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Neuropsychological function in young patients with unipolar major depression

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ABSTRACT

Background. While neuropsychological studies have consistently reported impaired cognition in elderly patients with unipolar depression, studies of cognitive function in younger patients with depression have produced equivocal results. The aim of this study was to examine the presence and nature of cognitive deficits in young patients with depression.

Methods. Neuropsychological function was assessed in 20 young patients with unipolar depression, in comparison to 20 age-, education- and IQ- matched controls. Subtests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) were employed, as this battery has proved sensitive to deficits in middle-aged and elderly patients with depression.

Results. The patients were not impaired for short-term memory capacity, spatial working memory, planning ability, cognitive speed, delayed matching to sample or recognition memory. Compared to controls, the patients showed impaired subsequent movement latencies on the Tower of London task, suggesting deficits in the ability to sustain motor responses in depression. The depression group were also impaired on the task of attentional set shifting, requiring more trials to criterion at the intradimensional stage of the task and being more likely to fail the task at the extradimensional shift stage than controls. Further analysis indicated that half of the depression group failed to complete all stages of the set shifting task. These patients were more likely to have required in-patient hospitalization at some time during their illness.

Conclusions. These results indicate that there are specific cognitive deficits in young patients with depression and that their presence may be related to a history of hospitalization.

INTRODUCTION

In addition to a significant lowering of mood, negative cognitive content and reduced affect and motivation, unipolar depression is characterized frequently by subjective accounts of diminished attentional or memory abilities and slowness of thinking (DSM-IV, APA, 1994). Given these clinical features, neuropsychological studies have recently begun to examine systematically cognitive function in patients with depression. Formal studies of cognition in depression are valuable, as they may guide putative brain–behaviour models of the disorder and may also aid in the understanding of the effects of co-morbid depression on neuropsychological performance in other neuropsychiatric disorders.

To date, neuropsychological studies of depression have predominantly examined performance in groups of elderly patients (e.g. > 65 years), although recent studies have also investigated whether cognitive deficits occur in younger patient groups. The studies in elderly patients with depression have consistently reported neuropsychological impairments. Using the Cambridge Neuropsychological Test Automated Battery (CANTAB; Morris *et al*. 1987), several studies have found impaired recognition mem-

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ory, delay dependent memory, conditional associative learning, executive function and psychomotor slowing (Abas *et al*. 1990; Beats *et al*. 1996). Impaired memory, attention and language function in elderly depressed patients was also reported by Brown *et al*. (1994*a*). Tarbuck & Paykel (1995) demonstrated that older patients with depression (mean age 69 years) were slower to respond on neuropsychological tasks compared to middle-aged depressed patients (mean age 41 years), although the groups did not differ for accuracy of performance.

The findings from neuropsychological studies of younger patients with depression have been equivocal. Several studies have failed to find major cognitive deficits in patients with unipolar depression whose mean age ranged between 33 and 40 years (Martin *et al*. 1991; DeLuca *et al*. 1995; Albus *et al*. 1996). In contrast, specific deficits in cognitive set shifting (Franke *et al*. 1993) and verbal memory and psychomotor speed (Ilsley *et al*. 1995) have been reported in depressed patients with a mean age between 42 and 47 years. Using CANTAB subtests, Elliott *et al*. (1996) also found middle-aged patients with depression (mean age 49 years) to be significantly impaired on tasks of executive and visual memory function and thinking speed. However, performance on tasks of attentional set shifting and motor speed was within normal limits.

Therefore, while studies have consistently identified impaired cognition in elderly patients with unipolar depression, there is less agreement on whether deficits in cognitive function occur in younger patients and, if so, what the nature of these deficits are. In the current study, we utilized a battery of neuropsychological tests previously found sensitive to cognitive deficits in elderly and middle-aged patients with depression to investigate the accuracy and speed of cognitive function in a younger group of patients with unipolar depression.

METHOD

Patient group

Twenty patients with unipolar depression who were consecutive referrals to the University of Melbourne/Royal Melbourne Hospital Psychology Outpatient Clinic, a tertiary referral service, were included in the study. One patient was an in-patient at the time of testing. The Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown *et al*. 1994*b*), which contains the Hamilton Depression Rating Scale (HAM-D; 24-item), was used to confirm the diagnosis of unipolar depression and to exclude other Axis I diagnoses. Patients reporting an history of hypomania, a neurological or major medical illness, or significant alcohol or substance abuse were excluded.

