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Cognitive function in depression: a distinct pattern of frontal impairment in melancholia?

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ABSTRACT

Background. Although depressed patients demonstrate impaired performance on a range of neuropsychological tests, there is little research that examines either frontal cognitive deficits or possible differences in test performance between melancholic and non-melancholic subtypes.

Methods. Depressed subjects were administered a broad neuropsychological battery. In an overall analysis, 77 depressed subjects were compared with 28 controls. In a second set of analyses, the depressed sample was divided into melancholic and non-melancholic subsets according to DSM-III-R, the CORE system and the Newcastle scale. These depressed subsets were contrasted to controls and with each other using ANCOVA controlling for age, IQ, simple reaction time and Hamilton Depression scores where appropriate.

Results. The total depressed sample was impaird on most mnemonic tasks, simple reaction time and Trails B. Similar findings applied to DSM-III-R melancholic and non-melancholic subjects. When defined by the CORE and Newcastle (narrower definitions of melancholia), melancholic patients were additionally impaired on WCST (perseverative response) and (for Newcastle) digit symbol substitution. In contrast, the cognitive performance of the CORE and Newcastle-defined non-melancholic patients was largely unimpaired.

Conclusions. Using narrower definitions of melancholia, i.e. CORE and (in particular) Newcastle, melancholic patients were impaired on mnemonic tasks and tasks of selective attention, and set-shifting while non-melancholic subjects were largely unimpaired in their cognitive performance. These differences may be due to impairment of specific neuroanatomical regions in narrowly defined melancholic patients, in particular the anterior cingulate.

INTRODUCTION

It is now commonly accepted that depression is associated with a number of deficits in cognitive function, especially memory (Sternberg & Jarvik, 1976; Stromgren, 1977; Weingartner *et al*. 1981; Cohen *et al*. 1982; Wolfe *et al*. 1987; Austin *et al*. 1992*a*). Impairment of 'frontal' or executive function has been examined less frequently, although this has been reported in more severely depressed subjects (see Goodwin 1997 for review; Raskin *et al*. 1982; Silberman *et al*. 1983; Jones *et al*. 1988).

Three studies are worthy of particular note (Jones *et al*. 1988; Beats *et al*. 1996; Elliott *et al*. 1996). The first was the small matched control study of Jones *et al*. (1988) in which severely depressed subjects awaiting ECT were tested on a large number of frontal tasks. These subjects were found to be impaired predominantly on those tasks examining set-shifting, such as the Wisconsin Card Sorting Task (WCST) and the 'Go – No Go' Task, but performed normally on the verbal fluency task.

Two more recent studies have also reported significant frontal deficits in depression. Elliott *et al*. (1996) administered the CANTAB to 28 medicated middle-aged subjects with moderate depression and without psychomotor impairment. They found significant deficits across all

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mnemonic tasks, the degree of which correlated with depression severity. Patients also demonstrated impairment on certain aspects of frontal performance such as planning and strategy, verbal fluency and spatial working memory. There was, however, no impairment on the attentional shifting task, a task which tests frontal domains similar to the WCST. Subjects showed no motor slowing.

In contrast, Beats *et al*. (1996), using the same cognitive battery in a more severely depressed elderly sample, found these subjects to be most prominently impaired on recognition memory, verbal fluency, and attentional set-shifting tasks. Those depressed subjects showed psychomotor retardation, as evidenced by significantly slower processing and movement time. They also showed some planning impairment.

There have been few studies that examine for differential patterns of cognitive function in depressive subtypes. Making such a distinction may be relevant, as there is some suggestion in the literature that severely depressed patients and especially those with significant psychomotor impairment are more cognitively impaired. A study that distinguishes between two subsets of depressed patients was undertaken by Austin *et al*. (1992*a*), who used a broad neuropsychological battery in a sample of patients defined as having endogenous and non-endogenous depression according to the Newcastle endogeneity scale. Austin *et al*. (1992*a*) found that while all subjects demonstrated memory impairment, only those with endogenous depression showed impairment on other tasks, i.e. Digit Symbol substitution and Trails B. Conceptual frontal tasks such as verbal fluency and block design were spared. Although psychomotor slowing, present in many of the 'endogenous' patients, may have theoretically accounted for the deficits on these timed tasks, relatively intact performance on Trails A (a measure of psychomotor speed) made it less likely that this alone accounted for the difference. Intact performance on another timed task – verbal fluency – also argued against any impairment being simply related to motor slowing.

Overall, little is known of the pattern of frontal task performance in depressed patients, and in particular, those with significant psychomotor impairment. On the basis of findings in a small number of studies (Jones *et al*. 1988; Austin *et al*. 1992*a*; Beats *et al*. 1996), it would appear that such patients appear to show impairment on frontal task performance.

The main aim of the present study was to investigate the pattern of cognitive task impairment in depressed subjects as a whole, and then contrast performance in melancholic and non-melancholic subjects defined by the DSM-III-R as well as two narrower systems for defining melancholia: CORE (Parker *et al*. 1994) and Newcastle (Carney *et al*. 1965).

While also examining memory impairment, we were particularly interested in identifying patterns of deficits on 'frontal' tasks for two purposes: first, to replicate and expand the findings of differential impairment in depressive subtypes reported by Austin *et al*. (1992*a*); and secondly, to examine for particular patterns of frontal impairment, which may suggest abnormalities of specific neuroanatomical pathways or regions.

METHOD

Depressed patients, 20 years of age and older, with a DSM-III-R Major Depressive Episode and Hamilton Depression Rating Scale 21-item (Hamilton, 1967) of $\geqslant 16$ were consecutively recruited. These subjects, the majority of whom were in-patients, were entered into the study after assessment at the Prince Henry Hospital Mood Disorders Unit in Sydney. Patients were excluded if they had inadequate English, a neurological disorder, a past or current history of alcohol abuse, ECT within 3 months, or substance abuse. All depressed subjects were categorized as being with, or without, melancholic features according to DSM-III-R (APA, 1987), the CORE system (Parker *et al*. 1994) and the Newcastle Endogeneity Scale (Carney *et al*. 1965) criteria. The CORE scale – an 18-item clinician-rated instrument – was used to assess for objective psychomotor disturbance. Depressed subjects were allocated to the CORE-defined melancholic group if they scored $\geqslant 8$ on the CORE scale (Parker *et al*. 1994). In order to compare our reults with the Austin *et al*. (1992*a*) study, the same Newcastle endogeneity scale cut-off of $\geqslant 6$ for endogeneity was applied. The presence of psychotic symptoms, age of onset of depression and medication status were also recorded.

