We studied 10 subjects each with melancholic depression evidencing significant motor retardation (RM), Parkinson's disease (PD) with bradykinesia, and normal healthy controls (NC), matched closely for age and gender, on measurements of motor function and depression, and their performance of simple and complex ballistic movements. The simple movements involved the execution of 10°, 20°, and 40° angular movements using a methodology adapted from Hallett and Khoshbin (1980). The complex movements involved the performance by the right arm and hand of a squeeze and a flexion movement, both sequentially and simultaneously, using a methodology adopted from Benecke et al (1986, 1987). The RM and PD groups demonstrated a smaller increase in the angular velocity as the angle of the movement increased from 10° to 40° than did the NC group. Many PD and RM subjects showed multiple electromyographic (EMG) bursts during the ballistic movements. The RM and PD subjects tended to take longer to perform the simultaneous and sequential movements, but nonsignificantly so. The RM group performed the squeeze movement slower when executed as part of the simultaneous movement than when performed as a simple movement. The pause time between the movements when performed sequentially was longer (nonsignificantly) for the RM subjects. Our study demonstrated a disturbance in the execution of simple and complex movements by RM subjects that resembled the disturbance seen in PD. This argues for a common pathophysiological basis for at least some aspects of motor retardation in the two disorders. Reduced dopamine function is one common abnormality that may partially account for these findings.

Key Words: Psychomotor retardation, bradykinesia, melancholia, Parkinson's disease, ballistic movements

Introduction

In the long-standing debate on the classification of depressive disorders (Kendell 1968), the syndrome variously called "endogenous," "biological," or "melancholic" depression has most consistently been regarded as a categorical entity with an imputed biological basis (Mendels and Cochrane 1968; Nelson and Charney 1981). Investigators have attempted to characterize the typical features of this entity, which we will refer to as melancholia (Davidson et al 1984), but a number of old controversies remain unresolved. Of the various strategies available to validate the diagnosis, the demonstration of an associated alteration in the physiological state has been considered to be one of the most powerful (Cowen and Wood 1991). In this paper we attempt to demonstrate a physiological disturbance in melancholic patients with motor retardation. The justification for this approach stems from two major observations reported in the literature: the importance of psychomotor change in melancholia, and the strong parallel this has with the bradykinesia of Parkinson's disease.

The defining features of melancholia are not consistently accepted by all researchers, and concordance between dif-
ferent systems such as DSM-III (American Psychiatric Association 1980), Newcastle (Carney et al 1985) and Michigan (Feinberg and Carroll 1982) discriminant indices is modest at best (Davidson et al 1984). Some influential reviews have held "psychomotor retardation" to an important discriminant variable between the categories of melancholic and nonmelancholic depressions (Mendels and Cochrane 1968; Nelson and Charny 1981). Widlöcher (1983) considered retardation to be the core behavioral pattern in affective disorders. Recent work by Parker et al (1990) places emphasis on psychomotor change as a core feature of melancholic depression. In spite of this increasing recent interest, descriptions of motor dysfunction in depression have been generally restricted to impressionistic, subjective observations, with perhaps a few exceptions (Greden and Carroll 1981; Widlöcher 1983; Parker et al 1990).

Although the slowness of movement in retarded melancholia (RM) has been largely ignored, its counterpart (bradykinesia) in Parkinson's disease (PD) has been extensively investigated. The parallel between the two has attracted the attention of neurologists and psychiatrists since the time of Charcot (Marsden 1989a). The RM patient with a stooped posture, expressionless face, reduced spontaneous motor activity, and slowed movement looks uncannily like the parkinsonian patient. Although PD is characterized by bradykinesia, rigidity, tremor, and postural instability, the slowness or loss of ability to move is considered to be the most characteristic and fundamental motor deficit (Marsden 1989b). Van Praag and colleagues (1975) have argued that similar behavioral syndromes in neuropsychiatry may have the same pathophysiology. Neurophysiological techniques that have proved useful in analyzing bradykinesia in PD may, therefore, be rewarding in RM.

Some disturbances thought to underlie the bradykinesia of PD are demonstrable in the execution of fast simple and complex limb movements (Marsden 1989b). When patients with PD attempt a self-paced, fast movement at one joint, not only is the reaction time increased, but the movement time is increased as well. PD patients do not increase the velocity when they make larger movements as much as normal subjects (Hallett and Khoshbin 1980). PD patients have an added difficulty when they try to execute two movements simultaneously (Benecke et al 1986) or sequentially (Benecke et al 1987). We argue in this paper that, if there are similarities in the pathophysiological basis of the motor disorder of RM and PD, RM patients should have similar disturbances in the execution of fast limb movements.