Patient characteristics

Twelve of the patients were female. The mean age of the patients was 37·5 years (range 18–52) and mean years of education was 13·5 (range 8–17). The National Adult Reading Test (NART; Nelson, 1982) was administered to provide an estimate of pre-morbid intellectual functioning (mean = 107·7; range 94–123). The mean age of onset of illness was 31·2 years (median = 30·0; range 16–48), while the mean duration of illness (including recurrent episodes) was 6·4 years (median = 3·5; range 1–20). Seven patients reported an history of in-patient hospitalization for the treatment of their illness, while the remaining 13 patients reported outpatient treatment only. The patients' mean score on the HAM-D was 22·6 (S.D. = 5·6; range 15–33), which reflects moderate depression severity. Twelve patients were medicated with antidepressants at the time of cognitive testing, while the remaining eight patients had been medication free for at least 2 months prior to testing. No subject had been treated with electroconvulsive therapy.

Control group

Normal controls were matched to depression patients on all descriptive variables. Twelve subjects were female. The mean age of controls was 37·2 years (range 21–60; $F(1,38) = 0{\cdot}01$, NS), mean years of education was 13·5 (range 10–17; $F(1,38) = 0{\cdot}01$, NS) and mean NART estimated full scale IQ was 108·6 (range 91–123; $F(1,38) = 0{\cdot}11$, NS). Control subjects were screened with the ADIS-IV to exclude any history of psychiatric illness, significant family history of mental illness or a history of alcohol or substance abuse, and were administered the HAM-D (mean = 1·85, S.D. = 2·06; $F(1,38) =$

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236·51, $P < 0·000$). Each patient and control subject provided written informed consent to participate in the study, which was approved by the RMH Board of Medical Research.

Procedure and tasks

Subjects completed the interview and neuropsychological assessment on separate days. In order to control for any possible effects of diurnal variation on neuropsychological performance (see Moffoot *et al*. 1994), each subject completed the clinical and neuropsychological assessments at approximately the same time of day (all assessments were conducted between 11.00 a.m. and 4.00 p.m.). The computerized CANTAB tasks were presented on a high resolution IBM colour monitor with a touch sensitive screen, in a testing session of approximately 90 min duration. These tasks have been extensively described elsewhere and their administration in this study was according to standard protocols (the reader is referred to Owen *et al*. 1990, 1991, 1993*a* and Beats *et al*. 1996 for detailed methodological descriptions of each task). The CANTAB tests employed were as follows.

'Executive function' tasks

(*a*) *Spatial span*

This task assessed the subject's spatial short term memory capacity. The spatial span was the highest level (minimum two/maximum nine) at which the subject successfully remembered at least one sequence of stimuli.

(*b*) *Spatial working memory*

This self-ordered searching task measured the accuracy of working memory (between-search-errors) and the subject's ability to adopt a systematic searching approach (strategy).

(*c*) *Tower of London planning task*

This test of planning required subjects to rearrange a set of balls in a specified minimum number of moves that increased in difficulty. The accuracy of planning was measured by the number of trials completed within the minimum number of moves (perfect solutions), and the total number of moves in excess of the minimum. The program recorded initial and subsequent thinking latencies during these trials to provide estimates of cognitive speed. For each planning trial, a yoked control condition was employed. During these 'following' trials, subjects were instructed to execute a sequence of single moves as quickly as possible. The task measured initial and subsequent movement latencies during these 'following' trials to provide estimates of motor speed.

(*d*) *Intradimensional/extradimensional* (*ID/ED*) *set shift*

This task assessed the subject's ability to maintain attention to different examples within a reinforced stimulus dimension (intradimensional stages) and to then shift attention to a previously irrelevant stimulus dimension (extradimensional stages). The task involved nine stages, with subjects proceeding to the next stage when a criterion of six consecutive correct responses had been attained. Performance was examined according to the percentage of subjects successfully completing each stage of the task, the mean number of stages completed and the number of trials required to attain criterion for each stage.