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Control subjects were recruited from among patients' relatives, staff and community volunteers. The controls were selected to be as close as possible to the CORE-defined melancholic subjects in age, gender ratio and years of education. Potential controls were excluded if there was a past history of depression or known neurological disorder.

Neuropsychological battery

The neuropsychological test battery was administered in the morning to standardize for any effect of diurnal mood variation (Moffoot *et al.* 1994) on test performance. It was given soon after admission before changes in medication had been instituted. We chose a test battery that would both optimize investigation of frontal–temporo–subcortical function and also be capable of being performed by severely depressed patients. Where patients were too unwell to perform the full battery, a shortened version was administered. This meant that there was missing data for some of the tasks. The full battery consisted of the following tests.

Mini-Mental State Examination (MMSE)

The MMSE (Folstein *et al.* 1975) is a screening tool for organic cognitive deficit. A score of < 25 is suggestive of significant cognitive deficit, but this is modified by psychosis, education, culture and other factors.

National Adult Reading test (NART)

The NART (Nelson, 1982): a list of 50 words in rising order of difficulty is read out aloud by subjects, the number of words incorrectly pronounced is used to estimate pre-morbid intelligence. The higher the score the better the intelligence quotient (IQ).

Digit span forwards and backwards (WMS-R, Wechsler, 1987)

Digit span forward is a test of attention and immediate recall, with digits backwards being an indication of working memory.

Reaction Time (Huppert, 1987)

This test is divided into simple reaction time (Reaction Time A), which relates purely to psychomotor speed, and choice reaction time (Reaction Time B), which relates to information processing speed and set-shifting ability.

Trails A and B (Army Battery, 1964)

In this test the subject consecutively connects numbered circles (Trails A) and then connects numbers and letters in alternating sequence (Trails B). Both are timed tests of visuomotor speed, with Trails B also being a test of set-switching. A high score indicates poor performance.

Stroop task (Golden, 1978)

This is a timed test of selective attention in which the subject is asked to read out three colour names printed in black ink as fast as possible. The subject is then presented with the same words printed in a colour different from the colour which it names. The subject is instructed to name, as fast as possible, the colour of the ink in which the word is printed. The time taken to complete the task increases significantly under these conditions and this is called the 'interference' effect. Suppressing this 'interference' and maintaining set, is thought to require pre-frontal input. This task tests ability to screen out automatic verbal responses that conflict with the required response. A higher score reflects better performance.

Verbal fluency (Borkowski *et al.* 1967)

This is a timed test in which the subject is asked to generate words starting with the letters F, A, and S as fast as possible. This task involves development of a strategy to produce the words (frontal) and is dependent on psychomotor speed. The total word score over three trials is reported in this study.

Abbreviated Wisconsin Card Sorting Test (WCST-64)

This test is adapted from the WCST (Heaton, 1981): 64 instead of 128 cards are administered in the usual fashion. The task is to match a series of cards to key cards varying in colour, shape and number according to 'correct/wrong' feedback. This is a test assessing ability to plan, devise problem solving strategies and appropriately shift and maintain set according to feedback. It has been shown to be sensitive to frontal lobe damage. It generates a number of measures but the most useful appear to be the number of completed categories, perseverative responses, and failure to maintain set.

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Similarities (WAIS-R, Wechsler, 1981)

This test requires the patient to describe how two objects/constructs are similar in increasing order of difficulty. It is a test of the patient's ability to conceptualize.

Rey Auditory Verbal Learning Task (RAVLT)

This is a test of verbal learning, and delayed recall and recognition (Rey, 1964). A list of 15 words is read out and repeated by the patient on five occasions. Delayed recall and recognition for the list are tested at 20 min. The test was administered according to instructions described in Lezak (1995). The main measures are: the sum of the five trials which gives an indication of learning ability; delayed recall at 20 min; and recognition. The RAVLT is thought to be a suitable test of memory in depressed subjects as learning information presented in a repeated fashion is less likely to be contaminated by poor attention span.

Visual reproduction (WMS-R, Wechsler, 1987)

In this task the subject is shown a series of four pictures for 10 s on each occasion and asked to reproduce each picture immediately after each viewing and then after a 30 min delay. Visual reproduction was included in the battery as the delayed recall component of this task has been considered by some authors to be more indicative of right than left front-temporal cortex function (Delaney *et al*. 1980).

Digit Symbol Substitution task (WAIS-R, Wechsler, 1981)

This is a timed task in which the subject is asked to match the numbers one to nine with a specific symbol. This is a test of visuomotor speed, selective attention and set shifting.

The short battery consisted of the NART, Digit Span forward and back, Reaction Time A and B, RAVLT, WCST-64, and (where possible) verbal fluency, the Stroop and Trails A and B.

Statistical analysis

Data were analysed with the SAS (1988) rather than the SPSS (Norušis 1993) as this allowed us to handle multiple contrasts more easily (as outlined below). First, comparisons between the total depressed group and controls were made using ANCOVA, covarying for age and, for timed tasks, Reaction Time A. Results are reported as raw means and standard deviations (i.e. before covariation).

In a second set of analyses, melancholic and non-melancholic subsets (defined according to the DSM-III-R, Newcastle scale and the CORE system) were compared with each other and controls, using ANCOVA and covarying for age, IQ (as defined by the NART) and Reaction Time A (where appropriate). Where differences emerged in the contrasts between melancholic and non-melancholic subjects, we also covaried for Hamilton score to assess the effect of depression severity on task performance.

As frontal task performance was extremely impaired in four elderly controls who performed at three or more standard deviations below the mean (and were thus distinct outliers), these subjects were excluded from all analyses as they may have had an early dementing process. This left 28 control subjects. Similarly, one melancholic subject – who was also clearly an outlier – was excluded.

Since correlations between psychometric variables were moderate, and there were six main subsets of tests (attention, memory, simple motor speed, set-shifting, WCST and conceptual), a Bonferroni correction factor of six was applied to control for possible false positive findings due to multiple analyses. Significant results are reported as $P < 0{\cdot}05$ after Bonferroni correction.