Methods

Subjects

The subjects comprised patients with retarded melancholia matched for gender and, as closely as possible, for age. All were right-handed individuals (score > +9 on the modified Annett's hand preference questionnaire (Briggs and Nebes 1975). The following inclusion criteria were used:

1. RM (Retarded Melancholic patients): (1) Satisfy DSM-III-R (American Psychiatric Association 1987) and Research Diagnostic Criteria (RDC) (Spitzer et al 1978) for melancholic/endogenous major depression. (2) A mood Disorders Unit (MDU) Core Score >16 (indicating high endogeneity). This rating scale of psychomotor function in depression has been developed by Parker et al (1990) at the Prince Henry Hospital, Sydney, and has been demonstrated to have high interrater reliability. The 24-item version was used. (3) A MDU Core Sign rating of ≥2 (i.e., moderate or severe abnormality) on at least four of the following items: facial immobility, postural slumping, delay in cognitive processing, immobility, slowed movements, delay in motor activity, and slowing of speech rate (indicating moderate to severe retardation). (4) Presence of retardation ≥1 week. (5) No other neurological or musculoskeletal abnormalities on examination (as judged by a neurologist) and a normal computed tomography (CT) scan of the head. (6) Absence of a medium frequency (4–6 Hz) tremor at rest as demonstrated on accelerometry. (7) On no neuroleptic medication for a minimum of 6 weeks (3 months in case of depot preparation), or lithium carbonate for 2 weeks. (8) Patients free of all medication were preferentially included, but antidepressants or benzodiazepines therapy did not lead to exclusion. (9) No history of parkinsonism, severe head injury, dementia, epilepsy, alcohol dependence, peripheral neuropathy, neuromuscular disorder, or other significant neurological disease. (10) No first-degree family history of Parkinson's disease, Progressive Supranuclear Palsy, Multiple System Atrophy, Huntington's disease. (11) Age <70 years. (12) Ability to give informed consent and complete the study.

2. PD (Parkinson's disease patients): (1) Patients diagnosed as having idiopathic PD by two independent neurologists, and who fulfilled the UK Parkinson's Disease Society Brain Bank Diagnostic Criteria (Rogers et al 1986). (2) Do not meet DSM-III-R or RDC criteria for major depression, dysthymia, or minor depression. (3) Zung Depression Scale (Zung 1965) score <40. (4) A rating of 2 on at least two of the following Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn et al 1987) items: facial expression, posture, gait, body bradykinesia, rapid alternating hand movements. (5) Absence of significant
with the study. (6) Absence of dementia (clinically judged) and no more than mild memory impairment, and Mini-Mental State (Folstein et al 1975) Score ≥ 25 (if there was doubt, a detailed neuropsychological evaluation was performed to rule out dementia). (7) Taken no medication on the day of assessment. (8) Ability to give informed consent.

3. NC (normal control subjects): (1) No current diagnosis on axes I and III of DSM-III-R and on RDC. (2) No significant current medical or neurological illness, in particular PD. (3) Zung score < 40. (4) No past history of affective disorder that required treatment. (5) Score of "zero" on all items of section III (motor examination) of the UPDRS. (6) On no medication.

Patients were administered section I (mentation, behavior, and mood) and III (motor examination) of the UPDRS, and a modified Hoehn and Yahr (1967) staging was performed on the PD group.

An MDU core signs rating was undertaken for each subject prior to the experiment. The following tests were also administered:

1. Finger Tapping Test (FTT), three 10-sec trials, using the right index finger (Reitan and Davidson 1974). The mean score for the 3 trials was obtained;
2. Purdue Pegboard test, three 30-sec trials using the right hand (Purdue Research Foundation 1948). The mean number of pegs placed correctly was obtained;
3. a Global rating of bradykinnesia on a 100-mm analogue scale designed for this study.

Investigations were carried out in the morning, after a light breakfast and with no medication on that morning.

Brief Description of the Sample

The principal clinical characteristics of the subjects are presented in Table 1. Three RM subjects, who met the criteria for inclusion, were subsequently excluded because of their inability to complete the investigations. A fourth RM subject was excluded because of her inability to generate ballistic movements. One RM subject failed to complete the study in the first instance, but was reexamined after 2 weeks of treatment with imipramine, with successful completion. The RM subjects had been ill for 3 months to 2 years. Four RM subjects were currently (at least 2 weeks) on no psychotropic medication, but one of these had received electroconvulsive therapy 2 days previously; the remaining six were on the following psychotropic drugs: desipramine 2, imipramine 2, nortriptyline 1, temazepam 1, diazepam 2. No subject had received a neuroleptic in the previous 3 months.

The PD subjects had been ill for 3 to 9 years, and were being treated with the following drugs: levodopa 9/10, bromocriptine 8/10, amantadine 2/10, benztropine 1/10, tricyclic antidepressant (small dose) 3/10, benzodiazepine 4/10. They rated as stages 2, 2.5, 3, or 4 on the Hoehn and Yahr (1967) scale.

Study 1

Simple Ballistic Movements

Ten matched retarded melancholic patients, Parkinson's disease patients, and normal controls were studied. These patients were assessed as above by the first investigator (PS). The measurements were performed by AMA who was not informed about the diagnostic category of the subject, although the nature of the disorders precluded complete blinding of the investigator.