Visual memory tasks

(*a*) *Delayed matching to sample* (*DMTS*)

This task assessed the subject's ability to remember a target stimulus after variable periods of delay (0, 4 or 12 s delay) between stimulus presentation and the presentation of response stimuli. Feedback regarding accuracy was presented after each of the 40 trials. Performance was analysed according to the percentage of correct responses at each delay level and the total percentage correct. The frequency of subsequent errors was also examined. Subsequent errors were defined as errors that occurred on the $n+1$ trial when feedback of failed performance had been given on trial n (see Elliott *et al*. 1996, for methodological description).

(*b*) *Spatial recognition*

This task assessed the subject's ability to recognize the correct spatial location of a target stimulus presented at different positions on the screen. Feedback regarding accuracy was presented after each of the 20 trials. Performance was analysed according to the percentage of correct responses, the mean latency of correct responses and the frequency of subsequent errors.

(*c*) *Pattern recognition*

This task measured the subject's ability to recognize a correct abstract coloured line pattern

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Table 1. *Comparison of neuropsychological performance in depressed patients and matched normal controls*

Measure	Depressed ($N = 20$) Mean	(S.D.)	Controls ($N = 20$) Mean	(S.D.)	Group comparison Statistic	Value	*P*
Spatial span	6·15	1·18	6·40	1·14	*t*	0·68	0·50
Spatial working memory							
Total between-search-errors	21·60	16·07	18·35	11·49	*t*	0·74	0·46
Strategy score	13·70	4·60	12·75	4·17	*t*	0·68	0·49
Tower of London							
Number of perfect solutions	8·45	1·84	8·50	2·18	*t*	0·08	0·93
Total moves in excess of the minimum	13·35	7·29	13·10	8·80	*t*	0·10	0·92
Initial thinking (log)	3·87	0·23	3·89	0·24	*F*	0·00	0·93
Subsequent thinking (log)	3·82	0·35	3·52	0·84	*F*	1·54	0·22
Initial movement (log)	3·19	0·09	3·14	0·12	*F*	1·46	0·23
Subsequent movement (log)	3·79	0·11	3·72	0·10	*F*	5·12	0·02
Attentional set shifting							
Stages completed	7·90	1·29	8·70	0·80	*t*	2·35	0·02
Intradimensional shift – trials to criterion	13·95	15·08	7·20	2·21	*t*	1·98	0·05
Extradimensional shift – trials to criterion	23·94	19·85	13·52	9·83	*t*	2·03	0·05
Delayed matching to sample							
0 s delay (% correct)	86·11	10·36	92·50	8·50	*t*	4·34	0·04
4 s delay (% correct)	91·11	12·78	91·00	9·67	*t*	0·00	0·97
12 s delay (% correct)	81·11	14·90	85·50	10·50	*t*	1·11	0·29
Total responses (% correct)	88·75	8·79	91·87	4·79	*t*	1·90	0·17
Spatial recognition							
Total responses (% correct)	80·00	8·57	83·25	12·06	*t*	0·95	0·35
Response latency (log)	3·37	0·12	3·35	0·09	*t*	0·54	0·59
Pattern recognition							
Total responses (% correct)	92·59	7·50	90·83	8·50	*t*	0·67	0·50
Response latency (log)	3·34	0·10	3·35	0·11	*t*	0·21	0·83

from a target stimulus presentation. Feedback of accuracy was presented after each of the 24 trials. Performance was examined according to the percentage of correct responses, the mean latency of correct responses and the frequency of subsequent errors.