RESULTS

Characteristics of clinical samples

Total depressed sample

The total depressed sample was significantly younger than the controls, but did not differ in terms of gender ratio, IQ or years of education (see Table 1). The total depressed sample was moderately depressed (mean Hamilton score of 23·1). Fifty-four depressed subjects were medicated at the time of testing. Of those who were medicated, all were on an antidepressant (mostly tricyclics or SSRIs) with 20 of these same patients also being on an antipsychotic or lithium. MMSE scores were slightly reduced in depressed subjects, in most cases due to poor performance in short-term memory.

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Table 1. *Demographic and clinical variables (means and S.D.s) for total depressed sample, DSM-III-R defined depressed subtypes and controls*

Variable	Total depressed ($N = 77$)	DSM-III-R subtypes: Melancholic ($N = 54$)	DSM-III-R subtypes: Non-melancholic ($N = 23$)	Controls ($N = 28$)
Age	50·7 (16·9)*	55·3 (16·9)*#	40·0 (12·4)	60·4 (12·5)
Sex (male:female)	24:53	13:26	11:27	9:19
IQ	106·6 (9·5)	105·3 (9·5)*#	109·1 (10·1)	109·0 (8·7)
Education (years)	11·7 (3·1)	12·1 (2·7)	10·6 (3·1)	11·1 (3·0)
CORE	8·3 (7·0)	10·0 (6·9)#	4·7 (6·1)	NA
Hamilton	23·1 (5·9)	24·4 (5·9)#	20·2 (5·2)	NA
Newcastle	4·0 (3·3)	4·9 (3·2)#	2·2 (2·6)	NA
MMSE	28·1 (1·7)	27·7 (2·0)	28·4 (1·6)	NA
Antidepressant (prescribed)	54	41#	13	NA

NA = not applicable.
* $P < 0{\cdot}05$ when compared with controls; # $P < 0{\cdot}05$ when melancholic compared with non-melancholic.

Table 2. *ANCOVA for total depressed sample, covarying for age and reaction time A where appropriate, raw means and standard deviations (S.D.s)*

Variable	Raw means (S.D.s): Depressed ($N = 77$)	Raw means (S.D.s): Controls ($N = 28$)	P
Attention			
Digits forward†	7·3 (2·6)	7·6 (2·0)	0·46
Immediate verbal recall†	5·5 (1·8)	5·9 (1·7)	0·09
Memory			
Digits backward†	6·1 (2·4)	7·0 (2·0)	0·06
Visual recall‡	29·6 (8·1)	34·2 (5·6)	0·0000***
Delayed visual recall‡	24·7 (11·4)	30·4 (9·3)	0·0000***
Verbal learning†	41·8 (12·9)	47·8 (9·5)	0·0002***
Verbal recognition†	12·6 (2·2)	13·5 (1·5)	0·01
Delayed verbal recall†	7·7 (3·7)	10·6 (2·9)	0·0003***
Motor speed			
Trail A‡	40·6 (18·7)	39·9 (15·4)	0·4
Reaction time A†	0·37 (0·14)	0·29 (0·06)	0·007*
Set shifting			
Trail B	96·9 (34·8)	91·5 (33·1)	0·005*
Reaction time B†	0·74 (0·18)	0·67 (0·1)	0·08
Digit symbol substitution‡	42·8 (16·0)	45·9 (12·8)	0·03
Stroop-interference‡	37·1 (8·4)	39·4 (10·4)	0·63
WCST			
Category†	2·4 (1·7)	2·86 (1·5)	0·16
Perseveration†	15·9 (11·6)	11·1 (6·3)	0·01
Set maintenance†	0·52 (0·87)	0·68 (0·86)	0·9
Set initiation†	17·4 (11·8)	13·6 (5·3)	0·052
Conceptual			
Verbal fluency‡	35·6 (14·2)	37·4 (11·6)	0·81
Similarities§	42·8 (16·0)	45·9 (12·8)	0·03

* $P < 0{\cdot}05$; *** $P < 0{\cdot}001$ after Bonferroni correction.
† All subjects tested.
‡ 45/54 melancholics, all non-melancholics, all controls tested.
§ 32/54 melancholics, all non-melancholics, all controls tested.

DSM-III-R-defined depressed groups

There were 54 DSM-III-R-defined melancholic and 23 non-melancholic subjects (see Table 1). The melancholic sample was significantly older than non-melancholics ($P < 0{\cdot}001$) but not significantly younger than controls ($P = 0{\cdot}14$). The mean IQ score of the melancholic subjects was 4

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points lower than the non-melancholic and control groups ($P = 0{\cdot}03$) on a three-way ANOVA.

CORE-defined depressed groups

There were 39 subjects with melancholic depression and 38 subjects with non-melancholic depression as defined by the CORE system. Comparisons of demographic and clinical variables in CORE-defined melancholic and non-melancholic patients were similar to DSM-III-R-defined comparisons. Melancholic patients defined by this system were older (60·2 *versus* 55·3 years) than those defined by DSM-III-R, but otherwise demographic features were similar. With respect to clinical variables, melancholic subjects had higher CORE and Hamilton scores (14·1 and 26·5 respectively) than DSM-III-R melancholics.

Newcastle-defined depressed groups

There were 28 endogenous (melancholic) and 49 non-endogenous (non-melancholic) subjects as defined by the Newcastle scale. Endogenous subjects defined by the Newcastle were a little older than controls but not significantly so (63·0 *v*. 60·4). They had, however, a significantly lower IQ (103·2, $P < 0{\cdot}02$) and less years of education (9·9, $P < 0{\cdot}006$).

Test performance

All significance levels are reported after Bonferroni correction.

Total depressed sample

Digit span forward and immediate recall on the RAVLT were unimpaired in the depressed subjects, indicating that they could attend to simple tasks as well as controls. When the total depressed group was compared with controls (see Table 2), impairment was found on predominantly mnemonic tasks: in particular verbal and visual learning and recall. Digit span backward and verbal recognition were spared. Reaction time A was also significantly impaired. Given this finding, we expected other time-limited tasks to be impaired and consequently covaried for Reaction time A on time limited tests. In spite of this covariation, Trails B remained significantly impaired. In contrast, no impairment was found on the Stroop and Digit symbol substitution tasks (also timed tasks). In particular, the expected 'interference' effect was not seen in the Stroop task, indicating that subjects were able to maintain set. There was no impairment on any aspects of the WCST, nor on either the verbal fluency or similarities task.

