Evidence for lateral premotor and parietal overactivity in Parkinson's disease during sequential and bimanual movements. A PET study

P. Praamstra,[1,2] D. F. Stegeman,[2] A. R. Cools,[3] A. S. Meyer[4] and M.W. I. M. Horstink[1]

Departments of [1]Neurology, [2]Clinical Neurophysiology and [3]Neuropsychopharmacology, University of Nijmegen and [4]Max Planck Institute for Psycholinguistics, Nijmegen, The Netherlands

Correspondence to: P. Praamstra, Department of Neurology, University Hospital Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands

In a recent issue of this journal, Samuel *et al.* (1997) reported deficient activation of the supplementary motor area along with overactivity of the lateral premotor and inferolateral parietal cortex during the performance of sequential movements by patients with Parkinson's disease. While there already existed evidence for deficient activation of medial premotor structures in Parkinson's disease, the overactivity of the lateral premotor and parietal cortex was reported as a

novel finding, associated specifically with the performance of sequential movements. However, there are reasons to question this association, as well as some other points that we wish to raise concerning this paper.

(i) With regard to deficient medial premotor cortex function, the authors discuss at some length the converging evidence from movement-related brain potentials (MRPs), including a recent study from their own laboratory (Jahanshahi *et al.*, 1995). In this context, we wish to point out that there is also MRP evidence bearing on their finding of overactive lateral premotor structures, including a directly relevant study of the time course and distribution of MRPs in a movement precueing task, also published in *Brain* (Praamstra *et al.*, 1996). We found differences between Parkinson's disease patients and controls that closely mirrored the findings of Samuel *et al.* (1997). In fact, our interpretation of differences in the distribution and amplitude of MRPs between patients and control subjects specified reduced supplementary motor area activity and increased activity of the primary motor, lateral premotor or ventral premotor area as the most likely cause of these changes. Naturally, the data did not allow a precise determination of the structures involved, because the neural sources of scalp-recorded potentials can only be estimated, not determined in a definitive way. Nevertheless, the evidence for increased activity in sensorimotor areas at the lateral convexity appeared strong enough to enable discussion, as in Samuel *et al.* (1997), of a possible relationship between our findings and PET evidence for motor reorganization after stroke (Weiller *et al.*, 1992). In addition, the temporal information provided by MRPs allowed us to localize the increased activity to a particular time window relative to the actual movement. As discussed below, this may be relevant to the interpretation of the PET results reported by Samuel *et al.* (1997).

(ii) Samuel *et al.* (1997) state that their movement task required high levels of mesial frontal cortex activation and therefore partially masked mesial frontal impairment in Parkinson's disease (p. 972). However, they also state that Parkinson's disease patients switch from the use of striato-mesial frontal to parietal-lateral premotor circuits for sequential movements (Summary, p. 963). The metaphor of switching between circuits suggests that these circuits normally operate in a mutually exclusive fashion. If this is indeed what the authors want to convey, it is difficult to maintain that mesial frontal impairment in Parkinson's disease is partially masked. The concept of two separate premotor systems mediating different kinds of movements was more or less abandoned in a previous study from the authors' group and traded for the idea of 'a more widely distributed volitional action system' (Jahanshahi *et al.*, 1995). Samuel *et al.* (1997) seem to vacillate between these different frameworks, as they do not make it clear whether they believe the lateral premotor-parietal circuit is invoked instead of or in addition to the impaired striato-mesial frontal circuit. Note that Cunnington *et al.* (1995), who the authors refer to in another context, have taken a strong position on this issue, claiming that the supplementary motor area can be bypassed when external cues are given.

(iii) Samuel *et al.* (1997) propose that the overactivity of lateral premotor and parietal areas in Parkinson's disease is related to the use of a sequential movement task, since earlier studies from their laboratory, using single ballistic (hand or finger) movements, failed to establish significant overactivity in these areas (Playford *et al.*, 1992; Jahanshahi *et al.*, 1995). We believe that other accounts need to be considered. The authors refer to Cunnington *et al.* (1995) as an MRP study supporting impaired supplementary motor area activation in Parkinson's disease, as it found a reduced MRP amplitude at the vertex. However, this study also contains other valuable information, as it likewise concerned sequential movements, investigated under various cueing conditions. In certain cueing conditions, Cunnington *et al.* (1995) found MRPs that were nearly flat in the premovement interval. Thus, we conclude that it is not the sequential nature of a movement alone, but at best this movement type in conjunction with particular cueing conditions that accounts for the recruitment of lateral premotor-parietal circuits. [Cunnington *et al.* (1995) used only a vertex electrode in most of the investigated subjects. However, given the volume conduction properties of the skull, this electrode should pick up activity from lateral premotor areas.]