Statistical analyses

Performance on the Tower of London, spatial working memory and DMTS tasks were compared between groups using a group by task difficulty analysis of variance (ANOVA) with repeated measures on the task difficulty factor. Performance on the spatial span, spatial and pattern recognition tasks and stages completed on the ID/ED set shifting task were compared between groups using independent groups *t* test. Latencies for the Tower of London, spatial and pattern recognition tasks were recorded as centiseconds (cs) and transformed into logarithms (base 10) to reduce skewness in the distribution. The frequency of subsequent errors on the DMTS and recognition tasks was examined using chi-square (2 [group: depression, control] × 3 [number of errors: 0, 1–2, > 3]). Performance on the ID/ED set shift was examined according to the percentage of subjects succeeding or failing to reach criterion at each stage of the task. The resulting contingency tables were analysed using the likelihood ratio method, which allows for use where cell frequencies were small, with the resulting statistic 2i being distributed as χ^2. Pearson's product moment correlation coefficients and Spearman's correlation coefficients were calculated to examine the relationship between the patients' clinical and demographic characteristics and the measures of impaired cognitive function. For *a priori* analyses comparing group performance on the CANTAB tasks, the error rate required to demonstrate significance was set at 0·05. However, as multiple *post hoc* comparisons were performed to examine the relationship between the patients' characteristics and their cognitive performance, we reduced the level of significance to 0·01, in order to protect against Type 1 error.

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RESULTS

The group mean performance and statistical comparisons for each cognitive task are summarized in Table 1. There were no differences between groups for performance on the measures of spatial span, spatial working memory, Tower of London planning accuracy, thinking times or initial movement time, delayed matching to sample and spatial and pattern recognition. Furthermore, there were no interactions between task difficulty and group for any of the analyses. However, in order to allow comparison with previous CANTAB studies, performance at each level of task difficulty on the DMTS task is shown in Table 1.

There was a significant group difference for subsequent movement times on the Tower of London ($F(1,38) = 5{\cdot}12$, $P < 0{\cdot}02$), with depressed patients (mean: 6442·03 cs, S.D. = 1971·77) being slower to complete the sequence of single moves on the yoked control 'following' trials compared to controls (mean = 5434·07 cs, S.D. = 1115·67). Patients with depression were also significantly impaired on the ID/ED set shifting task. Fig. 1*a* shows that 85% of control subjects were able to complete all stages successfully compared to 50% of depression patients ($2i = 5{\cdot}81$, $P < 0{\cdot}01$). The proportion of subjects passing each stage of the task was then analysed non-cumulatively; that is, only the data for those subjects attempting each stage were examined. Although the groups did not differ at the IDS ($2i = 1{\cdot}41$, NS) or IDR stages ($2i = 0{\cdot}42$, NS), more patients with depression failed the task at the EDS stage compared to controls ($2i = 4{\cdot}00$, $P < 0{\cdot}05$). The groups did not differ, however, at the EDR level, when only those subjects passing the EDS stage were included in the analysis ($2i = 0{\cdot}96$, NS). The number of trials required to attain criterion at each stage were also analysed non-cumulatively. Fig. 1*b* shows that in comparison to controls, patients with depression required more trials to reach criterion at both the IDS ($F(1,38) = 3{\cdot}96$, $P < 0{\cdot}05$) and EDS stages ($F(1,38) = 4{\cdot}11$, $P < 0{\cdot}05$).

The speed and accuracy of performance on the visual memory tasks did not differ between groups. Furthermore, there were no group differences for the frequency of subsequent errors on the DMTS task ($\chi^2 = 1{\cdot}10$, df = 2, NS), spatial recognition task ($\chi^2 = 1{\cdot}25$, df = 2, NS) or the pattern recognition task ($\chi^2 = 0{\cdot}50$, df = 2, NS).