Analyses of DSM-III-R-defined subtypes

Again depressed subjects were attending well. With respect to mnemonic tasks, both melancholic and non-melancholic subgroups were significantly impaired on all tasks (except digit span backwards and verbal recognition) compared with controls. Melancholic subjects were also significantly impaired on Reaction Time A and the Trails B task (see Table 3) while the non-melancholic sample were impaired on digit symbol substitution. When melancholic were compared to non-melancholic subjects, there was no difference in cognitive task performance between the two depressed subsets.

Analyses of CORE-defined subtypes

As was found for the total depressed sample and DSM-III-R melancholic subjects, CORE-defined melancholic subjects attended well but were significantly impaired on all memory tasks (see Table 4). They were also impaired on Trails B and the WCST perseverative response. The degree of perseveration on the WCST in the depressed group was similar to that found in patients with Alzheimer's disease (Robinson *et al*. 1991). This particular clustering of frontal deficits may indicate a selective inability to shift set, with set initiation and maintenance intact (as demonstrated by intact performance on the Stroop and remaining WCST variables). Non-melancholic subjects did not perform significantly differently from controls on any task except for visual recall ($P = 0{\cdot}02$).

Contrasts between melancholic and non-melancholic subjects revealed significant differences on delayed visual recall and verbal learning, recognition and delayed recall (see Table 4). After covariation for the Hamilton score, the only significant difference was on delayed verbal recall.

Analyses of Newcastle-defined subgroups

Results for Newcastle-defined endogenous patients were similar to the CORE-defined melancholics, with even more marked evidence

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Table 3. *ANCOVA for DSM-III-R samples, covarying for age, IQ and reaction time A where appropriate*

Variable	Raw means (S.D.)		Contrasts		
	Melancholic ($N = 54$)	Non-melancholic ($N = 23$)	Melancholic/ Control	Non-melancholic/ Control	Melancholic/ Non-melancholic
Attention					
Digits forward†	6·7 (2·5)	8·7 (2·4)	0·2	0·30	0·02
Immediate verbal recall†	5·3 (1·8)	6·0 (1·6)	0·12	0·16	0·8
Memory					
Digits backward†	5·8 (2·3)	6·7 (2·5)	0·05	0·24	0·7
Visual recall‡	28·2 (8·7)	32·3 (8·3)	0·00001***	0·0004*	0·97
Delayed visual recall‡	22·5 (11·4)	29 (10·4)	0·00001***	0·002*	0·66
Verbal learning†	40·0 (13·4)	46 (11·0)	0·0004***	0·002*	0·61
Verbal recognition†	12·4 (2·4)	13·4 (1·4)	0·009	0·16	0·48
Delayed verbal recall†	7·3 (3·8)	8·0 (3·4)	10^{-6}***	10^{-5}*	0·48
Motor speed					
Trail‡	42·5 (19·2)	36·4 (17)	0·6	0·20	0·34
Reaction time A†	0·4 (0·15)	0·3 (0·1)	0·0003*	0·22	0·22
Set shifting					
Trail B§	105·9 (36·8)	79·7 (23)	0·0003**	0·12	0·3
Reaction time B†	0·8 (0·2)	0·7 (0·1)	0·097	0·16	0·9
Digit symbol substitution‡	41·1 (16·4)	46·3 (15)	0·09	0·005*	0·08
Stroop interference‡	36·4 (8·3)	38·9 (8·5)	0·66	0·67	0·9
WCST					
Category†	2·3 (1·4)	2·7 (1·9)	0·2	0·13	0·47
Perseveration†	16·6 (11·6)	14 (11·6)	0·02	0·028	0·6
Set maintenance†	0·53 (0·9)	0·47 (0·8)	0·43	0·54	0·9
Set initiation†	19·5 (13·4)	12·7 (4·4)	0·02	0·77	0·1
Conceptual					
Verbal fluency‡	34·2 (14·2)	38·7 (14)	0·9	0·7	0·7
Similarities§	17·9 (5·9)	19·0 (6·7)	0·2	0·06	0·3

* $P < 0·05$; ** $P < 0·01$; *** $P < 0·001$ after Bonferroni corrections.
† All subjects tested.
‡ 45/54 melancholics, all non-melancholics, all controls tested.
§ 32/54 melancholics, all non-melancholics, all controls tested.

of frontal deficits. Thus, Newcastle melancholic subjects were impaired on all mnemonic tasks as well as Reaction time A, Trails B, perseveration on the WCST and also digit symbol substitution. As for CORE non-melancholic depressed subjects, Newcastle non-melancholic patients were not impaired on any tasks except for visual recall ($P = 0·03$) and delayed verbal recall ($P = 0·03$). Contrasts between endogenous and non-endogenous subjects revealed significant differences on delayed visual recall, verbal learning, verbal recognition and delayed verbal recall. These differences were no longer present after covariation for Hamilton score.

Correlations

Most of the psychometric variables (with the exception of WCST perseveration and Stroop) correlated moderately with each other ($r = 0·4$–$0·6$). Neuropsychological task scores were inversely correlated with depression severity as measured by the Hamilton scale ($r = -0·2$ to $-0·4$, $P < 0·001$) and psychomotor disturbance as measured by the CORE ($r \leqslant 0·5$, $P < 0·001$). Correlations between psychotic status and cognitive variables were only moderate ($r = -0·2$ to $-0·4$), and particularly weak for the WCST indices ($r = 0·05$, NS). Correlations between medication status and test performance were similarly weak.

Other analyses

The effects of a number of potential confounding factors on cognitive function were examined, as follows.

