Learning manual pursuit tracking skills in patients with Parkinson’s disease

P. Soliveri,1 R. G. Brown,2 M. Jahanshahi,2,3 T. Caraceni1 and C. D. Marsden2,3

1Centre for the Study and Treatment of Parkinson’s and Extrapyramidal Diseases, Neurological Institute ‘C. Besta’, Milan, Italy, 2Medical Research Council Human Movement and Balance Unit, The National Hospital for Neurology and Neurosurgery and 3Department of Clinical Neurology, Institute of Neurology, London, UK

Summary

Evidence from a number of sources identifies the putamen and its ultimate cortical projection sites as forming a possible substrate for motor learning. The present paper describes two experiments which explored motor learning of a pursuit tracking task under first (position) and second (velocity) order control dynamics, in patients with Parkinson’s disease on and off (experiment 2 only) their normal dopaminergic medication. In neither experiment did the medicated patients show evidence of significant impairment in learning the tasks. In the velocity tracking task, however, the patients off medication showed significantly less improvement in performance with practice. The discussion considers a number of possible interpretations of this finding. Contemporary cognitive theories of motor learning consider behavioural change with practice to be the combined action of an automatic procedural system, together with input from a conscious declarative system. Development of declarative knowledge about the task may have changed the nature of the process involved, from a visually guided task to a more predictive one based upon an internal representation. Evidence from various sources suggests that patients with Parkinson’s disease have particular problems with this mode of control, thus making the task more difficult. It is suggested that motor control deficits have not been adequately considered in previous studies on motor learning, and that the evidence from clinical studies for a role of the putamen/supplementary motor area in motor learning remains equivocal.

Keywords: dopamine; motor learning; Parkinson’s disease; pursuit tracking; striatum

Abbreviation: rCBF = regional cerebral blood flow

Introduction

The study of motor learning and skilled behaviour has waxed and waned over the decades of this century. It received particular attention with the development of behavioural and associationist theories. However, it fell from favour with the growth of cognitive psychology in the 1970s, when the focus of research shifted to verbal learning and memory. Even for psychologists still interested in movement, the growing influence of control and system theories meant that their investigations tended to concentrate on discrete movements, independent of the role of experience and practice. It is only relatively recently that motor learning has once again become a major focus of interest. In cognitive psychology the questions relate to the processes involved and the nature of the representation of knowledge. In neuroscience, the key question has been the neuroanatomical substrate underlying motor skill. The present paper will focus on the second of these two issues. However, we will return to contemporary cognitive theories of motor learning and to issues of motor control in the discussion.

Two primary methods have been employed to explore the functional anatomy of motor learning. First the effects of lesions and neurochemical dysfunction on motor learning, and second, the in vivo assessment of cerebral activity during the performance and acquisition of skilled motor tasks. The evidence from these two approaches will be considered in turn.
Dissociable learning systems: declarative and procedural learning

A key stage in the development of cognitive neuroscience was the discovery of the profound amnesia in patient H.M. caused by bilateral resection of the temporal lobes for the treatment of epilepsy (Milner, 1962). Although H.M. had lost the ability to acquire new factual information, it was evident that he retained the ability to learn certain types of information. Milner (1962) found normal learning on a perceptual-motor task (mirror drawing), while Corkin (1968) showed that H.M. was able to learn a manual pursuit tracking task. In each case, an improvement in performance with practice, and a retention of that performance gain between sessions provided evidence of learning. This was despite his failure to recall consciously these previous episodes.

Since then, study of H.M. and other amnesic patients has revealed largely intact learning on perceptual, perceptual-motor, motor and cognitive skill tasks, on priming paradigms, tests of series learning and (in most cases) classical conditioning (Graf et al., 1984). Based on the dissociation between these tasks and conventional measures of learning and memory, Graf and Schacter (1985) drew a distinction between ‘explicit’ and ‘implicit’ memory. Explicit memory refers to situations where performance on a task requires conscious recollection of previous experiences, while implicit memory is inferred when previous experience facilitates performance, even when conscious awareness is not present.

A similar distinction had been drawn by Cohen and Squire (1980) and Squire (1982) between ‘declarative’ memory for data-based information and ‘procedural’ memory for rule-based information. Procedural tasks included perceptual, cognitive and motor skill learning, priming and classical conditioning. Because amnesic patients were unimpaired on these procedural tasks, it was evident that the brain regions damaged in amnesia, i.e. the cortico-limbic-diencephalic system, were not essential for the learning involved. This led, inevitably, to the question of whether procedural learning was served by a separate neuronal system. Based upon lesion studies in primates, Mishkin et al. (1984) suggested that there was a ‘habit’ system for learning new sensori-motor associations, based around striatal structures and their cortical projection areas.

Attempts to test this hypothesis in man focused attention on patient groups with neurodegenerative diseases affecting the striatum: Huntington’s disease, Parkinson’s disease and Steel–Richardson–Olszewski disease (progressive supranuclear palsy), and more recently, schizophrenia. In general, however, this research has failed to offer support for a single ‘procedural system’ (for review see Brown et al., 1993a). The results showed that different paradigms (e.g. priming and motor learning) were dissociable both between and within striatal patient groups. Furthermore, patient groups with extra-striatal pathology such as that found in Alzheimer’s disease and cerebellar disease, have also shown deficits on certain procedural tasks. Together, this body of research argues strongly against the existence of a single procedural system based on the striatum and its frontal connections. An alternative model (Squire, 1987) is that each class of procedural or non-declarative learning, may be served by its own specific neuroanatomical substrate. This change suggests that we need to look, in detail, at specific types of non-declarative learning. The focus of the present paper is on motor learning and the possible contributions of the striatum and its associated cortical projection sites.