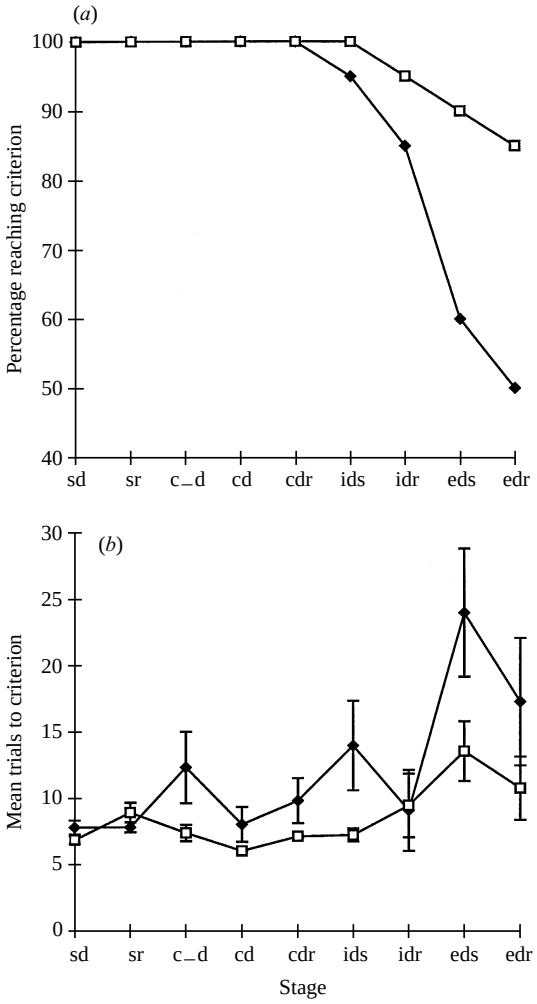


FIG. 1. ID/ED set shifting task. Stages: sd, simple discrimination; sr, simple reversal; c_d, compound discrimination; cd, superimposed compound discrimination; cdr, superimposed compound discrimination reversal; ids, intradimensional shift; idr, intradimensional reversal; eds, extradimensional shift; edr, extradimensional reversal. (*a*) The cumulative percentage of subjects reaching criterion at each stage of the task is shown for the depressed group (◆) and control group (□). (*b*) The non-cumulative number of trials required to criterion at each stage of the task is shown for the depressed group (◆) and control group (□).

Relationship between impaired neuropsychological performance and patient characteristics

Medicated and non-medicated patients did not differ for performance on the ID/ED task and

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Table 2. *Pearson's and Spearman's correlation coefficients of patient characteristics and impaired neuropsychological performance*

	Subsequent movement time*	ID/ED stages completed†
Age	0·44	−0·33
Education	−0·54	0·33
NART IQ	−0·29	0·06
Age of illness onset	0·21	−0·22
Length of illness	0·25	0·02
HAM-D	0·26	0·06

* Pearson's correlation coefficient.
† Spearman's correlation coefficient.

the Tower of London subsequent movement trials (data not shown). There were no significant correlations between the patients' age of onset of illness and length of illness and impaired cognitive performance. The severity of depression, according to clinician ratings on the HAM-D, did not correlate with performance on the measures of impaired cognitive function. Similarly, patient age was not related to impaired attentional set shifting or subsequent movement time. The patients' education and NART-estimated IQ scores were not associated with impaired set shifting or movement times (see Table 2).

Depression subgroup analyses

The initial analysis comparing the depression and control groups indicated that 50% of the depression group failed to complete all stages of the ID/ED set shifting task ('impaired group') while the remaining half performed the task successfully ('unimpaired group'). In light of this result, we examined the two patient subgroups in order to determine whether clinical or demographic characteristics could also distinguish these groups. Analysis of variance showed that the groups did not differ according to ratings on the HAM-D, age of onset of illness, length of illness, age, years of education, NART-IQ or medication status. However, patients in the 'impaired' subgroup were more likely to have reported an history of in-patient hospitalization for the treatment of depression in comparison to the unimpaired group ($2i = 5{\cdot}93$, $P < 0{\cdot}01$).

DISCUSSION

This study found that patients with unipolar depression were impaired on measures of motor speed and attentional set shifting, although their performance on the other tests of executive function, visual memory function and cognitive speed was within normal limits. This pattern of performance suggests that, while specific deficits in cognition occur in younger out-patients with moderate depression, the range and degree of this impairment is relatively mild.

Patients with depression were slower than controls to execute a sequence of motor responses on the subsequent movement trials of the Tower of London task. To perform this aspect of the task, the subject must compare two sets of stimuli, execute the necessary 'following' move and continue to repeat these following movements until the task is completed. In contrast, initial movement time reflects the execution of only the first 'following' move in the sequence. The patients' slower subsequent movement times and normal initiation of movement suggest that motor slowness in depression occurs when sustained motor responses to changing stimuli are required. This finding of a slowing in motor responses is consistent with observations of psychomotor slowing and increased reaction times both in middle-aged (Ilsley *et al*. 1995) and elderly depressed patients (Rogers *et al*. 1987; Tarbuck & Paykel, 1995; Beats *et al*. 1996). Although Elliott *et al*. (1996) did not find motor slowing in their middle-aged depression group, their patients exhibited slowed thinking latencies. Taken together, these results suggest that, while psychomotor retardation is commonly associated with depression in the elderly, in younger or middle-aged depressed patients, there may be some variability in the nature of this slowing (e.g. motor or cognitive).