The technique used was adapted from that previously described by Hallett and Khoshbin (1980). The subject sat in a chair facing an oscilloscope. Movements were made in the horizontal plane by abducting the shoulder to 90° and securing it firmly on a manipulandum constructed for this study. This consisted of a steel arm mounted on a wooden frame. The arm rotated freely at a hinge at the level of the elbow into which was incorporated a potentiometer to convert the rotation of the elbow into a variable voltage. The other end of the metal arm had a U-shaped metal bar for the subject to grip, which rotated the forearm into supination, so that the biceps remained the chief flexor of the elbow. The oscilloscope screen facing the subject displayed the voltage from the potentiometer as the height of the single beam, which ran rapidly to appear as a line. The graticule was illuminated, with the lowest line corresponding to an elbow angle of 120°, with further lines above at intervals of 10°. Subjects were asked to make rapid ("as quickly as possible"), accurate elbow flexion movements beginning at 120°, with the line under their control superimposed on the bottom of the graticule. Each movement was made in response to an auditory signal, which also triggered the recording device. Three movements of differing angular distance were studied (10°, 20°, 40°). Only well-practiced movements were studied, and during the course of the experiment the subjects were constantly urged to move as rapidly as possible. Electromyographs (EMG) with surface electrodes were recorded from biceps and triceps. The audio-trigger, the EMG activity, and the change in elbow angle were stored on magnetic tape for later analysis.

ANALYSIS OF DATA. The angular velocities of the movements were calculated from the angle and the time taken from onset of movement. The reaction times from the auditory signal to the start of the movements were calculated for the different groups. The reaction times and movement velocities for small and large amplitude movements were compared between the patient (RM and PD) groups and NC, using analyses of variance (ANOVA) with Tukey test for multiple comparisons. A repeated measures analysis
Table 1. Some Clinical Characteristics of the Three Groups: Retarded Melancholia (RM), Parkinson’s Disease (PD), Normal Controls (NC)*

<table>
<thead>
<tr>
<th></th>
<th>RM (n = 10)</th>
<th>PD (n = 10)</th>
<th>NC (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean (SD)b (years))</td>
<td>61.5 ± 9.3</td>
<td>61.5 ± 5.6</td>
<td>61.5 ± 7.2</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>5/5</td>
<td>5/5</td>
<td>5/5</td>
</tr>
<tr>
<td>Duration of illness (range)</td>
<td>3 mths–2 yrs</td>
<td>3–9 yrs</td>
<td>—</td>
</tr>
<tr>
<td>Bradykinesia rating</td>
<td>31.4 ± 15.2</td>
<td>41.1 ± 22.2</td>
<td>0*</td>
</tr>
<tr>
<td>MDU Core score</td>
<td>22.1 ± 11.4</td>
<td>12.1 ± 10.2</td>
<td>0*</td>
</tr>
<tr>
<td>FTT—R</td>
<td>11.22 ± 3.0</td>
<td>45.9 ± 9.7</td>
<td>47.4 ± 5.9</td>
</tr>
<tr>
<td>Purdue Pegboard score—R</td>
<td>11.7 ± 2.3</td>
<td>9.3 ± 3.0</td>
<td>13.4 ± 0.9</td>
</tr>
<tr>
<td>UPDR Scale score</td>
<td>6.4 ± 3.4</td>
<td>17.5 ± 11.9</td>
<td>0.5 ± 0.8</td>
</tr>
<tr>
<td>Zung Depression score</td>
<td>55.6 ± 10.1</td>
<td>33.5 ± 4.2</td>
<td>26.3 ± 5.1</td>
</tr>
</tbody>
</table>

*R = right hand; FTT = Finger Tapping Test; MDU = Mood Disorders Unit Core Scale score (Parker et al 1990); UPDR = Unified Parkinson’s Disease Rating Scale.

*See text for explanation of scales and references.

**Matched variable.

Contrasts using ANOVA with Tukey test for multiple comparisons.
(1) RM and PD versus NC 'p < 0.05; "p < 0.01; p < 0.001.
(2) RM versus NC 'p < 0.001.
(3) PD versus NC 'p < 0.05; "p < 0.01; p < 0.001.
(4) RM versus PD 'p < 0.001.

of variance was performed between NC and the two patient groups (RM and PD), with velocity at 10°, 20°, and 40° as the repeated measures factor, using the Wilks’ lambda test. The EMG burst patterns for the RM, PD, and NC groups were examined visually. Rank-order correlations were calculated between the MDU, UPDRS, Bradykinesia ratings, FIT, and Pegboard scores and the movement times and velocities for the different ballistic movements.