Medication status

A significant proportion (54/77) of depressed subjects were prescribed an antidepressant. The correlations between medication status and

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Table 4. *ANCOVA for CORE samples covarying for age, IQ and reaction time A where appropriate*

Variable	Raw means (S.D.)		Contrasts		
	Melancholic ($N = 39$)	Non-melancholic ($N = 38$)	Melancholic/ Control	Non-melancholic/ Control	Melancholic/ Non-melancholic
Attention					
Digits forward†	6·5 (2·5)	8·2 (2·5)	0·2	0·7	0·09
Immediate verbal recall†	4·7 (1·7)	6·4 (1·5)	0·015	0·9	0·03
Memory					
Digits backward†	5·3 (2·1)	6·9 (2·5)	0·004*	0·45	0·04
Visual recall‡	24·9 (9·7)	33·3 (5·7)	10^{-6}***	0·004*	0·04
Delayed visual recall‡	17·3 (11·3)	30·6 (7·7)	10^{-7}***	0·03	0·002*
Verbal learning†	34·9 (12·1)	49·0 (9·6)	10^{-4}***	0·12	0·005*
Verbal recognition†	11·6 (2·4)	13·7 (1·3)	0·0003**	0·8	0·002*
Delayed verbal recall†	5·4 (2·9)	10·1 (2·9)	10^{-9}***	0·03	10^{-4}**
Motor speed					
Trail A‡	50 (22·4)	32·4 (8·9)	0·12	0·8	0·07
Reaction time A†	0·4 (0·2)	0·3 (0·1)	0·002*	0·2	0·1
Set shifting					
Trail B§	116·5 (33)	84 (30·0)	0·002*	0·07	0·2
Reaction time B†	0·8 (0·2)	0·7 (0·1)	0·1	0·3	0·03
Digit symbol substitution‡	35·0 (14)	49·5 (14)	0·02	0·2	0·4
Stroop-interference‡	35·4 (7·9)	38·7 (3·6)	0·66	0·7	0·98
WCST					
Category†	2·1 (1·5)	2·8 (1·7)	0·2	0·3	0·9
Perseveration†	19 (13·3)	12·6 (8·6)	0·008*	0·14	0·31
Set maintenance†	0·5 (0·7)	0·5 (1·0)	0·34	0·7	0·6
Set initiation†	18·2 (12·4)	16·7 (11·4)	0·02	0·03	0·3
Conceptual					
Verbal fluency‡	31 (14·5)	40 (12·7)	0·6	0·8	0·4
Similarities§	15·8 (6·5)	20·3 (5·1)	0·04	0·54	0·2

* $P < 0·05$; ** $P < 0·01$; *** $P < 0·001$ after Bonferroni correction.
† All subjects tested.
‡ 45/54 melancholics, all non-melancholics, all controls tested.
§ 32/54 melancholics, all non-melancholics, all controls tested.

cognitive test performance were small ($r = -0·2$ to $-0·3$), indicating no substantive effect of medication on cognitive function.

Psychosis

When the sample was analysed without the 13 psychotic subjects (all of whom were melancholic) the results were very similar both in terms of means and significance levels. Furthermore, the correlations between test performance and psychotic status were modest ($r = -0·2$ to $-0·4$).

Sample age and age of onset

A recent study by Hickie *et al.* (1997) indicates that elderly depressed subjects with an older age of onset appear to have a high rate of persisting cognitive impairment in the ensuing 1 to 3 years. While some of these patients may have persistent deficits due to treatment-resistant depression, others may have developed a dementing illness, which could have been present to some degree when initially presenting with depression. The latter subjects would act as confounders in any study of cognitive deficits in depression. Since 25% of our sample was over 65 years of age, and 75% of these had late-onset depression (> 50 years old), we could not exclude the possibility that such a putative organic process in the elderly patients may have accentuated the impaired performance of the total sample. However, when subjects aged > 65 were excluded from the analyses, our results were again little different both in terms of mean values and significance levels.

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Table 5. *ANCOVA for Newcastle samples covarying for age, IQ and reaction time A where appropriate*

Variable	Raw means (S.D.)		Contrasts		
	Melancholic ($N = 28$)	Non-melancholic ($N = 49$)	Melancholic/ Control	Non-melancholic/ Control	Melancholic/ Non-melancholic
Attention					
Digits forward†	6·4 (2·7)	7·9 (2·5)	0·3	0·9	0·3
Immediate verbal recall†	4·6 (1·7)	6·1 (1·6)	0·02	0·55	0·1
Memory					
Digits backward†	4·9 (1·8)	6·9 (2·4)	0·0004**	0·3	0·004*
Visual recall‡	22·0 (9·2)	32·9 (6·0)	10^{-7}***	0·005*	0·0007**
Delayed visual recall‡	14·8 (9·8)	29·2 (9·1)	10^{-6}***	0·009	0·002*
Verbal learning†	33·5 (11·8)	47·2 (11)	0·00002***	0·03	0·03
Verbal recognition†	11·4 (2·5)	13·5 (1·4)	0·0002**	0·5	0·007*
Delayed verbal recall†	5·4 (2·7)	9·2 (3·5)	10^{-7}***	0·005*	0·03
Motor speed					
Trail A‡	53·4 (24·5)	34 (10·3)	0·06	0·8	0·03
Reaction time A†	0·4 (0·155)	0·35 (0·1)	0·002*	0·09	0·2
Set shifting					
Trail B§	121·5 (27·4)	87·5 (33)	0·005*	0·03	0·3
Reaction time B†	0·8 (0·2)	0·7 (0·1)	0·1	0·5	0·05
Digital symbol substitution‡	30·8 (12·7)	49·0 (14)	0·004*	0·3	0·06
Stroop-interference‡	34·1 (8·4)	38·8 (7·9)	0·4	0·9	0·5
WCST					
Category†	1·9 (1·3)	2·7 (1·7)	0·1	0·2	0·6
Perseveration†	21·2 (11·4)	12·6 (10·5)	0·002*	0·2	0·6
Set maintenance†	0·5 (0·8)	0·5 (0·9)	0·2	0·8	0·3
Set initiation†	19·5 (13·9)	16·3 (10·5)	0·2	0·05	0·6
Conceptual					
Verbal fluency†	27·8 (13·0)	40·2 (13·0)	0·2	0·55	0·08
Similarities§	15·0 (6·4)	19·8 (5·4)	0·05	0·4	0·5

* $P < 0·05$; ** $P < 0·01$; *** $P < 0·001$ after Bonferroni corrections.
† All subjects tested.
‡ 45/54 melancholics, all non-melancholics, all controls tested.
§ 32/54 melancholics, all non-melancholics, all controls tested.