The role of the fronto-striatal system in motor learning: clinical evidence

Corkin’s (1968) observation of intact motor learning in H.M. has now been replicated in other amnesic patients and groups with diverse sites of pathology (e.g. Cermak et al., 1973; Brooks and Baddeley, 1976; Heindel et al., 1988). Even patients with Alzheimer’s disease with their widespread neocortical degeneration and cholinergic dysfunction, show intact motor learning (e.g. Heindel et al., 1988, 1989; Deweer et al., 1994).

In the two studies of Heindel et al. (1988, 1989), patients with Huntington’s disease were also assessed. In contrast to the Alzheimer’s disease patients, the Huntington’s disease group were impaired on a pursuit rotor task, supporting a possible role of the caudate in the neuronal system subserving motor learning. Further evidence comes from a study of patients with schizophrenia (Granholm et al., 1993), where motor learning was associated with the degree of caudate pathology, as indicated by MRI T2 relaxation times. Other investigators have focused on the possible contribution of the putamen, using patients with Parkinson’s disease as their model. Heindel et al. (1989), using the pursuit rotor, assessed a group of Parkinson’s disease patients while on their normal dopaminergic medication. The patients were divided into a ‘demented’ and a ‘non-demented’ group. To equalize the starting level, the speed of the rotor was individually adjusted for each subject over four trials to give a baseline performance of 25% time on target. Although tracking at a slower speed than controls, the non-demented group showed normal improvement in performance across 24 trials. In contrast, the demented group showed very little evidence of learning. Harrington et al. (1990) assessed a group of non-demented patients, again while on their normal dopaminergic medication. Subjects were assessed over 3 days at each of three rotation speeds (30, 45 and 60 r.p.m.). At each speed, the Parkinson’s disease group exhibited less evidence of learning. However, when the Parkinson’s disease group was divided into those with relatively mild disability and those with more advanced disease, only the latter group were impaired, showing very little evidence of learning across the 3 days. Bondi and Kazniak (1991) employed a modified (computer based) version of the pursuit rotor which was used over 30 20-s trials. The Parkinson’s disease patients, who were medicated and had mild to moderate disease, showed...
normal motor learning. Together, these studies suggest that medicated, non-demented patients in the early to mid stages of illness show relatively normal learning on rotary pursuit type tasks. Impairments tend to be found in patients with more advanced disease and/or dementia, suggesting the possible contribution of extrastriatal pathology. None of the studies addressed the question of the role of medication on motor learning.

One other study provides evidence on learning pursuit tracking skill. Frith et al. (1986) employed complex two-dimensional bimanual tracking paradigms: a semi-predictable task and a mirror-reversed tracking task. While Parkinson’s disease patients showed evidence of learning across practice sessions, they failed to show the normal rapid improvement in performance at the start of each trial. This was interpreted as failure to acquire a ‘motor set’ which was thought to reflect the ‘modification of an existing motor programme for use in a new situation’.

The role of the fronto-striatal system in motor learning: evidence from rCBF studies

A number of studies have examined changes in regional cerebral blood flow (rCBF) associated with motor learning. The majority of early studies used a task involving the learning of a complex finger sequence, rather than pursuit tracking, making comparison with the clinical literature difficult.

Seitz et al. (1990) carried out the first study in which rCBF was measured at different stages during the learning a complex sequence of finger movements. Blood flow was measured during initial practice, and then on two subsequent occasions, between which the subject continued practising. Early practice was associated with a decrease in the rCBF, compared with rest, in the mid-sectors of the putamen—globus pallidus, together with the red nucleus and pontine regions. As practice proceeded, these decreases were reversed and rCBF increased steadily as the task was learned. Practice-contingent blood flow increases were also seen in the right anterior lobe of the cerebellum.

One methodological problem with this study was that the rate of movement increased with practice. At least some of the blood flow changes, therefore, may have been a result of increased motor activity rather than motor learning. However, it is worth noting that this suggestion cannot account for the initial decrease in activity in the striatum, despite the increase in motor activity compared with rest.

In two subsequent studies (Friston et al., 1992; Jenkins et al., 1994) subjects carried out a right-handed sequential keypress task, but on these occasions the rate was held constant. In the first study, Friston et al. (1992) showed a pattern of increased rCBF associated with task performance which involved the primary sensorimotor cortex, cerebellum, and left putamen, left thalamus and left claustrum-insular cortex. However, significant rCBF changes contingent upon practice were found only in the right lateral cerebellar cortex and medial cerebellum at the level of the cerebellar nuclei. In the second study (Jenkins et al., 1994) two separate finger sequence tasks were used, one which had been previously practised, and one which was learned during the rCBF measurement. Compared with rest, both tasks led to increased blood flow in a variety of cortical and subcortical areas including the cerebellum (hemispheres, vermis and cerebellar nuclei) and contralateral putamen. The evaluation of new learning per se; however, involved the comparison of rCBF in the prelearned versus new sequencing tasks. The new learning task was associated with greater relative blood flow in the cerebellum (vermis, cortex and nuclei bilaterally), the medial thalamus and red nuclei. Cortical areas of increased activation included various areas of prefrontal cortex (Brodmann area 47 on the right, and areas 9, 10 and 46 bilaterally), lateral premotor cortex bilaterally, anterior cingulate (area 32) and areas of parietal cortex (7 and 40) bilaterally. Other areas, however, showed greater relative blood flow during execution of the prelearned sequence. These included temporal cortex (areas 20, 21 and 37) and hippocampus bilaterally, posterior supplementary motor area and the adjacent cingulate area (24), as well as cortical areas 17, 18 and 40.