The patients with depression also performed poorly on the ID/ED set shifting task. For the intradimensional shift, the patients required more trials than controls to reach criterion, although the percentage of subjects completing this stage was equal in the two groups. This suggests that the patients were able to achieve a shift to a new exemplar of the reinforced dimension, albeit after more learning trials. Significantly fewer of the depressed group were able to learn the extradimensional set shift,

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which indicates that patients also experienced difficulty in shifting attention to a previously irrelevant stimulus dimension in order to discriminate between stimuli. The results demonstrated that half of the depression group were able to complete all nine stages successfully, although the remaining half were impaired in their ability to perform the task. A *post-hoc* analysis revealed that these two subgroups did not differ in relation to age, depression severity, duration of illness, education or estimated IQ. However, more patients who failed the ID/ED task had reported an history of in-patient hospitalization at some time during their illness. Therefore, these results suggest that younger patients with depression may not be impaired in attentional set shifting ability *per se*. Rather, set shifting deficits may be particularly evident among patients with a more severe history of depressive illness which has warranted in-patient treatment. These results, together with findings reported by Elliott *et al.* (1996), suggest that history of in-patient hospitalization is a better predictor of neuropsychological impairment than current illness severity. It is also possible that neuropsychological impairment may be an important indicator of the need for hospitalization in patients with depression. However, an alternative explanation is that in-patient treatment or other factors related to hospitalization may contribute to neuropsychological impairment. Prospective studies will be necessary to investigate the relationship between hospitalization and neuropsychological impairment.

Several studies have investigated attentional set shifting in patients with depression. One study reported deficits on the WCST in middle-aged patients (Franke *et al.* 1993), however, another study of patients of a similar age did not find deficits on this task (Martin *et al.* 1991). Elliott *et al.* (1996) also found that middle-aged patients with depression did not differ from controls on their measure of attentional set shifting. However, Elliott *et al.* administered a different, less stringent version of the CANTAB ID/ED task that requires subjects to perform under two conditions: (1) perseveration, and (2) learned irrelevance (see Owen *et al.* 1993*b* for task description). This version of the ID/ED task distinguishes between set shifting difficulties that occur due to perseveration or to learned irrelevance, which the CANTAB task employed in this study did not address. Given these task differences, direct comparison of the current results and those shown by Elliott *et al.* is not valid. Using the same CANTAB ID/ED set shifting task administered in the current study, Beats *et al.* (1996) found that elderly patients were more likely to fail at both the IDS and the EDS stages, suggesting difficulties with set maintenance and shifting in older patients with depression. Therefore, some of the variation in the results of studies examining attentional set shifting in patients with depression may be accounted for by the different tasks used to measure this ability. However, the consistency of our results with those of Beats *et al.* suggest that the current ID/ED task is sensitive to set shifting deficits in patients with depression, even though the appearance of such deficits on this task may depend on the history of depressive illness, the age of patients or both.

Comparison with previous CANTAB studies in depression

The results of the current study differ from recent investigations which have used the CANTAB battery to assess cognition in both middle-aged and elderly patients with depression in several ways. The patients in Elliott *et al.*'s sample (mean age of 49 years) and Beats *et al.*'s study (mean age of 72 years) showed significant deficits on the tasks of spatial working memory, planning, cognitive speed, DMTS and recognition memory. The older patients were also impaired on the tasks of attentional set shifting and motor speed, although these functions were not compromised in the middle-aged group. In contrast to these results, the younger patients in our study performed within normal limits on most measures. Similarly, while the middle-aged and elderly patients showed a specific impairment related to subsequent errors in the context of negative feedback, there was no evidence of a 'catastrophic response to failure' (Beats *et al.* p. 600, 1996) in our younger group. There may be several explanations for the differences between these previous studies and the current results. First, the finding of a catastrophic response to failure in the previous studies may have been associated with the patients' overall level of cognitive function. For example, the patients in the studies of Elliott *et al.* and Beats *et al.* showed performance deficits across each