Study 2

Simultaneous and Sequential Limb Movements in Melancholia

Ten subjects each of RM, PD, and NC were studied. The experimental procedure was adapted from Benecke et al (1986, 1987), and only a summary is presented here. Subjects were seated as in Study 1 and the angular movement was similarly monitored. A U-shaped metal bar at the end of the manipulandum, with a strain gauge attached to it, was grasped between the thumb and fingers. The different movements to be studied were as follows:

1. single flexion: of the elbow through an angle of 20° from a starting angle of 120° ("flex");
2. single squeezes of the strain gauge bar to exert a force 20% of the maximum voluntary contraction previously determined ("squeeze");
3. both these tasks at the same time ("squeeze and flex");
4. both tasks in sequence ("squeeze then flex").

The subjects were instructed to perform each movement as rapidly as possible, and this instruction was repeated periodically. For the sequential movements (squeeze then flex), the subjects were instructed to perform the squeeze and immediately on its completion, flex the elbow.

The elbow position and force of grip were displayed as two horizontal bars on an oscilloscope screen in front of the patient. After a series of practice trials, 10 single trials of each task were collected. Trials were excluded from analysis if they were not simultaneous or sequential, as the case may be, or if the movements were performed in the wrong order. EMG activity was monitored in the biceps and triceps muscles using surface electrodes. The velocity of the elbow movement (electronically derived from the position signal), the force of hand squeeze, and rectified EMG were recorded. Reaction times were measured from the go signal to movement onset, for both "flex and squeeze. For both the simultaneous and sequential tasks, the interval between the onset of the first and second movements (the interonset latency, IOL) was measured. The movement time of the first movement was subtracted from the IOL of the sequential task to give the pause time between the two movements. The times taken for flexion and squeeze movements to be performed, independently and as part of the complex simultaneous movement, were calculated.

**ANALYSIS OF DATA.** The movement times for the "flex," "squeeze," "flex and squeeze," "squeeze then flex," the IOL for both tasks, and the pause time were compared between patient (RM and PD) groups and NC subjects using analysis of variance with Tukey test for mul-
Multiple comparisons. Spearman’s test of rank correlations were used to test the relation between scores on FTT, Pegboard test, MDU, UPDRS, Zung, and the Bradykinesia scores with the parameters of simultaneous and sequential movements.

Results

For the entire sample, the correlations between the different measures of bradykinesia and depression were calculated, along with one-tailed levels of significance. These results are presented in Table 2. The global rating of bradykinesia had a highly significant positive correlation with the MDU Core score and the UPDRS Section 3 score, and a negative correlation with FTT and Pegboard scores. The MDU Core score also correlated significantly with the Zung depression score and the FTT and Pegboard scores. When the following scores: MDU Core, UPDRS section 3, global bradykinesia, Zung depression, FTT and Pegboard were subjected to a factor analysis to determine if they measured similar or different constructs, two factors emerged. The rotated factor matrix revealed high factor loadings for Zung (0.93) and MDU Core (0.79) scores on Factor 1 (interpreted as the Depression factor), and UPDRS (0.92) and global bradykinesia (0.72) scores on Factor 2 (interpreted as the bradykinesia factor). There was a high correlation between the two factors (r = 0.61) indicating a great overlap between the two constructs.

Study 1

The movement and reaction times, and the angular velocities for the three movements are given in Table 3. The NC subjects significantly increased the angular velocity as the movement angle increased from 10° to 20° to 40° (repeated measures ANOVA, n = 10, df = 2, F = 121.23, p < 0.001), as has been demonstrated previously (Hallett and Marsden 1979). The PD (n = 10, df = 2, F = 52.86, p < 0.001) and RM (n = 10, df = 2, F = 24.38, p = 0.003) subjects similarly increased the velocity, but not to the same extent. For the 10° movement, the mean angular velocity was nonsignificantly lower for the PD group, but no different for the RM group, when compared with controls. There was no significant difference for the 20° angular velocity between the patient groups and the controls, but for the 40° angular velocity, RM and PD was significantly slower than the controls (p < 0.05), and the difference between RM and PD was not significant. When the RM group was compared with the NC group using repeated measures ANOVA with angular velocities at 10°, 20° and 40° as the repeated measure, the group by angle effect was highly significant (SS = 1410.00, df = 1, MS = 705.00, F = 6.44, p = 0.004). The PD group also differed significantly from the controls (SS = 589.05, df = 1, MS = 294.13, F = 3.29, p = 0.049). The conclusion drawn was that both patient groups failed to show as great an increase in angular velocity as did the NC group, and this was most evident when the angle of movement increased to 40°. Figure 1 is a graphic representation of the angular velocities for the three groups for different angles.

NC subjects performed the flexion movements with a biphasic or triphasic pattern of EMG activity in the agonist and antagonist muscles (Figure 2). Many of the PD subjects showed 3–5 bursts of EMG activity during the movements. The RM subjects showed a similar abnormality in some movements (Figure 2). Because of the poor definition of the onset and offset of the first agonist burst in many cases, enough measurements of its duration could not be obtained for a valid analysis.