Two published studies have employed pursuit tracking tasks. Lang et al. (1988) employed a pseudo-random two-dimensional tracking task. In one condition, the subject tracked the target with normal movement dynamics, while in the second condition the horizontal component was mirror-reversed (as in the study of Frith et al., 1986). rCBF was measured using single photon emission computerized tomography. It was assumed that learning would be reflected most in changes in the more difficult, mirror tracking conditions. Learning-related activation across successive scans were shown for fronto-medial cortex (including the supplementary motor area), left and right mid frontal gyrus (mainly area 6, but including parts of areas 8, 9 and 46), right basal ganglia and left cerebellum.

Grafton et al. (1992) employed the conventional pursuit-rotor paradigm. Subjects were assessed at ‘rest’, while watching the movement of the pursuit rotor, then over four trials of manual pursuit (with further intervening practice) and finally at ‘rest’ once more. Compared with ‘rest’, tracking performance was associated with significant increases in rCBF in the contralateral motor cortex, supplementary motor area, putamen and substantia nigra, together with large increases in the middle and right parasagittal zones of the cerebellum. However, practice-contingent increases in rCBF (across the four tracking scans) were observed only in contralateral motor cortex, supplementary motor area and thalamus (putinar). Of these motor areas, only the supplementary motor area showed a persistent increase in rCBF across all four practice trials, the other areas showing only an increase in early practice. Unlike the previous studies with finger sequence learning, no practice-contingent rCBF changes were observed in cerebellar structures, although this was only partially imaged in the
scanner. Interpretation of these rCBF data, however, are complicated by the statistical technique employed. This was biased to detecting systematic linear changes in blood flow, using contrasts derived from each subject’s performance on the tracking task. It follows that non-linear and certainly non-monotonic rCBF changes across the four scans would not be detected. It is unwise and probably inaccurate to assume that the monotonic change in performance represents the action of a single ‘skill acquisition’ process. It is probably based instead on the summation of a series of processes, with different time courses and each with their own neuronal substrate (see Discussion). As the authors themselves note, there were quantitative as well as qualitative changes in performance as the pursuit task was learned. Therefore, it may well be that other brain areas, including the putamen and cerebellum, might have shown more complex practice-contingent changes. Indeed, Grafton and colleagues themselves take care to point out that their results do not exclude other structures, including the putamen, having a role in motor learning.

Other factors may also contribute to inconsistencies between the various rCBF studies, particularly in relation to learning-contingent changes in striatal structures. Subtle changes in task may have an important impact on the pattern of relative rCBF. Indeed, even within the same task, subjects may use different strategies and thus involve different brain regions (Schlaug et al., 1994). Another factor may be the inherent neuronal heterogeneity of the striatum. The putamen and caudate have many different populations of neurons, with distinct firing patterns, and presumably have distinct functions. It is possible that different populations may be involved early and late in practice (e.g. Schultz et al., 1993; Aosaki et al., 1994), with the result that net metabolite activity shows no change across time (Jenkins et al., 1994). Thus, although brain imaging techniques provide us with powerful tools to examine the functional anatomy of motor learning, there is still a place for clinical studies with selected patient samples.

To return to the question of Parkinson’s disease as a model of motor learning dysfunction, the clinical and rCBF evidence reviewed so far leaves unresolved the possible contribution (if any) of putaminal dysfunction to motor learning, and particularly manual pursuit tasks. However, the rCBF evidence for an involvement of supplementary motor area is more consistent. The supplementary motor area is the main cortical projection site of the putamen via the ventrolateral thalamus. Both the putamen and supplementary motor area are known to be underactivated in Parkinson’s disease during voluntary movement (Playford et al., 1992; Jahanshahi et al., 1995), and that these changes are reversed by the administration of dopamine agonists (Jenkins et al., 1992).

The present paper describes a pair of studies which examined the ability of non-demented patients with Parkinson’s disease to learn a new manual pursuit tracking skill. Between them they address the issues of task specific effects on learning and the possible role of dopaminergic medication.

**Experiment 1**

**Subjects**

Ten patients with Parkinson’s disease and 10 aged-matched controls were recruited (Table 1). Patients were selected from out-patients attending the National Hospital for Neurology and Neurosurgery (London, UK) and normal control subjects from a panel of volunteers. Diagnosis of Parkinson’s disease was based on the presence of bradykinesia and at least one other of the following: rest tremor, rigidity and postural instability (Hughes, 1992), and the absence of any other possible aetiological factor for parkinsonism. All patients responded well to l-dopa and had mild or moderate illness as assessed by Hoehn and Yahr (1967) stage and the King’s College Hospital Parkinson’s Disease Rating Scale (Parkes, 1981). At the time of testing patients were on their normal antiparkinsonian medication. All subjects were right-handed. The study was conducted with ethical permission (National Hospital for Neurology and Neurosurgery, London) and all subjects gave informed consent.

**Methods**

Subjects sat ~1 m from a computer VDU screen. The target was a 1.5 cm wide rectangle moving horizontally on the screen in a predictable, repetitive sine wave of 0.25 Hz frequency, with a full oscillation subtending a visual angle of approximately 14°. Each trial commenced with a warning tone, followed after 1 s by target movement. The initial direction of movement (left or right) was randomized. The subject’s task was to track the target by moving the position of a pointer on a screen. Subjects controlled the position of this pointer by moving their right arm which rested on a manipulandum and pivoted at the elbow with a maximum displacement of 60°.

