British Journal of Psychiatry (1990), **157**, 50–54

Cognitive Inflexibility and Pre-frontal Dysfunction in Schizophrenia and Mania

RODNEY MORICE

The ability to shift cognitive set, which is probably subserved, at least in part, by the pre-frontal cortex, was determined for schizophrenic, bipolar (manic) and control subjects, using the Wisconsin Card Sorting Test (WCST). The schizophrenic and manic subjects both demonstrated poor performance on the WCST, suggesting that cognitive inflexibility and/or pre-frontal dysfunction, is not specific to schizophrenia (although laterality differences could exist). Moderate levels of poor performance in the non-psychiatric control group suggest the need for a review of the cut-off figures in the WCST currently used for predicting 'brain damage' and 'focal frontal involvement', especially given the trend for the increasing use of cognitive assessment and rehabilitation in the major psychoses.

The Wisconsin Card Sorting Test (WCST; Berg, 1948; Heaton, 1981) has recently come into greater prominence with reference to schizophrenia following the studies and reports of Weinberger and colleagues (Berman *et al*, 1986; Weinberger *et al*, 1986; Goldberg *et al*, 1987; Weinberger, 1987; Weinberger *et al*, 1988). Measuring regional cerebral blood flow under different test conditions, they have demonstrated hypoactivation of the dorsolateral pre-frontal cortex in schizophrenia. Specifically, schizophrenic patients, unlike controls, did not show an increase in regional cerebral blood flow to that area of brain when attempting to perform a modified version of the WCST. Additionally, patients could not be trained to improve their performance on the WCST, leading Goldberg *et al* (1987) to speculate on the presence of a "dementia of the prefrontal type in schizophrenia".

Since its introduction as a neuropsychological test (Berg, 1948), the WCST increasingly has been regarded as the best single measure of pre-frontal cortical function. Devised as a measure of abstraction ability, but now regarded more as a test of cognitive flexibility, this reputation was gained following a series of studies that demonstrated impaired performance in patients with focal lesions affecting the pre-frontal lobes (Milner, 1963; Drewe, 1974; Robinson *et al*, 1980). Some studies reported equivalent impairment following left- and right-sided lesions (Milner, 1963), and others for focal frontal and diffuse brain lesions (Robinson *et al*, 1980).

Prior to the studies of Weinberger and colleagues at The National Institute of Mental Health (NIMH), occasional studies had demonstrated impaired WCST performance in schizophrenic patients (Fey, 1951; Malmo, 1974), with Fey having matched patients and controls for full-scale IQ. Kolb & Wishaw (1983) also found that schizophrenic patients completed fewer categories on the WCST than controls, but in Fey's (1951) study patients recorded a significantly lower mean full-scale IQ than the non-patient controls. This lower full-scale IQ was due to a lower mean performance rather than verbal IQ.

Impaired WCST performance also has been demonstrated in alcoholic subjects (Tarter & Parsons, 1971; Malmo, 1974), but not, to the author's knowledge, in patients with bipolar illness.

Because of the increasing role for neuropsychological tests as cognitive tasks used in conjunction with brain imaging techniques and of the increasing relevance of cognitive impairments for treatment and rehabilitation, this study sought to examine the specificity of impaired WCST performance (and putative pre-frontal cortical dysfunction) for schizophrenia *vis-à-vis* bipolar illness (mania), and to determine the prevalence of impairment in both disorders. Further, possible relationships between general intelligence (IQ) and WCST performance were sought.

Method

Subjects

Subjects comprised 60 schizophrenic patients, 20 bipolar (manic) patients and 34 non-patient controls. All were administered the Diagnostic Interview Schedule (DIS; Robins *et al*, 1981) to confirm DSM-III (American Psychiatric Association, 1980) diagnoses of schizophrenia or mania, and to exclude subjects with any psychiatric diagnoses from the non-patient control group. Any subjects with a known history of primary mental retardation, head injury, epilepsy or drug or alcohol dependence were excluded from the study.

https://doi.org/10.1192/bjp.157.1.50 Published online by Cambridge University Press

The main sociodemographic data for the three groups are listed in Table I. Sex differences between the groups were significant ($\chi^2 = 14.3$, 2 d.f., $P < 0.001$), but those between the two patient groups reflect clinical realities. Manic subjects were significantly older than both other groups ($P < 0.01$), and there were significant differences between groups with respect to marital status ($\chi^2 = 33.8$, 4 d.f., $P < 0.001$). Education level attained was fairly uniform across the groups, except that ten (17%) schizophrenics had only completed primary education.

Patient subjects were selected both from in-patient and out-patient populations. In-patients were from either the acute admissions ward or the longer-stay wards in the two psychiatric hospitals servicing the Hunter Area of New South Wales, Australia. Out-patients were selected from attenders at several community mental health clinics. No patient was tested during an acute psychotic episode, in particular no patient was so thought-disordered as to make standardised diagnosis or formal testing impossible. All patients were fairly stable mentally, in a state of chronic psychosis, 'near-recovery' from an acute psychotic episode or, especially in the case of most manic subjects, in 'remission'. Six (30%) manic and 23 (38%) schizophrenic patients were tested while in hospital. Control subjects were selected from a variety of subgroups, including mine workers and unemployed people, the aim being to select a control group with a mean IQ lower than that usually obtained for control groups in psychiatric research.