DISCUSSION

This study undertaken at the Prince Henry Hospital Mood Disorders Unit in Sydney extends the report of Austin *et al.* (1992*a*). When depressed subjects were analysed as a whole (and also when using the DSM-III-R system to identify melancholic and non-melancholic subjects), the main finding was impairment on most aspects of memory. However, when analyses were performed after applying narrow definitions of melancholia (i.e. the CORE and the Newcastle systems) only melancholic subjects were substantially cognitively impaired when compared to controls, demonstrating both broad mnemonic and selective frontal task deficits. CORE and Newcastle-define non-melancholic subjects demonstrated limited mnemonic impairment. This finding contrasts with reports of broad impairment of mnemonic performance in non-melancholics in the earlier Austin *et al.* (1992*a*) study and the Elliott *et al.* (1996) study also looking at a moderately depressed sample without psychomotor impairment.

The pattern of frontal task impairment in narrowly-defined melancholic patients appeared to be fairly specific. When performing the WCST, these subjects had great difficulty with set-shifting while demonstrating no deficit in set initiation and maintenance. This intriguing dissociation between set shifting and set maintenance was further highlighted by the ability of CORE and Newcastle melancholic subjects to maintain set on the Stroop task such that the 'interference' effect was not seen. Further difficulty with set-shifting was demosntrated on the Trails B and digit symbol substitution tasks (the latter only impaired in Newcastle melancholic patients). Finally, there was no im-

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pairment on tasks of conceptualization and strategy not requiring set shifting – as tested by the verbal fluency and similarities tasks. These results were independent of age, IQ, the presence of psychosis, medication status or psychomotor retardation. Findings for the narrowly defined melancholic subjects were comparable to those found in the Beats *et al*. (1996) study (described in the Introduction), where deficits in recognition memory, attentional set shifting (similar to the perseveration seen on the WCST in this study) and planning were found.

When performance between narrowly defined melancholic and non-melancholic subjects was directly contrasted, highly significant differences persisted at the level of the mnemonic tasks. These differences, however, were no longer significant after covarying for the Hamilton score.

This finding raises an important conceptual issue. Do the cognitive differences found reflect qualitative or quantitative distinctions between melancholic and non-melancholic subgroups? Most historical descriptions and formal definitions of melancholia indicate that this is both a more severely depressed, and phenomenologically distinct group, for example in terms of psychomotor disturbance. Thus, both quantitative and qualitative differences are usually implied. It is not possible to resolve this debate on the basis of our data. On the one hand, differences between melancholic and non-melancholic subjects were no longer significant after covarying for Hamilton scores, which may suggest a simple quantitative difference. On the other hand, the virtual absence of cognitive impairment in non-melancholic subjects, and distinct pattern of frontal deficits in melancholic subjects found when using two very different systems (one sign based; the CORE, the other symptom based; the Newcastle) for strictly defined melancholia, lends support to the possibility that this difference between the two groups is truly qualitative rather than quantitative.

With regard to neuroanatomical localization, the pattern of psychometric deficits demonstrated in the narrowly defined melancholic subjects – a combination of broad deficits in mnemonic function and highly selective deficits in executive function – is suggestive of both frontal-subcortical and temporal impairment. Although earlier studies claimed that verbal recognition tasks were unimpaired (Weingartner *et al*. 1981), the current study, using stricter criteria for defining melancholia, and that of Austin *et al*. (1992*a*) would suggest impairment in both recall and recognition in melancholia. Whereas recall of information relies on the use of working memory (Goldman-Rakic, 1993) – a fundamental function of the pre-frontal cortex – recognition is more reliant on intact temporal lobe function. The impairment in recognition, thus, argues for the involvement of both fronto-subcortical and temporal regions. This is in keeping with the findings of Elliott *et al*. (1996) who also suggest combined pre-frontal-subcortical and temporal impairment.

The intriguing dissociation between impairment on tasks of set-shifting and other frontal tasks, implies that quite specific regions and/or functional neuronal networks may be impaired in patients with narrowly defined melancholic depression. This finding could well be explained within the framework suggested by Alexander *et al*. (1986) who proposed the existence of a number of fronto-subcortical neural networks (or loops) impacting upon motor function, cognitive processes and mood. Cummings (1993) further postulated that specific patterns of impairment in parts of the dorsolateral prefrontal network (as described by Alexander *et al*. 1986) might be associated with specific disorders such as depression, and frontal cognitive deficits. The application of this hypothesis to melancholic depression, was further expanded in an earlier paper by Austin & Mitchell (1995).

In depressed subjects, functional imaging studies indicate alterations in cerebral blood flow in prefrontal cortex (PFC), more so in the orbito-medial than the dorsolateral prefrontal cortex (DLPFC) (see review of Goodwin, 1997). A number of resting studies (Austin *et al*. 1992*b*; Bench *et al*. 1992; Dolan *et al*. 1994; Drevets *et al*. 1997; Ebert & Ebmeier, 1996) and one treatment study (Mayberg, 1997) in depressed patients, implicate disturbed PFC function – especially of the anterior cingulate (AC), which is situated in the orbitomedial PFC – related to both the affective and cognitive components of depression.

The various functional regions of the anterior cingulate (AC) have now been mapped in a highly sophisticated fashion (Devinsky *et al*. 1995). Their relationship to the various symptom

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clusters of the depressive syndrome have also been elegantly postulated by Mayberg *et al.* (1997). Thus, two main components of the AC have been distinguished: the dorsal AC which has connections to the DLPFC, and the ventral AC, which connects to other components of the orbitomedial PFC such as the rostral and subgenual PFC. The dorsal AC (in conjunction with the DLPFC) has been postulated to modulate the cognitive and psychomotor aspects of depression while the ventral AC is thought to modulate vegetative, autonomic and affective aspects of depression, via the modulation of the subgenual PFC (Mayberg *et al.* 1997).