A mixed between-groups and within-subjects design was used. A distributed practice procedure was employed (Stelmach, 1969). Subjects performed three blocks of 10 trials (blocks A, B and C) representing the practice phase. Each trial lasted 36 s and comprised nine complete cycles of target movement. After each trial the subject had a break of 40 s during which time he/she was given knowledge of results in the form of bar graphs displaying the percentage time-on-target for that trial, and preceding trials. Each block was separated by a 10-min break. Subjects were tested for a further five trials after a rest period of 1 h (block D).

The test procedures employed in the present study were designed to maximize learning in all subjects. Distributed practice, transfer and knowledge of results helped to ensure that any deficits observed could be more confidently attributed to learning rather than to fatigue or lack of motivation.

Arm position during tracking was sampled at a rate of
Table 1 Clinical and demographic data of Parkinson’s disease patients and controls: experiment 1

<table>
<thead>
<tr>
<th></th>
<th>Parkinson’s disease patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male : female)</td>
<td>6 : 4</td>
<td>3 : 7</td>
</tr>
<tr>
<td>Hand (right : left)</td>
<td>10 : 0</td>
<td>10 : 0</td>
</tr>
<tr>
<td>Mini-Mental State Score</td>
<td>28.6 ± 2.8</td>
<td>29.1 ± 1.2</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.1 ± 8.7</td>
<td>69.7 ± 7.1</td>
</tr>
<tr>
<td>Parkinson’s disease duration (years)</td>
<td>6.8 ± 5.4</td>
<td>—</td>
</tr>
<tr>
<td>Hoehn and Yahr Stage</td>
<td>I 1</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>II 5</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>III 4</td>
<td>—</td>
</tr>
<tr>
<td>King’s College Hospital Scale</td>
<td>26.0 ± 13.1</td>
<td>—</td>
</tr>
<tr>
<td>L-Dopa dose (mg/day)</td>
<td>480 ± 312</td>
<td>—</td>
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150 Hz. Performance was measured in terms of percentage time-on-target. In calculating time-on-target for each trial, the data from the first cycle were excluded. Repeated measures analysis of variance employed Group (Parkinson’s disease patients and controls) as the between-subject factor and Trial or Block as the within-subject factors. For the within-subject and interaction terms, the $F$ values refer to averaged $F$ statistics, with Huyn Feldt correction of the degrees of freedom (Norušis, 1992).

**Results**

The two groups differed significantly in terms of age with the patients being younger ($P < 0.05$). There was no difference in the Mini-Mental State Score (Folstein et al., 1975) ($P > 0.10$). There was a higher proportion of males in the patient group, but the difference was not statistically significant ($P > 0.10$). Given the age difference between the groups, age was employed as a covariate in all of the analyses of variance.

Effect of Trial within Blocks A to D

The data for the individual trials are shown in Fig. 1. The trial data were analysed for each block in turn. In none of the blocks was the main effect for Group significant (in all cases $P > 0.10$). We will therefore consider only the effects of Trial and Group $\times$ Trial interactions.

In block A, there was a significant main effect for Trial ($P < 0.001$), but no significant Group $\times$ Trial interaction ($P > 0.10$). From Fig. 1, the greatest increase in time-on-target occurred over the first few trials in both groups. The cubic trend offered the best fit from the polynomial contrasts ($P < 0.001$), although the linear and quadratic trends were also highly significant. For block B there was a significant effect of Trial ($P < 0.01$), once again best described by the cubic trend, while the Group $\times$ Trial interaction approached significance ($P = 0.06$). Time-on-target appeared to decrease for the first trial of the block, although in this case only for the Parkinson’s disease group. For block C, neither the Trial effect nor Group $\times$ Trial effects were significant ($P > 0.10$). Finally, for block D a significant decrease in time-on-target was seen across the five trials ($P < 0.05$), but no significant Group $\times$ Trial interaction.

Effect of Block

Figure 2 shows the mean time-on-target for each block. Average time-on-target was calculated for each set of five trials (A1, A2, B1, B2, C1, C2 and D). Neither the main effects of Group, nor any Group $\times$ Block interaction was significant ($P > 0.10$). Therefore, we consider here only the main effects of Block, averaged across Group. There was a significant increase in time-on-target across blocks A1 to C2 ($P < 0.001$), with the trend best described by the linear contrast. One deviation from this general linear trend was the final five practice trials (C2) in both groups, a result that might have been attributed to fatigue. Excluding this data-point revealed a linear function with an $r^2$ value of 0.94 with...
a slope of 2.5% increase in time-on-target per five trials. Next the difference between blocks C2 and D was assessed. This revealed a further slight decrease in time-on-target after the delay ($P < 0.05$).

**Summary and comments**

With one exception (the warm-up decrement in block B), the performance of the medicated Parkinson’s disease group was not significantly different from that of the control group. Both groups showed the greatest improvements in performance over the first few trials. However, it seems unlikely that a performance ceiling had been reached. Maximum mean time-on-target was in the range of 60–70%, and (with the exception of the last few trials), performance showed slow but steady improvement across blocks.

Overall, therefore, the data provided no evidence for a deficit in motor learning. However, some caution is necessary in generalizing from these results. Although showing evidence of learning in both groups, the task itself may have been insufficiently sensitive to detect group differences. Another aspect of the results that raises doubts about the task, was the failure of either group to maintain the full performance gains after a 1 h delay. Finally, the fact that the patient group were maintained on their normal antiparkinsonian medication at the time of testing may, again have contributed to the lack of any significant between-group effects.