Clinical characteristics

Some basic clinical characteristics for both patient groups are listed in Table II. The younger mean age at onset for the schizophrenic group was expected. The older mean age for the manic group (Table I) probably explains the significant differences with respect to duration of illness and number of previous admissions to hospital. The difference in mean scores on the Expanded Brief Psychiatric Rating Scale (BPRS; Lukoff *et al*, 1986) reflects the differences in cross-sectional symptoms between the two groups, particularly the presence of fewer symptoms in 'remitted' manics than in stable, or 'remitted', schizophrenics. The significant difference in the mean dose of antipsychotic medication, as measured by chlorpromazine equivalents, again probably reflects the greater propensity for schizophrenics to be maintained on an antipsychotic.

TABLE I
Sociodemographic data for subject groups

	Schizophrenics (n = 60)	*Manics (n = 20)*	*Controls (n = 34)*
Sex			
male	46	6	21
female	14	14	13
Age			
mean (s.d.)	32.0(9.1)	45.0(10.9)	29.0(10.6)
Marital status			
single	45	4	17
married	8	7	16
divorced/separated	7	9	1

Neuropsychological tests

All subjects were administered the full-scale Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981) and the WCST. In the latter, subjects are required to sort cards according to categories of colour, form or number. They are not informed of the target category. When a subject has sorted ten consecutive cards into the correct category, the nature of category is changed without informing the subject, who is told merely that a sort is correct or incorrect. Some versions of the WCST (e.g. Nelson, 1976) inform subjects when the sorting category is changed. We used the more standard version (Heaton, 1981).

We report WCST results in terms of 'categories completed', a measure of overall performance, and 'perseverative errors', a measure of perseveration or the inability to 'shift cognitive set', one of the putative functions of the pre-frontal cortex, especially its dorsolateral aspect (Fuster, 1989).

Results

Mean values for WAIS-R and WCST scores were compared for in-patient and out-patient schizophrenic and manic groups separately, using two-tail *t*-tests. After applying the Bonferroni correction (Godfrey, 1985), no significant differences were found for either diagnostic group. Accordingly, for subsequent analyses, results for in-patient and out-patient groups were combined.

As the control group comprised employed and unemployed subjects, WAIS-R and WCST results were compared for these two subgroups. The unemployed group recorded a significantly lower full-scale IQ than the employed group (91.9 v. 108.7, 32 d.f., $t = 3.82$, $P < 0.01$). There were no significant differences between the two groups with respect

TABLE II
Comparisons (two-tail t-tests) between the two patient groups for main clinical characteristics

Clinical characteristics	*Schizophrenics (n = 60)*	*Manics (n = 20)*	t	P
Age at onset: years (s.d.)	22.9(5.6)	29.1(8.2)	3.78	0.000
Duration of illness: years (s.d.)	9.6(9.4)	16.1(9.2)	2.65	0.01
Previous admissions: *n* (s.d.)	4.8(4.4)	9.6(7.5)	3.40	0.001
Expanded BPRS:[1] mean score (s.d.)	20.7(14.3)	8.7(10.2)	3.46	0.001
Chlorpromazine equivalents: mg (s.d.)	519.6(498.3)	84.5(120.6)	3.85	0.000

1. Expanded Brief Psychiatric Rating Scale (Lukoff *et al*, 1986).

https://doi.org/10.1192/bjp.157.1.50 Published online by Cambridge University Press

to WCST results ('categories completed': 5.8 v. 4.9, 31 d.f., $t=1.85$, $P<0.1$; 'perseverative errors': 15.1 v. 15.6, 31 d.f., $t=0.15$, $P>0.1$).

Group means, standard deviations, and one-way ANOVA results for the WCST results are presented in Table III. Significant group differences were present. Multiple range tests using the Scheffe procedure revealed that both schizophrenic and manic groups performed significantly ($P<0.01$) worse than the control group. There were no differences between the two patient groups.

A plot of individual scores for perseverative errors for the three groups is presented in Fig. 1. Heaton (1981) suggests optimal perseverative error score cut-offs of above 13 for predicting 'brain damage', and of above 16 for predicting 'focal frontal involvement'. Using these criteria, 'brain damage' would be predicted in 55 (91.6%) schizophrenics, 15 (75%) manics and 18 (52.9%) controls, and 'focal frontal involvement' in 53 (88.3%) schizophrenics, 15 (75%) manics and 16 (47.1%) controls.