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cognitive domain assessed. This generalized lowering of function may have contributed to the specific impairment observed in the context of negative feedback. In contrast, cognitive function in our sample was not generally compromised. With this higher level of function, patients may have been less susceptible to the consequences of negative feedback. Secondly, the different results may be related to sample characteristics, including depression severity. Most patients in Beats *et al.*'s study were in-patients or day patients, while approximately 40% of Elliott *et al.*'s patients were in-patients at the time of testing. Elliott *et al.* found that the in-patients were more impaired on the measures of DMTS, spatial span and response to failure in comparison to the out-patients. All but one of the patients in our study were out-patients and hence this factor may account for their relatively normal cognitive performance. Consistent with this was the observation that deficits in attentional set shifting in our group were more likely to occur in patients who reported an history of in-patient treatment. This again suggests that a history of depression requiring hospitalization may be a more important predictor of neuropsychological function than current illness severity. Finally, the different results may be related to patient age. Depression in younger patients appears to be associated only with mild and specific impairments in set shifting and psychomotor speed. Middle-aged patients with depression show a greater range and severity of deficits, including impaired executive and visual memory function, as well as psychomotor slowing. Elderly patients with depression also show these deficits, in addition to impairment across a wide range of neuropsychological domains (see Brown *et al.* 1994; Palmer *et al.* 1996). While each of these factors may have contributed to the different results, these explanations are not mutually exclusive, and differences between the current and previous studies of cognitive function in depression may have arisen from the interaction between these factors.

Neural correlates of cognitive deficits in young patients with depression

Impaired set shifting in the ID/ED task and slow subsequent motor responses have been ascribed to impaired frontal lobe function or to disruption of the fronto-striatal circuitry which connects the frontal cortex to the basal ganglia. Patients with focal lesions of the frontal lobes or with neurodegenerative diseases which preferentially involve the basal ganglia also show impaired performance on the ID/ED set shifting task and a slowing of motor responses (Owen *et al.* 1990, 1991; Robbins *et al.* 1994). However, the severity of these impairments is usually much greater than that observed in the current sample and is also accompanied by performance deficits on the spatial working memory, spatial recognition and Tower of London tasks. Therefore, the cognitive deficits found in the current group suggest that there may be only subtle disruption to fronto-striatal brain pathways in younger patients with unipolar depression, or disruption of specific fronto-striatal pathways. For example, the dorsolateral prefrontal cortex (DLPFC) has been proposed as important in set shifting ability (Rezai *et al.* 1993; Berman *et al.* 1995). That the patients were impaired on this function suggests that the DLPFC may be implicated in depression, consistent with the findings of functional neuroimaging studies which have reported hypometabolism of the (predominantly left) DLPFC (see Biver *et al.* 1994; Bench *et al.* 1995). However, on the basis of the current results it is not possible to determine whether the cognitive deficits found reflect the earliest stages of a degeneration in the integrity of the DLPFC and its connections with the basal ganglia that may progress with age or disease severity, or whether these deficits reflect a 'state' change in the functional integrity of the fronto-striatal pathways that would resolve with recovery from depression (e.g. Bench *et al.* 1995).

Conclusion

This study demonstrated specific neuropsychological deficits in motor slowing and attentional set shifting in young patients with depression. However, there was no general decline in the speed or accuracy of visual memory or executive function. Taken together with the results of previous neuropsychological studies, these results suggest that there is considerable variability in the nature and severity of cognitive impairment in depression, which may be explained in part by patient age and factors associated with hospitalization. Future neuro-

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psychological studies should examine prospectively young patients with depressive illness in order to determine the relationship between neuropsychological performance and patient, illness or treatment related factors. Finally, the results of this study should be considered when interpreting attentional shifting performance or performance on timed tasks that require ongoing motor responses in young patients with neuropsychiatric diseases where there is co-morbid depression.

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