To address these issues a second experiment was designed. There were two main changes. Firstly, the possible effect of antiparkinsonian medication was examined by assessing both medicated and unmedicated patients. Secondly, the task was made more difficult in an attempt to make it a more sensitive measure of motor learning. A number of options were available to increase the task difficulty. The most obvious was to increase the target frequency from 0.25 Hz. However, it was felt that such a strategy might differentially handicap the patient groups, regardless of their ability to learn the task. Instead, it was decided to keep the sensory and motor aspects of the task identical, i.e. to track a 0.25 Hz sine wave. Complexity was increased by changing the control dynamic from position (zero order) to velocity (first order), with an additional directional component (see below). From pilot work in normal subjects, this task was shown to be associated with much higher initial error rates, and a more gradual and sustained learning curve. Most importantly, however, the motor demands of the task were identical to those employed in experiment 1.

**Experiment 2**

**Subjects**

Eight medicated (Parkinson’s disease-on) and eight unmediated (Parkinson’s disease-off) Parkinson’s disease patients were chosen from those attending the out-patient clinic of the National Neurological Institute (Milan, Italy). The Parkinson’s disease-off patients withheld anti-parkinsonian therapy from the evening prior to testing (~12–14 h). Eight age-matched normal controls were also tested. These were either spouses of the patients, or patients hospitalized for lumbar disc surgery. Inclusion criteria were as for experiment 1. Table 2 gives clinical and demographic features of the three groups. Illness severity (King’s College Hospital scale) and Hoehn and Yahr ratings were assessed at the start of testing. The study was conducted with ethical permission (National Neurological Institute, Milan) and all subjects gave informed consent.

**Method**

The equipment, experimental design, and data sampling method were identical to those used in the experiment 1.
The difference between this task, and that used in experiment 1, was that the position of the response manipulandum determined the direction and velocity of the response cursor on the VDU (first order or velocity control dynamic). Moving the manipulandum to the left, led to a leftward movement of the cursor. The further to the left it was moved, the faster the cursor moved in that direction. To stop the cursor, the manipulandum had to be moved back to the mid-position.

Rightward movement of the manipulandum then led to rightward movement of the cursor with increasing velocity. Therefore, to track the target with 100% accuracy the subject had to move the manipulandum in a 0.25 Hz sine wave (as in experiment 1), but 90° (i.e. 1 s) phase-advanced on the target.

The response dynamics of the tracking control were briefly demonstrated to each subject before commencing the task. They were told how the manipulandum controlled both the direction and speed of the response cursor. However, they were not allowed any practice, nor was the ordered relationship between the stimulus and response waveforms made explicit. Statistical analysis of the tracking data was carried out using repeated measures analysis of variance. No covariates were employed. Two independent comparisons were made, comparing each patient group in turn with the controls.

Results
The three groups did not differ in terms of age (P > 0.10) or years of education (P > 0.10). The proportion of males to females did not differ between the three groups (P > 0.10). All subjects were right handed. The Mini-Mental State was not assessed in all control subjects. None, however, showed any signs of clinically significant cognitive impairment. Comparing the Parkinson’s disease-on and Parkinson’s disease-off groups, there were no differences in disease duration or mean dopa daily dose (P > 0.10). Although the mean symptom severity rating (King’s College Hospital scale) of the Parkinson’s disease-off group was somewhat higher than that of the Parkinson’s disease-on group, the difference was not statistically significant (P > 0.10). Patients in both groups had mild to moderate Parkinson’s disease (Hoehn and Yahr stages I—III). There was no significant difference between the distribution of stages in the two patient groups.

The initial performance levels of the three groups clearly indicate the increased difficulty of the new task compared with the version used in experiment 1. The mean time-on-target for controls was 10.3% (SD 5.4), for the Parkinson’s disease-on group 10.5% (SD 5.3), and for the Parkinson’s disease-off group 7.5% (SD 2.4). Analysis of variance revealed that neither patient group differed significantly from the controls (P > 0.10). There was a significant increase in time-on-target across the 10 trials (P < 0.001), best fit by the quadratic polynomial contrast. A significant effect of trial was also found for block B (P < 0.05), together with a group×trial interaction that approached significance (P < 0.06). Examination of the data failed to reveal any simple explanation for this interaction. Rather it seemed to reflect a complex pattern of convergence and divergence between the two groups’ means across the 10 trials. For blocks C and D, significant effects of trial again
were found ($P < 0.05$). These were best explained by the improvement in performance between the first and second trial of each block, with a relatively stable performance for remaining trials.

(ii) Parkinson’s disease-off compared with controls. Analysis of block A revealed a significant effect of Trial ($P < 0.001$) together with a significant Group $\times$ Trial interaction ($P < 0.01$). The Group effect approached significance ($P < 0.09$). One possible cause of this interaction was the marked improvement in performance shown by the patients, but not the controls, in the final trial of the block. However, analysing only trial 1–9 still revealed a significant interaction effect ($P < 0.001$). Beyond block A, none of the Group $\times$ Trial interactions were significant ($P < 0.10$), and the main effects for Trial were similar to those described previously. For each block, however, there was a significant overall difference between the time-on-target of the controls and Parkinson’s disease-off group ($P < 0.05$).

Effect of Block

Next, the overall change in tracking performance across blocks was assessed (Fig. 4). As in experiment 1, blocks A–C were split into two parts, each of five trials. Across block A1–C2, the analyses revealed the same general pattern of results obtained by the analysis of the individual trials, with no significant difference between the Parkinson’s disease-on and control groups, but with significant Group ($P < 0.05$) and Group $\times$ Block ($P < 0.001$) interactions when considering controls and Parkinson’s disease-off.

