of clinical involvement in Parkinson's disease is caused by asymmetry of degeneration of neurons in the substantia nigra. Assuming that lateralised motor disability affecting upper limb motor function is a consequence of nigral degeneration in the contralateral half of the midbrain, comparison of body sides in patients with asymmetric motor disability allows direct comparison of two different stages in the progression of Parkinson's disease. If the duration of effect of exogenous levodopa is dependent on storage and synaptic release of dopamine in surviving nigral neuronal terminals, it should be possible to detect some difference in the duration of motor response between body sides in asymmetric cases.

Rodriguez *et al*¹ have evaluated asymmetry of motor response to levodopa and apomorphine in 14 cases and concluded that the motor response is more prolonged on the less affected body side. By contrast, our previous study of levodopa motor responses in asymmetric cases showed that the onset and wearing off of the motor response to levodopa occur simultaneously for each side of the body.² There are differences in patient selection and methods that may be relevant to understanding this discrepancy.

Parkinson's disease often begins with exclusively unilateral involvement and patients then retain obvious motor asymmetry for the first few years of their disease course. Eventually, motor involvement becomes bilateral and clinical asymmetry is more subtle, although differences in upper limb motor function in accordance with first affected body side are still present in many cases. By choosing relatively early cases (untreated patients and patients with moderate motor fluctuations after a mean period of levodopa treatment of 4.9 years), Rodriguez *et al* were able to study a patient group with obvious asymmetric Parkinsonism. It needs to be recognised, however, that when the amplitude of motor response is relatively low, as it will be in milder cases, differences in motor scores before and after pharmacological agents will not be great and the precise determination of time points of onset and wearing off of motor response will be difficult. In these studies, the estimation of the duration of motor response on the less affected body side is more prone to error because of this factor. The low negative gradients of the lines representing wearing off phases on the motor function *v* time graphs

presented by Rodriguez *et al* illustrate this difficulty.

By contrast, we studied patients with more advanced disease and well developed motor fluctuations (mean duration of levodopa treatment 9.9 years) who retained clinical asymmetry in accordance with the first affected body side. A large amplitude of motor responses and unequivocal wearing off phases allowed accurate measurement of duration of motor response for each body side, as represented by the graphs of individual patient data published with our results. We presented evidence to show that such cases with advanced and bilateral Parkinson's disease should still retain asymmetry of neuronal degeneration in the substantia nigra with about 25% difference between nigral neuronal counts on opposite brainstem halves. Readers wishing to confirm the fact that body sides do not fluctuate out of phase in advanced cases can do so by observing any patient with asymmetric disease onset and severe "on-off" motor oscillations.

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- Rodriguez M, Lera G, Vaamonde J, Luquin MR, Obeso JA. Motor response to apomorphine and levodopa in asymmetric Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1994;57:562-6.
- Kempster PA, Gibb WR, Stern GM, Lees AJ. Asymmetry of substantia nigra neuronal loss in Parkinson's disease and its relevance to the mechanism of levodopa related motor fluctuations. *J Neurol Neurosurg Psychiatry* 1989;52:72-6.

Rodriguez *et al* reply:

The problems in assessing motor response during pharmacological tests are well known. We admitted such difficulties in the discussion of our paper. We do not believe, however, that the findings we reported are erroneous, for the asymmetric response to apomorphine and levodopa was consistent and independently evaluated by several members of the team during the study. It should be noted that the asymmetry in the response involved not only duration but also magnitude and latency.

Several studies using intravenous levodopa in patients with Parkinson's disease have conclusively shown that greater disease severity, which is directly correlated with longer disease duration and time under levodopa treatment, is associated with shorter response duration and increased magnitude. The lack of difference observed by Kempster *et al* probably reflected a relatively symmetric disease in advanced cases. Thus patients with recent disease onset will be more prone to show an asymmetric response than those with a long evolution. We agree with Kempster and Lees in how to confirm this assertion. Select a recently diagnosed patient, usually young, with severe bradykinesia and rigidity in one limb or hemibody and compare the response to one Sinemet-275 (250 mg levodopa, 25 mg

carbidopa) tablet with that of a patient who has had Parkinson's disease for many years and the motor signs are bilateral. The asymmetry in the response will be obvious in the first but not in the second patient.

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SHORT NOTICES

Readers may be interested in **Manual of Nerve Conduction Velocity and Clinical Neurophysiology—third edition**. By JOEL A DELISA, HANG J LEE, ERNES M BARAN, KA-SIU LAI and NEIL SPIELHOLZ. (Pp 508; \$60.50.) Published by Raven Press, New York 1994. ISBN 0-7817-0138-4.

Monoamine Oxidase Inhibitors in Neurological Diseases (Neurological Disease and Therapy Series/21). Edited by ABRAHAM LIEBERMAN, C WARREN OLANOW, MOUSSA B H YOUSSEF and KEITH TIPTON (Pp 371; \$150.00.) Published by Marcel Dekker Inc, New York 1993. ISBN 0-8247-9082-0.

Manual Therapy for Chronic Headache, Second Edition. By JOY EDELING. (Pp 170; £18.95.) Published by Butterworth Heinemann, Oxford 1994. ISBN 0-7506-1619-9.

Cognitive-Behavioral Therapy of Schizophrenia. By DAVID G KINGDON and DOUGLAS TURKINGTON. (Pp 212; £25.00.) Published by Lawrence Erlbaum Associates, Hove 1994. ISBN 0-86377-328-1.

Linguistic Disorders and Pathologies—An International Handbook. Edited by GERHARD BLANKEN, JURGEN DITTMANN, HANNELORE GRIMM, JOHN C MARSHALL and CLAUS-W WALLECH. (Pp 962; DM830,00.) Published by Walter De Gruyter and Co, Berlin 1993. ISBN 3-11-011324-4.

Language of the Elderly By KAREN L BRYAN and JANE MAXIM. (Pp 285; £19.50.) Published by Whurr Publishers Ltd, London 1994. ISBN 1-870332-35-0.