Study 2

The results of the simultaneous (squeeze and flex) and sequential (squeeze then flex) movements are presented in Table 4.

The RM and PD groups were slower to complete the

Table 2. Spearman’s Correlation Coefficients Matrix of Scores for the Entire Sample (n = 30)4

<table>
<thead>
<tr>
<th>Variable</th>
<th>MDU score</th>
<th>UPDRS score</th>
<th>FTT score</th>
<th>Pegboard score</th>
<th>Bradykinesia score</th>
<th>Zung score</th>
<th>10° Velocity</th>
<th>20° Velocity</th>
<th>40° Velocity</th>
<th>Reaction time (40°) Simultaneous</th>
<th>Complex excess squeeze flexion</th>
<th>Sequential Movements IOL</th>
<th>IOL Pause</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDU Core score</td>
<td>—</td>
<td>0.32</td>
<td>-0.63a</td>
<td>-0.40a</td>
<td>0.76a</td>
<td>0.69a</td>
<td>15</td>
<td>-0.00</td>
<td>-0.33</td>
<td>0.35a</td>
<td>0.30</td>
<td>0.11</td>
<td>0.49a</td>
</tr>
<tr>
<td>UPDRS (Factor 3)</td>
<td>0.32</td>
<td>—</td>
<td>-0.02</td>
<td>-0.54b</td>
<td>0.62a</td>
<td>0.04</td>
<td>-0.05</td>
<td>-0.23</td>
<td>-0.20</td>
<td>0.45a</td>
<td>0.49a</td>
<td>0.27</td>
<td>0.83b</td>
</tr>
<tr>
<td>Bradykinesia</td>
<td>0.76c</td>
<td>0.62b</td>
<td>-0.50a</td>
<td>-0.52a</td>
<td>—</td>
<td>0.48a</td>
<td>-0.06</td>
<td>0.05</td>
<td>-0.16</td>
<td>0.40a</td>
<td>0.24</td>
<td>0.22</td>
<td>0.61a</td>
</tr>
<tr>
<td>Zung score</td>
<td>0.69b</td>
<td>-0.04</td>
<td>-0.78a</td>
<td>-0.12</td>
<td>0.48a</td>
<td>—</td>
<td>0.02</td>
<td>0.01</td>
<td>-0.30</td>
<td>-0.06</td>
<td>0.01</td>
<td>0.01</td>
<td>0.10</td>
</tr>
</tbody>
</table>

One-tailed significance, *p < 0.05 **p < 0.01 ***p < 0.001.

4Some data missing in 3 cases.

4The difference in time for complex and simple squeeze and flexion movements.

MDU = Mood Disorders Unit Core Score; UPDRS = Unified Parkinson’s Disease Rating Scale; FTT = Finger Tapping Test; Bradykin = Bradykinesia Analogue Score; Zung = Zung Depression Rating Scale; IOL = Interonset Latency; Complex excess = Difference between movement times for complex and simple execution.
Table 3. Some Characteristics of the Simple Angular Movements for the Three Groups: Retarded Melancholia (RM), Parkinson’s Disease (PD) and Normal Controls (NC)

<table>
<thead>
<tr>
<th>Movement / Angle</th>
<th>RM (n = 10)</th>
<th>PD (n = 10)</th>
<th>NC (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10° RT (msec)</td>
<td>338.8 ± 91.6</td>
<td>352.2 ± 69.7</td>
<td>292.3 ± 139.3</td>
</tr>
<tr>
<td>MT (sec)</td>
<td>361.9 ± 105.5</td>
<td>423.9 ± 193.5</td>
<td>353.7 ± 75.5</td>
</tr>
<tr>
<td>AV (%/sec)</td>
<td>30.0 ± 9.5</td>
<td>26.7 ± 8.2</td>
<td>29.6 ± 6.8</td>
</tr>
<tr>
<td>20° RT (msec)</td>
<td>331.4 ± 105.7</td>
<td>345.4 ± 119.4</td>
<td>294.8 ± 127.8</td>
</tr>
<tr>
<td>MT (sec)</td>
<td>483.3 ± 211.0</td>
<td>449.1 ± 158.1</td>
<td>427.8 ± 98.9</td>
</tr>
<tr>
<td>AV (%/sec)</td>
<td>48.0 ± 18.1</td>
<td>49.0 ± 14.5</td>
<td>49.4 ± 12.9</td>
</tr>
<tr>
<td>40° RT (msec)</td>
<td>367 ± 156</td>
<td>346.0 ± 112.4</td>
<td>290.3 ± 98.8</td>
</tr>
<tr>
<td>MT (sec)</td>
<td>721.9 ± 386.5c</td>
<td>587.6 ± 190.1r</td>
<td>470.7 ± 92.9a</td>
</tr>
<tr>
<td>AV (%/sec)</td>
<td>67.6 ± 27.7c</td>
<td>73.8 ± 20.3</td>
<td>88.7 ± 20.4b</td>
</tr>
<tr>
<td>20°-10° MT (msec)</td>
<td>121.4 ± 163.0</td>
<td>25.2 ± 137.2</td>
<td>71.4 ± 76.2</td>
</tr>
<tr>
<td>AV (%/sec)</td>
<td>18.0 ± 14.4</td>
<td>22.2 ± 12.0</td>
<td>19.8 ± 9.5</td>
</tr>
<tr>
<td>40°-10° MT</td>
<td>360.0 ± 329.2d</td>
<td>163.7 ± 81.8</td>
<td>117 ± 67.9a</td>
</tr>
<tr>
<td>AV (%/sec)</td>
<td>37.5 ± 22.3d</td>
<td>47.0 ± 14.5e</td>
<td>59.1 ± 15.9b</td>
</tr>
</tbody>
</table>