Considering each group individually, all showed steady and significant improvement in performance across blocks A1–C2. For the controls and Parkinson’s disease-on groups, the best curve fit was obtained with a power function (controls $r^2 = 0.95$, Parkinson’s disease-on $r^2 = 0.98$). The data for each group, however, could be reasonably fitted to a linear trend (controls $r^2 = 0.87$, Parkinson’s disease-on $r^2 = 0.93$, Parkinson’s disease-off $r^2 = 0.98$) with slopes of 3.9% increase in time-on-target for controls for each block of 5 trials, 3.3% for Parkinson’s disease-on and only 1.7% for Parkinson’s disease-off.

Finally, performance for block C2 at the end of training was compared with performance for block D after the transfer period. time-on-target remained relatively constant ($P < 0.001$) together with a significant Group ($P < 0.01$) and Group $\times$ Block ($P < 0.001$) interactions when considering controls and Parkinson’s disease-off.

Summary

Percentage time-on-target error showed a steady improvement in all three groups across the 30 training trials, although the degree of improvement in the Parkinson’s disease-off group was significantly less than that shown by the controls. In contrast, the performance of the Parkinson’s disease-on group showed no significant impairment. Performance gains were well maintained after a delay in both control and Parkinson’s disease-on groups, but showed a significant deterioration in the Parkinson’s disease-off patients.

Discussion

After a general consideration of the findings, this discussion will focus on the implication of the results for two main issues: (i) the effect of task specific factors on motor learning and motor performance in Parkinson’s disease; (ii) the place of the striatum in the neuronal system(s) underlying motor learning.

How did the pursuit tracking task employed in experiment 1 compare with the pursuit rotor task employed in previous studies? As with the pursuit rotor, a simple position (zero order) tracking dynamic was used, although it was easier in that the arm was supported and it involved only single degree-of freedom movement. However, it was perhaps slightly more difficult in that the subject was having to use
the manipulandum to control an on-screen cursor with an amplitude gain of ~4, compared with the more direct control employed in the pursuit rotor. These differences, however, appeared to have little impact on the pattern of results obtained. As in the previous studies, a group of mild-to-moderately disabled Parkinson’s disease patients, without clinical evidence of dementia and on their normal anti-parkinsonian medication, showed no appreciable evidence of impairment in motor learning. The results of the first experiment, therefore, confirmed that a deficit in motor learning is not inevitable in Parkinson’s disease.

As noted in the comments on experiment 1, a number of aspects to the results suggest that caution is necessary in generalizing from this result. First, the rate of performance improvement with practice was slow beyond the first few trials and, secondly, there was no evidence that those performance gains were retained after a delay without practice, an important criterion for motor learning. Thus, although generally supportive of previous evidence, further investigation was judged appropriate.

In experiment 2, the complexity of the task to be learned was increased in an attempt to improve sensitivity. Unlike studies employing the pursuit rotor which manipulated target frequency, the present study altered the dynamics of the system transforming arm position into response cursor position. Increasing the control order is known to have a dramatic effect on tracking performance (Wickens, 1986). Comparing the performance of the control group in experiment 1 with that of the control group in experiment 2 illustrates the greater difficulty of velocity over position control. This reveals an almost four-fold decrease in % time-on-target error at trial 1.

Although this experimental manipulation was effective in increasing task difficulty for all subjects, it did not change the main pattern of results for the medicated patients with Parkinson’s disease. As in experiment 1, the Parkinson’s disease-on group showed a normal rate of learning across the 30 trials of practice. Both Parkinson’s disease-on and control groups showed a steady improvement in tracking performance across the first 10 trials more than doubling % time-on-target. In subsequent blocks, tracking performance continued to show significant, if slower, improvement. Unlike experiment 1, both groups maintained a large proportion of the improvement across the transfer period to block D.

These data support the conclusion from experiment 1 that medicated, non-demented and mild-to-moderately impaired patients with Parkinson’s disease appear to show normal motor learning. Previous research suggests that deficits might have been found if we had assessed patients with clinically significant intellectual impairment, or patients with more severe motor signs. However, these issues lie outside the scope of the present investigation. One important question which was tackled, however, was the possible impact of dopaminergic medication on motor learning.

The Parkinson’s disease-off patients showed clear evidence of learning, but the degree of performance gain across trials was substantially reduced. Furthermore, there was some deterioration in tracking performance after a delay in which the subject rested.

Superficially, these results suggest that motor learning is indeed impaired in patients with Parkinson’s disease, at least when withdrawn from dopaminergic medication. However, before accepting this conclusion, it is useful to consider some alternative explanations.

**Psychological theories of motor learning**

In one broad class of theory, motor learning is seen as a relatively automatic build-up of adaptive response patterns through experience. Such approaches range from the early associationist theories of Thorndike (1903) and Lashley (1917), to contemporary neural network models (see Masson, 1990). Although varying considerably in detail, these theories or models stress the importance of stimulus–response or input–output pairings, together with some shaping feedback such as reward or an error signal. The second class of theories can be broadly termed cognitive theories of skill acquisition. In the tradition of cognitive psychology, these theories are concerned with (i) the processes involved in skill, (ii) how information is represented and transformed, and (iii) how the nature of the representation and associated processes changes with practice.

A common strand that runs through cognitive theories of motor learning is that different processes and modes of representation are involved at different phases of learning, i.e. that the smooth transition in motor performance does not reflect an equivalent transition in a single underlying process. Although varying in detail, most theories draw a distinction between an initial phase, demanding conscious processing, working memory, attention, hypothesis testing, etc., and a later more automatic phase, where the attentional demands are reduced or even absent. For example, Fitts (1964) described a transition from ‘cognitive’ to ‘associative’ to ‘autonomous’ stages. Adams (1971) described ‘verbal–motor’ and ‘motor’ stages; Logan (1988) ‘algorithm-based’ and ‘memory-based’ performance, while Anderson (1983) distinguished between ‘declarative’ and ‘procedural’ based knowledge systems.

