Reliance on external cues during serial sequential movement in major depression

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Abstract
Maintenance of motor set in patients with unipolar major depression was examined. Twelve melancholic and 12 non-melancholic depressed patients and 24 age matched controls performed a serial choice reaction time task while external cues aiding maintenance of a motor set were systematically removed. Melancholic patients were significantly slower than controls with no reduction in external cues and with a moderate reduction in external cues. At a high level of reduction in external cues, seven of 12 melancholic patients (but only three of 12 non-melancholic patients and controls) were unable to complete the task; suggesting a greater reliance on external cues, perhaps implicating a failure of motor planning ability in melancholic patients. This, in turn, may point to a prefrontal (premotor) deficit in melancholic depression, with possible commonalities with Parkinson's disease.

Keywords: major depression; parkinsonism; motor sequencing

The cognitive and motor slowing, or psychomotor retardation, of patients with melancholic major depression may not be entirely secondary, but rather a direct consequence of underlying neurophysiological disturbance. Findings from neuropsychology; functional, and to a lesser extent structural, imaging; and from neurochemistry and lesion studies' implicate frontostriatal impairment in major depression. Thus motor slowing in such patients may be viewed as arising from dysfunction of the basal ganglia-thalamocortical motor circuit. Indeed there is a similarity in the clinical presentation of psychomotor retardation in patients with depression and that of bradykinesia in Parkinson's disease, a disorder involving the basal ganglia.

This apparent similarity between psychomotor retardation and bradykinesia, and the fact that patients with Parkinson's disease (and other basal ganglia disorders) show abnormally high rates of depression may reflect some commonality of causation between the two disorders. The depth of this similarity has, however, been little studied and findings are contradictory. Sachdev and Annis' found similarities in performance of patients with Parkinson's disease and depressed patients with psychomotor retardation during simultaneous and sequential movement, suggesting common elements of neuropathology. Fleminger, however, found that depressed patients with psychomotor retardation did not show difficulty with simultaneous movements or the rapid fatiguing effect shown by patients with Parkinson's disease.

To consider the underlying nature of any motor slowing common to Parkinson's disease and depression we examined performance on a serial choice reaction time task previously validated on patients with basal ganglia disorders. These disorders lead to a greater reliance on external cues to initiate and maintain movement. The present study employed the same task to assess whether patients with major depression also show a deficit in maintenance of motor set when external cues aiding maintenance were systematically removed. Undue reliance on external cues might indicate impaired ability to maintain motor set.

Method and participants
Participants performed a serial choice reaction time button pressing task involving 10 two way choice button presses along a response board. The correct “pathway” to follow was initially illuminated thereby providing external cues to aid maintenance of motor set. External cues were progressively removed in advance of each movement according to three protocols: no reduction in advance information, where the next correct button remained illuminated until the current button was released; moderate reduction in advance information, where the next correct button extinguished when the current button was pressed; finally, at a high level of reduction in advance information, the next correct button was extinguished when the previous button was released. Eight equidistant pathways appeared in random order, each occurring twice at each level of reduction in advance information. The three cue reduction conditions were therefore matched for sequence difficulty. Order of presentation of conditions was counterbalanced. The measure obtained, “interbutton time”, was the mean...
time between depression of one button and that of the next. Participants were 24 patients with unipolar major depression (DSM-IV) and 24 age-matched controls. All were dextral, with 10 men and 14 women in each group. The patient and control groups were matched for age (patients: mean 57.15, range 24–85 years; controls: mean 57.70, range 24–85 years; t(46) = −0.09, p > 0.05); and according to the new adult reading test (NART) estimate of premorbid IQ (patients: mean 57.15, range 24–85 years, controls: mean 57.70, range 24–85 years, t(46) = −0.52, p > 0.05). All patients had a primary diagnosis of unipolar major depression and a Beck depression inventory score of nine or greater at time of testing. Exclusion criteria were high potency anticholinergic medications, neurological impairment, dementia, musculoskeletal pathology, and poor corrected vision. Controls had no known psychiatric history. The patient group was divided into melancholic and non-melancholic subgroups on the basis of DSM-IV criteria for melancholic features, and the CORE measure of psychomotor disturbance (table). A CORE rating of 8 or greater was considered an indication of melancholic depression.1 The melancholic group (mean 14.2, range 8–22) had a significantly higher mean CORE score than the non-melancholic group (mean 2.6, range 0–6) (t(22) = 7.80, p < 0.001). The melancholic group (mean 29.2, range 12–47) and non-melancholic group (mean 24.3, range 10–44) did not differ in their mean Beck score measures of depression severity (t(22) = −1.01, p > 0.05). All patients were tested within 2 months of diagnosis except five melancholic and six non-melancholic patients tested between 6 and 12 months after diagnosis. Patients were in their first episode except for four melancholic and four non-melancholic patients.

Results
Ten patients (seven melancholic and three non-melancholic) and three controls were unable to complete the high level of reduction in advance information condition. Fisher’s exact test (two tailed) showed that significantly more melancholic (p = 0.007), but not non-melancholic (p = 0.300) patients were unable to complete this condition relative to controls. To avoid unequal sample sizes the data for that level were not included in the overall analysis. A two way mixed model analysis of variance (ANOVA) with factors of group (controls vs. melancholic vs. non-melancholic) and reduction (None vs. Moderate) was carried out. There was a significant effect of group (F(2,45) = 9.09, p < 0.001; fig). There were no significant effects between controls (mean 265 (SD 48.73)) and non-melancholic patients (mean 304 (SD 85.60)) (F(1,34) = 3.052, p > 0.05). There was, however, a significant main effect between controls and melancholic patients (mean 516 (SD 323.48)) (F(1,34) = 14.160, p < 0.001). Finally a direct comparison showed that melancholic patients (mean 516 (SD 323.48) ms) were significantly slower than non-melancholic patients (mean 304 (SD 85.60) ms) (F(1,22) = 6.70, p < 0.05). There was no significant effect of cue (F(1,46) = 0.39, p > 0.05) nor of group x cue (F(1,46) = 0.89, p < 0.05).

Discussion
Maintenance of motor set in patients with major depression was examined. Melancholic, but not non-melancholic, patients were slow overall relative to controls. A moderate reduction in external cues did not further degrade melancholic patients’ performance, indicating that they were able to retain at least one movement ahead in a motor set. When advance information was further reduced, however, 10 patients and three controls...
were unable to complete the task. Of the 10 patients who failed at this condition, seven were melancholic and only three were non-melancholic. This reflects the overall finding that non-melancholic patients performed at about the level of the controls, whereas performance of melancholic patients was poor.

That over half the melancholic group was unable to perform with a high level of reduction in advance information suggests a difficulty in maintaining a motor set involving more than one element or movement. Melancholic patients therefore showed a qualitatively similar, though more severe, pattern of deficits to that previously found in patients with Parkinson’s disease and Huntington’s disease who, while able to complete the high level of reduction condition, did so significantly slower than in the other conditions. Such deficits in self initiated movements in Parkinson’s disease are associated with reduced motor circuit activity. The presence of similar behavioural deficits in melancholic depression might indicate a functionally similar motor circuit deficit. That non-melancholic patients were indistinguishable from controls indicates that they do not share the motor deficits of the melancholic patients.

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