RT = reaction time; MT = movement time; AV = average velocity (degrees per sec).

Comparisons using ANOVA with Tukey test for multiple comparisons.

1. RM and PD versus NC: *p < 0.1; **p < 0.05.
2. RM versus NC: *p < 0.1; **p < 0.05.
3. PD versus NC: *p < 0.1.
4. RM versus PD: *p < 0.01.

simultaneous movements, but the differences from the controls were not significant. All subjects tended to initiate the squeeze a little before the flexion movement even when instructed to perform them simultaneously, and the interonset latencies did not differ between the three groups.

The time taken to perform the flexion and squeeze movements as part of the simultaneous movements (complex flexion and squeeze) were compared with the times for the movements when performed alone (simple flexion and squeeze). The complex squeeze was slower than the simple squeeze in all three groups, but the difference was significant for only the RM group (*p < 0.05). When the RM group was compared to the NC group by repeated measures ANOVA, using simple and complex squeeze time as the repeated measure, the difference was not significant (df = 1, F = 2.26, *p = 0.15). The complex flexion was significantly slower than simple flexion for all three groups, but RM and PD again did not differ from the controls on repeated measures multivariate analysis of variance (MANOVA).

The movement times for the sequential task were again greater for the RM and PD groups, tending toward a significant level (ANOVA, *p = 0.12 and 0.08, respectively) of difference from the NC group. The IOL was marginally greater for the RM (*p < 0.1) and PD (*p < 0.1) groups, with the RM and PD subjects showing a longer pause time that tended to approach statistical significance.

Discussion

The pathophysiology of the slowness of movement in both PD and RM is incompletely understood. As stated in the Introduction, there are similarities in the slowness seen in the two disorders. It is important to decide whether these similarities are superficial, or whether they can withstand a careful analysis of movement in the two disorders. If the latter is true, it has implications for the understanding of the pathogenesis of either disorder. Our PD subjects, who were judged by us to be free of depression, received a mean score...
of 12.1 on the MDU Core rating scale (Parker et al 1990)—a scale constructed to measure the retardation, and to a lesser extent agitation, seen in melancholia—which was lower than that for RM but much higher than the score of zero for the NC group. Conversely, RM subjects rated a mean 6.4 on section 3 of UPDRS, significantly different from the controls but not from PD (one way ANOVA, p = 0.07). A complete concordance of ratings for PD and RM on the two scales was unlikely, as melancholia does not include rigidity, resting tremor, or postural instability as its features, and sustained mood change, loss of emotional reactivity, and guilt feelings are not defining features of PD. The parallels between the two disorders must, therefore, be restricted to those features that explain bradykinesia, in so far as this can be distinguished from the other cardinal features of either disorder.

In our study we have demonstrated that the motor disorder of RM bears a number of similarities with that of PD. The RM subjects showed an increased movement time for the larger ballistic movements, and did not show the same increase in velocity when increasing the angle of movement from 10° to 40° as normal subjects. Their ballistic movements were often characterised by multiple agonist and antagonist bursts, and some were unable to generate ballistic movements at the nadir of the depression. These difficulties in ballistic movements cannot be explained simply on the basis of volitional disturbance in RM. The subjects made a satisfactory effort to complete the tasks; the reaction

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**Table 4. Some Characteristics of the Simultaneous (Squeeze and Flex) and Sequential (Squeeze then Flex) Movements of the Three Groups; Retarded Melancholia (RM), Parkinson’s disease (PD), Normal Controls (NC)**