There have been a number of studies examining the potential anatomical correlates of tasks dependent on cognitive flexibility and selective attention. Pardo *et al.* (1990) – using PET imaging – demonstrated that performance on the Stroop task involved selective activation of the anterior cingulate and a number of subcortical structures. Grattan *et al.* (1994) studied impairment on a task of cognitive flexibility (WCST) and affective response in patients with three types of PFC lesions: 'dorsolateral' (DLPFC); 'mesial' (in which the authors included dorsal anterior cingulate and posterior cingulate); and 'orbital' (in which they included ventral anterior cingulate). They found that 'mesial' lesions impaired cognitive flexibility (as assessed by perseverative response on the WCST) without impacting on empathy; 'dorsolateral' prefrontal cortex (DLPFC) lesions affected both; and 'orbital' lesions only impacted upon empathy. Finally, a cognitive activation study in depressed patients demonstrated that impaired performance on the more demanding or 'willed' aspect of a planning task was associated with failure to activate the anterior cingulate, caudate nucleus and rostral PFC (Elliott *et al.* 1997) while activation in the DLPFC was unimpaired. These studies highlight the putative involvement of the AC, and the dorsal AC in particular, in the performance of complex cognitive tasks.

Given these recent insights into the functions and connections of the anterior cingulate, one might speculate that all depressed patients (whether melancholic or not) demonstrate impaired function in the ventral AC (which governs the affective, autonomic and vegetative aspects common to depression). In narrowly defined melancholia, abnormalities on a number of tasks and in particular those requiring the involvement of selective attention and cognitive flexibility, may implicate additional dysfunction in the ventral AC, rostral (or orbitomedial) PFC and subcortical regions. Such speculation must remain tentative but could be further tested by appropriate imaging studies.

Some of the methodological limitations of this study should be acknowledged. Almost all the subjects were tested on the most informative tests in the battery – namely the RAVLT, verbal fluency, the Stroop and the WCST. Any missing data were limited to melancholic patients, and to the Similarities and Trails B tasks in particular (see Tables 3–5). It should also be recognized that the tasks used in this study were originally devised to test brain-damaged patients. Applying them to patients with functional psychiatric disorders, therefore, calls for caution in interpreting test results. Furthermore, the greater the task complexity the more difficult it is to interpret findings. This applies especially to the WCST. On the other hand, the various components of the WCST (set initiation, maintenance and shifting) are well differentiated. In this study the distinction between these subtests allowed detection of a dissociation between set shifting and set initiation or maintenance. The set shifting difficulties elicited by the WCST were further supported by similar findings in simpler tasks reliant on set shifting, i.e. Digit Symbol substitution (in Newcastle defined subjects) and Trails B.

Another theoretical limitation of the WCST is the use of negative feed-back, which is inherent in the task instructions. This could have reinforced the depressed patients' pre-existing 'negative cognitive set' (Beck *et al.* 1979) and thus adversely affected performance. If that were the case, however, other tasks assessing set-shifting – but independent of feedback for their performance – should not have been impaired. The fact that the reverse was true, however, argues against the possibility of negative task feed-back acting as a confounder.

In conclusion, the present study highlights the utility of the neurocognitive approach as a tool in clarifying the neuroanatomical basis of depression, thereby offering a means of 'dissecting out' particular dysfunctional pathways or regions. Furthermore, it confirms the value of

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focussing upon strictly defined melancholic patients in whom a pattern of cognitive dysfunction may be more readily demonstrable than in more heterogeneous depressed samples.

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REFERENCES

Alexander, G. E., De Long, M. R. & Strick, P. L. (1986). Parallel organisation of functionally segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience* **9**, 357–381.

American Psychiatric Association (1987). *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III-R*). Washington, DC: APA.

Army Individual Test Battery (1964). *Manual of Directions and Scoring*. War Department, Adjutant General's Office: Washington, DC.

Austin, M.-P. & Mitchell, P. (1995). The anatomy of melancholia: does frontal subcortical pathophysiology underpin its psychomotor and cognitive manifestations? *Psychological Medicine* **25**, 665–672.

Austin, M.-P., Ross, M., Murray, C., O'Carroll, R. E., Ebmeier, K. P. & Goodwin, G. M. (1992*a*). Cognitive function in major depression. *Journal of Affective Disorders* **25**, 21–30.

Austin, M.-P., Dougall, N., Ross, M., Murray, C., O'Carroll, R. E., Moffott, A., Ebmeier, K. P. & Goodwin, G. M. (1992*b*). Single photon emission tomography with ^{99m}Tc-exametazime in major depression and the pattern of brain activity underlying the psychotic/neurotic continuum. *Journal of Affective Disorders* **26**, 31–44.

Beats, B. C., Sahakian, B. J. & Levy, R. (1996). Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. *Psychological Medicine* **26**, 591–603.

Beck, A. T., Rush, A. J., Shaw, B. F. & Emery, G. (1979). *Cognitive Therapy of Depression*. Academic Press: New York.

Bench, C. J., Friston, K. M., Brown, R. G., Scott, L. C., Frackowiak, S. J. & Dolan, E. J. (1992). The anatomy of melancholia – focal abnormalities of cerebral blood flow in major depression. *Psychological Medicine* **22**, 606–615.

Borkowski, J. G., Benton, A. L. & Spreen, O. (1967). Word fluency and brain damage. *Neuropsychologia* **5**, 135–140.

Carney, M. P. W., Roth, M. & Garside, R. F. (1965). The diagnosis of depressive syndromes and the prediction of ECT response. *British Journal of Psychiatry* **111**, 659–674.

Cohen, R., Weingartner, H., Smallberg, S., Pickar, D. & Murphy, D. (1982). Effort and cognition in depression. *Archives of General Psychiatry* **39**, 593–598.

Cummings, J. L. (1993). Frontal-subcortical circuits and human behaviour. *Archives of Neurology* **50**, 873–880.

Delaney, R. C., Roen, A. J., Mattson, R. H. & Novelly, R. A. (1980). Memory function in focal epilepsy: a comparison of nonsurgical, unilateral temporal lobe and frontal lobe samples. *Cortex* **16**, 103–117.

Devinsky, O., Morrell, M. J. & Brent, A. V. (1995). Contribuitons of anterior cingulate cortex to behaviour. *Brain* **118**, 279–306.

Dolan, R. J., Bench, C. J., Brown, R. G., Scott, L. C. & Frackowiak, R. S. J. (1994). Neuropsychological dysfunction in depression: the relationship to regional cerebral blood flow. *Psychological Medicine* **24**, 849–857.

Drevets, W. C., Price, J. L., Simpson, J. R. Jr., Todd, R. D., Reich, T., Vannier, M. & Raichle, M. E. (1997). Subgenual prefrontal cortex abnormalities in mood disorders. *Nature* **386**, 824–827.

