On the basis of the data presented in our Table 4, which shows an inverse correlation between the latency to nadir of symptoms and the chance of complete recovery, we agree with Professor Hughes and colleagues that a longer latency to nadir was an adverse prognostic factor in our study. However, the duration of active disease (measured as the time from onset to remission or stabilization of symptoms) also seemed to adversely affect the prognosis of Guillain–Barré syndrome in our cases (see Table 4 in Italian Guillain–Barré Study Group, 1996). This latter finding is in keeping with other reports (Ravn, 1967; Kaur et al., 1986; Raphael et al., 1986; Winer et al., 1988) and is mentioned in the Discussion of the Italian Guillain–Barré Study Group (1996) as the feature our data confirmed. Probably, the sentence ‘We confirmed these findings’ should be changed to ‘We partly confirmed these findings’.

Although details of the neurological examination are given for most patients, arm disability was not specifically assessed as a prognostic variable. However, the report of an adverse effect of complete paralysis of the arms is in agreement with personal observations and with clinical experience.

We agree with Professor Hughes’ criticism that there is incompatibility between the text (reporting a faster recovery among patients receiving immunoglobulins) and Fig. 3 (showing that people treated with plasma exchange had a faster recovery). This was due to an erroneous label in the figure (plasma exchange and immunoglobulins were the wrong way round).

Finally, at the time of submission of this paper, the results of the trial of plasma exchange, intravenous immunoglobulins and combined treatments in Guillain–Barré syndrome (Plasma Exchange/Sandoglobulin Guillain–Barré Syndrome Trial Group, 1997) were not available. At that time, the need for comparative trials was justified as only plasma exchange was known to be superior to placebo (Guillain–Barré Syndrome Study Group, 1985; French Cooperative Group on Plasma Exchange in Guillain–Barré Syndrome, 1992), there was only one study comparing immunoglobulins and plasma exchange (van der Meché et al., 1991), and evidence of a long-term efficacy of this therapeutic strategy was insufficient (French Cooperative Group on Plasma Exchange in Guillain Barre Syndrome, 1992).

References


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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. Meyer4 and M.W. I. M. Horstink1

Departments of 1Neurology, 2Clinical Neurophysiology and 3Neuropsychopharmacology, University of Nijmegen and 4Max 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 precuing task, also published in Brain (Pramstra 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., 1996). 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 (Pramstra 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


Reply
Michael Samuel and David J. Brooks

Correspondence to: Dr Michael Samuel, MRC Cyclotron Unit, Imperial College School of Medicine, Hammersmith Hospital, DuCane Road, London W12 0NN, UK

We wish to thank Praamstra et al. for expressing their interest in our work and for their valuable discussion. We would like to make the following comments concerning our manuscript (Samuel et al., 1997) and their discussion.

The findings of the recent paper of Praamstra et al. (1996), documenting an increase in measurable movement-related brain potential activity over the lateral convexity of patients with Parkinson’s disease during index and middle finger movements, are in keeping with the findings of our regional cerebral blood flow study with PET and are discussed in terms of a possible ‘shift’ from an underactive mesial frontal cortical system to a lateral (pre)motor cortical system. It would appear, however, that Praamstra et al. wish us to take a stronger position on whether a lateral (pre)motor cortical system acts ‘instead of’ or ‘in addition to’ the impaired mesial frontal cortical system in Parkinson’s disease. At present we do not believe that such a distinction can be justified on the basis of currently available functional imaging data.

The main results from our study derive from between-group comparisons (Parkinson’s disease with controls) which demonstrated relatively impaired mesial frontal cortex activation associated with relative overactivity of lateral premotor-parietal cortex in patients with Parkinson’s disease during performance of paced sequential finger movements. In order to interpret between-group findings, it is also imperative to refer to the within-group data, and it was for this reason that we included the within-group data. To be in
a position to specify that the lateral (pre)motor cortical system acts ‘instead of’ the mesial frontal cortical system in patients with Parkinson’s disease, we would need to have shown that in the control group task performance was associated with activation of the mesial frontal but not the lateral premotor cortex while in the Parkinson’s disease group there was activation of the lateral premotor but not the mesial frontal cortex. This was not the case, as it can be seen from the within-group results of our Parkinson’s disease group that task performance activated both the mesial frontal cortex and the lateral premotor-parietal cortex. This, therefore, dismisses the possibility that one system operates ‘instead of’ another in Parkinson’s disease. However, the fact that in Parkinson’s disease the two cortical systems are activated concurrently should not be interpreted as indicating that their function is to operate in combined fashion to allow correct task performance to occur, since we cannot determine whether activation of the mesial frontal cortex in Parkinson’s disease represents correct and appropriate neuronal signalling as opposed to inappropriate synaptic metabolism. Put simply, although we provide evidence that the lateral premotor-parietal cortex is relatively more active in Parkinson’s disease during task performance, the level and nature of the ‘switch’ or ‘shift’ from one system to another—whether partial or complete—cannot be determined with accuracy. It is for these reasons that we did not mention the completeness of the ‘switch’ in our manuscript, and we believe that being asked to take such a strong position in the light of currently available evidence is inappropriate.

We fully acknowledge the difficulty in interpretation of studies (like ours) which have so far employed paradigms involving regular pacing and performance of sequential tasks. We point out in our introduction that ‘... the supplementary motor area is involved more with generation of volitional movements, particularly sequential patterns...’, indicating that both preparation and sequential movements per se may contribute to the previously documented activity observed in this region. Like ours, the study of Jahanshahi et al. (1995) used predictable tones and ballistic index finger extensions associated with movement-related brain potential generation but failed to detect significant lateral premotor overactivity, which we observed during performance of sequential movements. This would support the notion that movements of a sequential nature are associated with recruitment of the lateral premotor-parietal cortex. Any sequential finger movements, however, involve several components, some of which are difficult to define and measure, such as timing, attention to the order in which to recruit and cycle through muscular activity, spatial awareness of the position of one finger in relation to the previous and the next, and, as Praamstra et al. (1996) note, possible attentive differences with respect to the relative difficulty of recruitment of some muscle groups compared with others. In this respect, the activation patterns may reflect cortical correlates of either the timing of contraction of muscle groups, or the unconscious selection of muscle groups or the predictive load applied to the tasks. In order to determine which component of a sequential nature is specifically responsible for cortical activity, sequential tasks need to be considered in terms of basic components and studies performed using only one variable. Our study did not attempt this and our conclusion, therefore, applies to the combined components which constitute sequential finger movements.

Praamstra et al. very importantly point out that there was ~2.5 s of muscle quiescence between pacing tones in our study, i.e. ~2.5 s of every 3 s (~83%) during the collection of PET data was attributed to cortical activity occurring between finger movements. It cannot be assumed that this period of muscle quiescence exactly coincided with cortical quiescence, but this is likely as co-operative subjects who agree to take part in research studies are likely to perform the tasks as instructed. The subjects in our study were instructed to press a keypad on hearing a tone, and it is inevitable that some preparation/anticipation occurred. If this were the case, it would be in keeping with the findings of Praamstra et al. (1996), in which there was increased activity over the lateral convexity during non-sequential tasks where the variable employed was the presence of predictive information. We would, therefore, like to congratulate Praamstra et al. on performing what is a most valuable study.

References

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