<table>
<thead>
<tr>
<th>Movement Type</th>
<th>RM (n = 10)</th>
<th>PD (n = 10)</th>
<th>NC (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squeeze RT (msec)</td>
<td>236.2 ± 62.0</td>
<td>257.2 ± 122.4</td>
<td>215.8 ± 47.2</td>
</tr>
<tr>
<td>MT (msec)</td>
<td>386.1 ± 327.0</td>
<td>351.2 ± 157.3</td>
<td>251.7 ± 84.8</td>
</tr>
<tr>
<td>Flexion 20° RT (msec)</td>
<td>331.4 ± 105.7</td>
<td>345.4 ± 119.4</td>
<td>294.8 ± 127.8</td>
</tr>
<tr>
<td>MT (msec)</td>
<td>483.3 ± 211.0</td>
<td>449.1 ± 158.1</td>
<td>427.8 ± 98.9</td>
</tr>
<tr>
<td>Squeeze and flex MT (msec)</td>
<td>1129.4 ± 919.9</td>
<td>1049.3 ± 615.6</td>
<td>710.5 ± 190.3</td>
</tr>
<tr>
<td>IOL (msec)</td>
<td>211.3 ± 169.1</td>
<td>163.1 ± 139.7</td>
<td>143.3 ± 88.5</td>
</tr>
<tr>
<td>Squeeze then flex MT (msec)</td>
<td>1625 ± 1315.1</td>
<td>1562 ± 857.8</td>
<td>1044.3 ± 204.7</td>
</tr>
<tr>
<td>IOL (msec)</td>
<td>1044.4 ± 954.1</td>
<td>714.3 ± 331.4</td>
<td>510.7 ± 186.9</td>
</tr>
<tr>
<td>Pause DT (msec)</td>
<td>562.2 ± 668.7</td>
<td>326.4 ± 191.8</td>
<td>226.2 ± 153.0</td>
</tr>
<tr>
<td>Complex x squeeze MT (msec)</td>
<td>470.2 ± 306.1</td>
<td>388.0 ± 190.2</td>
<td>305.8 ± 119.8</td>
</tr>
<tr>
<td>Complex x flexion MT (msec)</td>
<td>714.9 ± 380.9</td>
<td>847.9 ± 561.4</td>
<td>530.9 ± 100.6</td>
</tr>
</tbody>
</table>

RT = reaction time; MT = movement time; IOL = Interoonset latency.

* Movements when part of simultaneous movement.

Contrasts using ANOVA with Tukey test for multiple comparisons.
(1) RM and PD versus NC
(2) RM versus NC
(3) PD versus NC
(4) RM versus PD

NS.
times, which may be seen as partial indicators of volition and cooperativeness, even though increased, were not statistically different from the controls; and the movement times for the smaller movements (10°, and less so 20°) were not much larger than the NC group. The difficulty was, therefore, in the inability to increase the velocity of movement as the angle increased, a disturbance similar to that shown by the PD group.

The RM and PD groups tended to show similar disturbances in the execution of complex movements. Because the patient groups showed greater variation, the power of the study to detect significant differences was reduced, but the trends were in the predicted direction. The flexion and squeeze movements were slower when performed jointly with another movement, although the RM group differed significantly from the NC only for the difference between complex and simple squeeze times. In performing two movements sequentially, the RM and PD subjects again demonstrated an added difficulty, and a longer pause time, which tended toward significance at the 0.05 level.

We would like to emphasize the great care taken in the selection of subjects, which took over 2 years. The RM subjects were neuroleptic-free, and drug-induced parkinsonism cannot therefore be considered the basis for the disturbance. No RM subject had muscular rigidity, tremor, or loss of postural reflexes, and there was no suspicion of PD in them. Some subjects failed to complete the study or had an inability to generate ballistic movements, that is, the EMG agonist burst did not cease before the completion of the movement. These subjects were excluded, but the inability to execute a ballistic movement in RM is worthy of note as it may reflect a disturbance in the execution of a motor plan. The criticism that is often raised against such studies is that the data reflect a lack of attention, or that of interest and motivation, in the RM group. We counter this with the data that the disturbances we report here are specific and not across the board. A future strategy would be to compare depressives with similar motivational difficulties but different degrees of retardation in order to substantiate our findings. Our subject numbers were too small to examine correlations between ratings of bradykinesia and the movement measurements for each group, but when the entire group was examined, there were significant correlations with some measures as detailed in Table 2. We do not have an adequate explanation for some of our observations:

1. The RM subjects performed very poorly on the FTT relative to their performance on the Pegboard and their overall bradykinesia ratings. This may relate to the nature of the FTT task.
2. The NC group took longer to perform complex flexion and squeeze movements compared to the simple movements (Table 4). This is unlike the previous

One possible explanation is that our subjects were older, and age may be a factor. Our RM subjects demonstrated an added difficulty in switching from simple to complex movements.

We do not intend to argue in this paper that the abnormalities we report explain entirely the slowness of movement seen in RM. Like PD, there are many aspects to the slowness of a depressed patient. What we intend to put forward is that the bradykinesia of RM is more than what Wilmanns viewed as “intrapsychic inhibition,” or the outward expression of an “unpleasant mood-tone” (Lewis 1934). We tend to agree with the French psychiatrist Widlölcher (1983) that motor change in melancholia should not be viewed as secondary to mood change, with retardation being construed as the patient’s unwillingness to move because of loss of interest or a paralysis of will. Instead, it should be seen as a “core behavioral pattern, not merely a symptom.” If this is accepted, then one can move from a global and impressionistic description of motor change in depression toward a more detailed and fine analysis of the patterns of motor disturbance. Such an approach has been advocated by Widlölcher (1983) and more recently by Parker et al (1990).