(iv) Although Samuel *et al.* (1997) used external (auditory) signals to pace movements, their role is not discussed. They propose that '... patients engaged the lateral premotor-parietal cortex loop subconsciously via tactile or sensory proprioceptive inputs' (p. 973). This proposal seems plausible in view of the sequential movement task that was used. However, the task involved sequential finger press movements on four response keys located under the index, middle, ring and little fingers, respectively. Given that the pacing tones were presented every 3 s and that the response times were <0.5 s, a period of ~ 2.5 s of muscle quiescence remained between each finger movement. Rather than a sequential movement, this is more like a predictable series of discrete movements, each triggered by an external timing signal. Thus, the 'sequential' nature of the movement task used by Samuel *et al.* (1997), compared with the ballistic movements used by Jahanshahi *et al.* (1995), is not a very convincing explanation for the absence of overactivity in parietal and lateral premotor structures in the latter study.

To summarize, we do not believe that the interpretation Samuel *et al.* (1997) propose for their data is the only feasible one. We will briefly discuss movement-related potentials data that invite another view. Our own data (Praamstra *et al.*, 1996) show that when Parkinson's disease patients know in advance (i.e. before the occurrence of a reaction signal) which hand to move, they recruit more activity in areas located at the lateral convexity than control subjects, relative to a condition in which they do not know in advance which hand to move. We suggested in that paper that such evidence for overactivity in lateral premotor areas had not been seen in previous PET studies in Parkinson's disease because less

emphasis had been placed on response speed than in our investigation. We might have added that the duration of the activity was perhaps too short to be seen by PET. The main points for the present discussion are that the movements eliciting overactivity in Parkinson's disease were single movements, and that they were predictably timed by an external signal. The first point contradicts the interpretation offered by Samuel *et al.* (1997), as it implies that sequential movements are not a necessary precondition for overactivation of lateral premotor areas. The second point might imply that their auditory pacing signal was more important than they assumed. This signal allowed subjects, given the fixed order in which they had to move different fingers, to prepare each movement in advance. As suggested in our study, differences between Parkinson's disease patients and control subjects occurred during the advance preparation, involving a shift in balance between the activity in mesial frontal structures and activity in motor and lateral premotor structures. While the opportunity for advance movement preparation was also present in the study by Jahanshahi *et al.* (1995), activation of the lateral premotor cortex may have been stronger in the study of Samuel *et al.* (1997) not because of the sequential nature of their movement task but because the isolated finger movements required in their task were more difficult, and thus more likely to elicit preparatory activity in advance of the auditory cue. This hypothesis is supported by the findings of Kitamura *et al.* (1993), who found that isolated movements of the index and middle finger (i.e. extension movements) were accompanied by higher amplitude MRPs at lateral electrode sites than was simultaneous movement of the same fingers. Moreover, isolated middle finger movement was judged more difficult than isolated index finger movement and yielded higher premovement potentials at lateral electrode sites.

In conclusion, we agree with the statement of Samuel *et al.* (1997) that 'the mechanism of . . . abnormal recruitment of alternative sensorimotor cortical areas and its exact physiological role still remains uncertain' (p. 974). However, we disagree with their claim that sequential or complex movements are required for the recruitment of these alternative sensorimotor areas, as recent neurophysiological studies suggest that sequential movements are neither a necessary nor a sufficient requirement for the recruitment of these areas.

References

Cunnington R, Iansek R, Bradshaw JL, Phillips JG. Movement-related potentials in Parkinson's disease. Presence and predictability of temporal and spatial cues. Brain 1995; 118: 935–50.

Jahanshahi M, Jenkins IH, Brown RG, Marsden CD, Passingham RE, Brooks DJ. Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects [see comment]. Brain 1995; 118: 913–33. Comment in: Brain 1996; 119: 1045–8.

Kitamura J, Shibasaki H, Kondo T. A cortical slow potential is larger before an isolated movement of a single finger than simultaneous movement of two fingers. Electroencephalogr Clin Neurophysiol 1993; 86: 252–8.

Playford ED, Jenkins IH, Passingham RE, Nutt J, Frackowiak RS, Brooks DJ. Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study. Ann Neurol 1992; 32: 151–61.

Praamstra P, Meyer AS, Cools AR, Horstink MW, Stegeman DF. Movement preparation in Parkinson's disease. Time course and distribution of movement-related potentials in a movement precueing task. Brain 1996; 119: 1689–704.

Samuel M, Ceballos-Baumann AO, Blin J, Uema T, Boecker H, Passingham RE, et al. Evidence for lateral premotor and parietal overactivity in Parkinson's disease during sequential and bimanual movements. A PET study. Brain 1997; 120: 963–76.

Weiller C, Chollet F, Friston KJ, Wise RJ, Frackowiak RS. Functional reorganization of the brain in recovery from striatocapsular infarction in man. Ann Neurol 1992; 31: 463–72.