One difference between these theories is whether they propose successive, serial stages (e.g. Fitts, 1964), or the action of essentially independent processes (e.g. Anderson, 1983). For Anderson, the acquisition of a skill depends ultimately of the ‘produralisation’ of knowledge. This is based on so-called ‘production systems’ of condition–action (IF–THEN) pairs, represented in long-term memory, but not verbalizable or open to conscious interpretation. However, coexistent with this system, is declarative knowledge about the task. This can be described verbally, retained and manipulated in working memory, and represented in the form of propositions or mental images. While both systems coexist, their relative importance changes during learning. Early in practice, the declarative system might be expected to have
the greatest impact on performance. Later, however, the procedural system could safely take over, releasing the limited resources demanded by the declarative system for other tasks. The reduction in the number of systems involved, and the shift in their relative importance, are referred to as ‘constriction’ and ‘displacement’ (Heuer, 1984), and are a common feature of many models of skill acquisition.

Although Anderson’s (1983) model is only one of many, it has certain attractions in considering the functional anatomy of motor learning. Most obvious is the tie-in between Squire’s (1982) suggestion of anatomically distinct ‘declarative’ and ‘procedural’ systems, and Anderson’s description of ‘declarative’ and ‘procedural’ information. It is important to note, however, that declarative knowledge is not synonymous with declarative learning or memory. As stated, Anderson’s declarative system is one based around working memory. It allows conscious access to and manipulation of information, both current and stored. The declarative memory system, in contrast, is usually taken to refer to the system involved in the acquisition, long-term storage and retrieval of information. While the two sets of systems overlap conceptually, and probably anatomically, they are not the same. The most obvious illustration of this is that amnesic patients who have a deficit in declarative learning and memory (in Squire’s sense), nevertheless seem to have a functioning declarative system (in Anderson’s sense). They appear able to hold and manipulate information in working memory, verbalize the contents and formulate plans and strategies on the results. The difference is their declarative (working memory) system does not have access to declarative (long-term) memory.

One further implication of Anderson’s (1983) model, and other similar ones, is that there is no such thing as a pure procedural task, a fact increasingly appreciated in the literature on procedural learning. All forms of so-called procedural or implicit learning, including motor learning, will probably involve the declarative system, particularly early on. While access to declarative knowledge may not be necessary for the process of proceduralization, that knowledge can offer a strong advantage for the rate of behaviour change.

Adopting this model requires that we redefine our task in looking for the anatomical substrate of motor learning. Many areas will be involved in the learning of a new motor task. Precisely which areas will depend upon the nature of that task, and the stage of learning. However, to say that an area is involved at a particular stage in the learning process, is not the same as saying that the area forms part of a ‘procedural system’.

Declarative and procedural knowledge, and motor learning in Parkinson’s disease

How do the perspectives offered by the cognitive approach help in understanding the results of experiment 2? In particular, how might they help in explaining the poorer performance gains shown by the Parkinson’s disease-off group?

When first starting to perform the velocity tracking task used in experiment 2, the subject is faced with a novel situation. The ‘automatic’ tendency to employ a position tracking response produces a large error. Despite having information that the manipulandum controls both the speed and direction of the response cursor, this knowledge does not immediately suggest any systematic strategies for dealing with the problem. At this stage we may consider that performance improvement may be largely under the control of the procedural system, and that the declarative system is still ‘looking’ for the information that will help it control behaviour. As described previously, the most effective strategy is to move the tracking arm precisely one-quarter cycle ahead of the target. We cannot be sure whether and when a subject has explicitly discovered this rule. However the possibility remains that control subjects and the Parkinson’s disease-off patients did discover this new strategy and used it to improve their tracking performance, whereas the Parkinson’s disease-off group did not. This hypothesis provides an alternative perspective on the results of experiment 2, namely that the Parkinson’s disease-off group did not show impaired learning per se. Rather, they were using less than optimum strategies for solving the problem of velocity tracking. In effect, there was a failure of the declarative system, resulting in them trying to learn a more difficult task.

An alternative account, however, and one which we favour, is that the solution of the tracking problem and the application of declarative knowledge essentially changed the nature of the task. The subject now had to exert more deliberate control over the tracking response, employing a phase-advanced strategy, rather than employing more ‘intuitive’ approaches to minimize the tracking error. This strategy would require the subject deliberately to ignore the visual signal provided by the target, but to track instead an ‘imaginary’ target moving one-quarter cycle ahead. It is well known that Parkinson’s disease patients are more dependent on visual information for motor control (e.g. Cooke et al., 1978), and that they show increased error in tracking even simple patterns without vision (e.g. Flowers, 1978; Stern et al., 1984). Furthermore, even in discrete movements, patients are slowed relative to controls when they have to make a choice response signalled by a spatially incompatible stimulus (Brown et al., 1993b). The combined demands of (i) ignoring or devaluing a misleading (incompatible) visual stimulus, while (ii) simultaneously tracking a spatially displaced internal model of the target movement, would present the patients with an extremely difficult task.

Thus we suggest that, in experiment 2, the development of declarative knowledge about the tracking dynamics may have placed the Parkinson’s disease-off group at a disadvantage compared with the other two groups. In the control and medicated Parkinson’s disease groups, this new
knowledge could be rapidly utilized. In the Parkinson’s disease-off group it could not.