At the neurochemical level, the motor disorder in PD correlates best with deficits in DA. Dopamine function in PD is disturbed in both the nigrostriatal and the mesocortico-limbic regions, but the precise pathoatomic correlate with bradykinesia is uncertain. Early pathological data tended to correlate bradykinesia with cell loss in the nigrostriatal DA system ( Hornykiewicz 1979). Bradykinesia is produced in humans and lower primates with lesions of the substantia nigra induced by N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) (Langston et al 1983; Burns et al 1983). It has been suggested by some authors (Javoy-Agid and Agid 1980) that DA deficiency in the mesocortical projections may be the basis of at least some aspects of bradykinesia, for example, defect in initiation and strategy of movement. Still other investigators suggest that DA may, in fact, have a more general homeostatic and regulatory role in the brain. Le Moal and Simon (1991) argue, “it is not yet possible to define the fundamental deficit(s) that characterizes the absence of dopaminergic neurons in terms other than total behavioral disorganization and inability to initiate and adapt: incapacity to evaluate changes in environments, inability to purposefully initiate a motor response, and incapacity to perceive goals and organize responses, all disturbances that can be labelled, broadly speaking, as revealing incentive and motivational disturbances. Paradoxically all these capacities are virtually present and latent, although not expressed anymore after dopaminergic lesions” (p 209).

What is the evidence that DA and basal ganglia function is disturbed in melancholia? Although the neurochemical research in depression has largely focused on α-repineph-
important neurotransmitter in the neuronal circuits associated with mood modulation (Holcomb 1985). Much of the evidence comes from the behavioral effects of drugs such as amphetamine, L-dopa, apomorphine, bromocriptine, alpha-methyl-para-tyrosine, reserpine, and the neuroleptics. Many effective antidepressants, for example, nomifensine, maprotiline, butriptyline, Irimipramine, iprindole, mianserin, etc., are potent inhibitors of 3H-DA uptake and this may indeed be related to their antidepressant property (Randrup and Braestrup 1977). The investigations of the behavioral effects of L-dopa have produced diverse results (Holcomb 1985) with one study from the National Institute of Mental Health (Goodwin et al 1970) reporting improvement mainly in the psychomotor retardation rather than the mood state. Direct DA agonists, such as piribedil (Post et al 1978) and bromocriptine (Nordin et al 1981), have been reported to have measurable antidepressant effects in some studies. Direct evidence for the role of DA comes from the studies of Van Praag and colleagues, which demonstrated decreased turnover of DA in the cerebrospinal fluid in patients with melancholia and retardation, and this was comparable in magnitude to that reported in parkinsonian patients (Olsson and Roos 1968). DA deficiency is possibly only one of the many neurotransmitter disturbances that occur in depression, but it may be of particular importance in melancholia, especially in the presence of retardation.

Other evidence of basal ganglia dysfunction in depression comes from recent brain imaging studies. Structural imaging studies using magnetic resonance imaging have reported a higher prevalence of white matter and basal ganglia hyperintensities in depressives (Krishnan et al 1988; Coffey et al 1990; Brown et al 1992). Positron emission tomographic studies report reduced metabolism and blood flow to the prefrontal cortex and the caudate nucleus in depression (Baxter et al 1989; Martinot et al 1990; Buchsbaum et al 1986; Hageman et al 1990). Affective disturbance has often been reported in patients with basal ganglia lesions (Ali-Cherif et al 1984; Laplane et al 1989). All these reports suggest that disturbances in the basal ganglia-frontal lobe circuits are important in the pathogenesis of depression. Laplane et al (1989), in their description of eight patients with bilateral basal ganglia lesions, concluded: “Similarities existed between some symptoms in our patients and certain features of major psychiatric illnesses such as severe depression... this raises the hypothesis that some aspects of these psychiatric disorders could be related to structural disturbances in the systems linking the frontal associative cortex and the basal ganglia” (p 699). Striatothalamicocortical circuits are the focus of attention in PD (Albin et al 1989), and commonality of disturbances between PD and RM is therefore not unexpected. DA deficiency may well be the common link, transient and reversible in the case of RM, and progressive and irreversible in PD.

We conclude, therefore, from our study that the slowness of melancholia possibly has similar pathogenetic mechanisms to that of bradykinesia in PD. It would be important to explore further the motor abnormalities in depression with strategies that have been fruitful in PD (Marsden 1989b). Functional neuroimaging and neuropsychological studies of both depression and PD will contribute to our understanding of the mood, behavioral, and cognitive features that these disorders share. Our study also suggests that dopaminergic mechanisms deserve further investigation in depressive disorders.

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