Ebert, D. & Ebmeier, K. P. (1996). The role of the cingulate gyrus in depression: from functional anatomy to neurochemistry. *Biological Psychiatry* **39**, 1044–1050.

Elliott, R., Sahakian, B. J., McKay, A. P., Herrod, J. J., Robbins, T. W. & Paykel, E. S. (1996). Neuropsychological impairments in unipolar depression: the influence of perceived failure on subsequent performance. *Psychological Medicine* **26**, 975–989.

Elliott, R., Baker, S. C., Rogers, R. D., O'Leary, D. A., Paykel, E. S., Frith, C. D., Dolan, R. J. & Sahakian, B. J. (1997). Prefrontal dysfunction in depressed patients performing a complex planning task: a study positron emission tomography. *Psychological Medicine* **27**, 931–942.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975). Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* **12**, 189–198.

Golden, C. J. (1978). *Stroop Color and Word Test*. Stoelting: Chicago, IL.

Goldman-Rakic, P. S. (1993). Specification of higher cortical functions. *Journal of Head Trauma Rehabilitation* **8**, 13–23.

Goodwin, G. M. (1997). Neuropsychological and neuroimaging evidence for the involvement of the frontal lobes in depression. *Journal of Psychopharmacology* **11**, 115–122.

Grattan, L. M., Bloomer, R. H., Archambault, F. X. & Eslinger, P. J. (1994). Cognitive flexibility and empathy after frontal lobe lesion. *Neuropsychiatry*, *Neuropsychology*, *and Behavioural Neurology* **7**, 251–259.

Hamilton, M. (1967). Development of a rating scale of primary depressive illness. *British Journal of Social and Clinical Psychology* **6**, 278–296.

Heaton, R. K. (1981). *Wisconsin Card Sorting Test* (*WCST*). Psychological Assessment Resources: Odessa, FL.

Hickie, I., Scott, E., Wilhelm, K. & Brodaty, H. (1997). Subcortical hyperintensities on magnetic resonance imaging in patients with severe depression. A longitudinal evaluation. *Biological Psychiatry* **42**, 367–374.

Huppert, F. A. (1987). Cognitive function. In *The Health and Lifestyle Survey: Preliminary Report of a Nationwide Survey of the Physical and Mental Health*, *Attitudes and Lifestyle of a Random Sample of 9003 British Adults* (ed. B. D. Cox), pp. 43–50. Health Promotion Research Trust: London.

Jones, B., Henderson, M. & Welch, C. A. (1988). Executive functions in unipolar depression before and after electroconvulsive therapy. *International Journal of Neuroscience* **38**, 287–297.

Lezak, M. D. (1995). *Neuropsychological Assessment*, *3rd edn*. Oxford University Press; New York.

Mayberg, H. S. (1997). Limbic-cortical dysregulation: a proposed model of depression. *Journal of Neuropsychiatry* **9**, 471–481.

Mayberg, H. S., Brannan, S. K., Mahurin, R. K., Jerabek, P. A., Brickman, J. S., Tekell, J. L., Silva, J. S., McGinnis, S., Glass, T. G., Martin, C. C. & Fox, P. T. (1997). Cingulate function in depression: a potential predictor of treatment response. *Neuro-Report* **8**, 1057–1061.

Moffoot, A. P. R., O'Carroll, R. E., Bennie, J., Carroll, S., Dicj, H., Ebmeier, K. P. & Goodwin, G. M. (1994). Diurnal variation of mood and neuropsychological function in major depression with melancholia. *Journal of Affective Disorders* **32**, 257–269.

Nelson, H. E. (1982). *National Adult Reading Test* (*NART*): *Test Manual*. NFER-Nelson: Windsor.

Norušis, M. J. (1993). *Statistical Packet for the Social Sciences for Windows* (*SPSS*) *Base System Users Guide 6.0*. SPSS: Chicago, IL.

Pardo, J. V., Pardo, P. J., Janer, K. W. & Raichle, M. E. (1990). The

https://doi.org/10.1017/S0033291798007788 Published online by Cambridge University Press

anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. *Proceedings of the National Academy of Science* **87**, 256–259.
Parker, G., Hadzi-Pavlovic, D., Wilhelm, K., Hickie, I., Brodaty, H., Boyce, P., Mitchell, P. & Eyers, K. (1994). Defining melancholia: properties of a refined sign-based measure. *British Journal of Psychiatry* **164**, 316–326.
Raskin, A., Friedman, A. S. & DeMascio, A. (1982). Cognitive and performance deficits in depression. *Psychopharmacology Bulletin* **18**, 196–202.
Rey, A. (1964). *L'examen clinique en psychologie*. Presses Universitaires de France: Paris.
Robinson, L. J., Kester, D. B., Saykin, A. J., Kaplan, E. F. & Gur, R. C. (1991). Comparison of two short forms of the Wisconsin Card Sorting Test. *Archives of Clinical Neuropsychology* **6**, 27–33.
SAS Institute (1988). *SAS/STAT. User's Guide*, *Release 6.03 Edition*. SAS: Cary NC.
Silberman, E. K., Weingartner, H. & Post, R. M. (1983). Thinking disorder in depression. *Archives of General Psychiatry* **40**, 775–780.
Sternberg, D. E. & Jarvik, M. E. (1976). Memory functions in depression. *Archives of General Psychiatry* **33**, 219–224.
Stromgren, L. S. (1977). The influence of depression on memory. *Acta Psychiatrica Scandinavica* **56**, 109–128.
Wechsler, D. A. (1981). *Wechsler Adult Intelligence Scale-Revised Test Manual*. The Psychological Corporation: New York.
Wechsler, D. A. (1987). *Wechsler Memory Scale-Revised Manual*. The Psychological Corporation: New York.
Weingartner, H., Cohen, R. M., Murphy, D. L., Martello, J. & Gerdt, C. (1981). Cognitive processes in depression. *Archives of General Psychiatry* **38**, 42–47.
Wolfe, J., Granholm, E., Butters, N., Saunders, E. & Janowski, D. (1987). Verbal memory deficits associated with major affective disorders: a comparison of unipolar and bipolar patients. *Journal of Affective Disorders* **13**, 83–92.

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