It is acknowledged that this interpretation is post hoc, and subjects were not questioned about their insight into the task dynamics, nor their strategy in performing the task. However, a number of testable predictions are suggested. Firstly, if patients were somehow impaired in acquiring the relevant declarative knowledge, then informing all subjects at the start of the session should equalize performance gains in the three groups. If, however, the patients problem was in utilizing this knowledge to control performance, then the information might lead to an even greater initial deficit. Secondly, if subjects were given an attention demanding secondary task, and thus inhibited from developing the declarative knowledge, performance gains would be restricted to the action of the procedural system. While this might lead to a slower rate of improvement in the control and Parkinson’s disease-on patients, Parkinson’s disease-off patients should show an enhancement in performance, and a rate of learning equalized to the other two groups.

Such an analysis, although derived from the present results, can be applied equally to any study on motor learning. If we accept the concept that learning occurs through the combined action of both procedural and declarative knowledge, then it is necessary to think in these terms for all tasks. Specifically, what possible impact might declarative knowledge have on the task? In particular, we need to ask the following questions: what conscious strategy is the subject using in trying to perform the task? How is that strategy altered by different degrees (or accuracy) of declarative knowledge? What are the implications of the chosen strategy for the patient’s motor performance, i.e. does choosing a particular strategy disadvantage a patient’s performance because of motor control problems independent of any difﬁculties in motor learning?

Although the data on performance change with practice provides only equivocal support for a deficit in motor learning, one final aspect of the results needs to be considered. This is the deterioration in performance shown by the Parkinson’s disease-off group after the transfer period. Such a decline suggests that impaired motor learning may have made some contribution to the performance deﬁcits, although alternative explanations such as a worsening in the patients motor symptoms with time off medication must also be considered.

Motor learning: the role of the fronto-striatal system and dopamine?
The starting point of the present investigation was to explore the hypothesis that the putamen plays an important role in a system of procedural learning, and speciﬁcally in motor learning. We suggest that our ﬁndings offer only equivocal support for the hypothesis that the putamen or its cortical projection sites are critical structures in a system subserving motor learning, at least for the type of tasks involved in the present studies. Rather, putaminal dopamine depletion may exert its inﬂuence on behaviour, and behavioural change with practice, through other mechanisms related to motor control and the processing of information. In the present investigation, a deﬁcit was observed in a task which could be optimally performed by switching from an external (visually guided) mode of tracking to one in which motor control is based on an internal representation uncoupled from the visual information. In functional anatomical terms, this could be understood as a transfer of control at a cortical level from lateral premotor cortex to supplementary motor area (Passingham, 1985). Thus in the unmedicated patients with Parkinson’s disease, the under-functioning of the putamen—supplementary motor area circuit would interfere with the ability to employ this mode of control.

This conclusion runs counter to some recent suggestions from other investigators. For example, Saint-Cyr and Taylor (1992) see the striatum (although not speciﬁcally the putamen) as having a critical role in a procedural or ‘habit’ system. They, like us and other authors, focus upon the interplay between different sources of procedural and declarative knowledge. They propose that the striatum is ‘... transiently involved during the early stage of procedural learning (mobilization phase), and that this system is designed to function intuitively and nonconsciously. ... the fundamental role of the striatum is to mobilize new procedures and to select among known procedures by acting as a procedural memory buffer.’ In accounting for skill deﬁcits in patients with Parkinson’s disease, Saint-Cyr and Taylor (1992) see patients as potentially compromised in two ways: (i) an ineffective conscious cortical system (based on the prefrontal cortex), and (ii) a dopamine-poor striatal circuit, which has to ‘limp along ineffectively’.

It should be noted that our own data do not necessarily support this hypothesis. We would agree that, in some tasks, a conscious cortical process such as problem solving may be inefficient and place limits on behaviour. However, we would add other limitations, including the ability to use accurate declarative knowledge to guide and control motor behaviour. However, while these various task-speciﬁc limitations may slow the rate of behavioural change with practice, this is not the same as saying that the underlying processes of procedural learning are fundamentally impaired.

Conclusions
The results show that on a complex tracking task involving a velocity control dynamic, unmedicated patients with Parkinson’s disease show a slower rate of improvement in performance with practice and fail to maintain gains after a delay compared with medicated patients with Parkinson’s disease and controls. It is unclear, however, from this and previous studies, whether these deﬁcits reﬂect an impairment in proceduralization, or problems in acquiring or utilizing declarative knowledge to assist in performing the task more efﬁciently. We favour the parsimonious conclusion, consistent with data obtained from many sources, that the deﬁcit found
in the present study was associated with the need to employ an internal rather than stimulus-bound representation of motor control, and it is this that sets limits on the performance gains shown by the Parkinson’s disease-off group. This has important implications for the assessment of motor learning, and indeed any skill, in patients with neurological disease. It also has implications for our concept of a discrete ‘procedural system’.

Motor learning has been defined as long lasting behavioural change as a result of experience. This is seen as the concerted action of a basic and largely autonomous process of proceduralization, combined with conscious application of task-specific knowledge. If the acquisition or utilization of this latter declarative knowledge is impaired through disease, there may be a deficit in the rate of behavioural change with practice. In other words, there will be a deficit in ‘motor learning’ at the behavioural level. However, this does not imply that the rate of proceduralization is impaired, nor that the affected brain regions are part of any coherent ‘procedural system’. The definition of a procedural system, assuming that one exists, requires that we identify lesions that produce robust impairments in the rate of learning independent of the particular characteristics of the task.

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