Group means, standard deviations and one-way ANOVA results for all subtests and composite scores of the WAIS-R are presented in Table IV. Significant differences between the three groups were recorded for all subtests, and for the three composite scores (verbal, performance and full-scale IQ). Multiple range tests using the Scheffe procedure revealed that the schizophrenic group performed significantly worse than the control group on all scores except for object assembly ($P<0.05$ information, $P<0.01$ all other subtests). The manic group performed significantly worse than the control group on all performance IQ subtests except object assembly ($P<0.05$ picture completion, block design, $P<0.01$ picture arrangement, digit symbol), but there were no significant differences with respect to the composite measures of verbal, performance and full-scale IQs. The schizophrenic group performed significantly worse than the manic group on verbal, performance and full-scale IQs ($P<0.01$), but the only significant differences on subtest scores between the two patient groups occurred with respect to information ($P<0.05$) and vocabulary ($P<0.01$). It is to be remembered that the Scheffe procedure is a fairly conservative one.

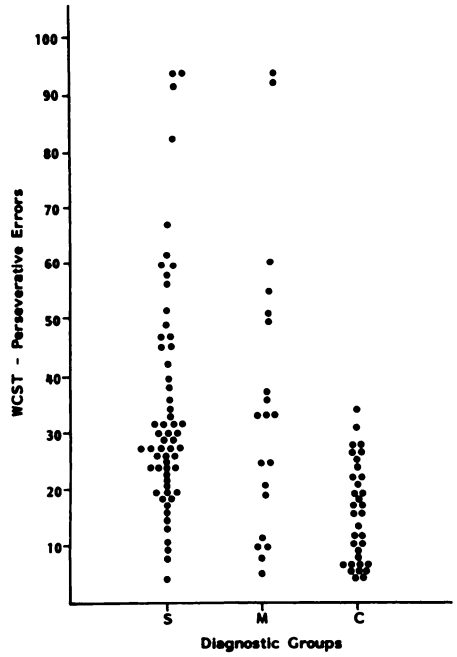


FIG. 1 Plot of individual WCST 'perseverative errors' scores for schizophrenic (S), manic (M) and control (C) subjects.

Discussion

These results confirm previous findings that schizophrenic subjects, as a group, perform poorly on the WCST. By recording high perseverative error scores, the schizophrenic subjects demonstrated relative degrees of cognitive inflexibility. Once a 'cognitive set' had been formed, they experienced difficulty in shifting to another set, despite being constantly informed that their current set was no longer correct.

This psychological function, the ability to shift cognitive set, is believed to be subserved by the pre-frontal cortex, especially the left dorsolateral cortex (Fuster, 1989). As such then, it could be postulated that schizophrenia involves (at least) a dysfunction of the left dorsolateral pre-frontal cortex, or of one of its neural circuits.

An unexpected finding to emerge from this research was an equivalent level of WCST performance in bipolar (manic) subjects, both in those recovering from an acute episode and in those in remission. Subjects with bipolar disorder also had difficulty with shifting cognitive set. This psychological dysfunction cannot therefore be considered specific to schizophrenia among the functional psychoses.

Doubt must also be raised as to the specificity of the left dorsolateral cortex for cognitive shift,

TABLE III

One-way ANOVA results for mean WCST scores recorded by schizophrenic, manic and control subjects

	Mean scores (s.d.)				
	Schizophrenics (n = 60)	*Manics (n = 20)*	*Controls (n = 34)*	F *ratio*	F *probability*
Categories completed	3.1(1.8)	3.3(2.3)	5.2(1.3)	14.93	0.0000
Perseverative errors	34.7(20.5)	35.0(25.3)	15.5(8.8)	12.22	0.0000

https://doi.org/10.1192/bjp.157.1.50 Published online by Cambridge University Press

TABLE IV
One-way ANOVA results for WAIS–R subtest and composite scores recorded by schizophrenic, manic, and control subjects

	Mean scores (s.d.)				
	Schizophrenics (n = 60)	*Manics (n = 20)*	*Controls (n = 34)*	F *ratio*	F *probability*
Verbal IQ subtest					
Information	8.4(3.2)	10.8(2.9)	10.4(2.9)	7.19	0.0012
Digit span	8.2(2.8)	9.2(2.3)	10.4(3.0)	6.53	0.0021
Vocabulary	7.8(3.4)	10.7(2.5)	10.4(3.3)	9.82	0.0001
Arithmetic	7.6(2.8)	9.4(2.9)	10.9(2.9)	14.95	0.0000
Comprehension	7.6(3.3)	9.5(3.2)	10.8(2.8)	11.64	0.0000
Similarities	7.2(3.0)	8.7(2.5)	10.4(3.2)	12.21	0.0000
Performance IQ subtest					
Picture completion	7.3(2.3)	8.4(2.3)	10.3(2.6)	16.02	0.0000
Picture arrangement	7.0(2.8)	8.7(2.7)	11.6(3.0)	28.20	0.0000
Block design	8.0(2.4)	8.2(2.7)	10.1(2.4)	8.56	0.0004
Object assembly	7.3(5.8)	8.3(2.8)	9.1(2.8)	4.44	0.0140
Digit symbol	5.7(1.7)	6.5(2.2)	9.3(2.7)	30.45	0.0000
Composite scores					
Verbal IQ	87.6(14.1)	99.9(13.9)	104.5(15.2)	16.58	0.0000
Performance IQ	83.0(10.8)	94.4(12.3)	101.7(12.1)	30.12	0.0000
Full-scale IQ	84.5(11.9)	97.3(12.2)	103.7(13.9)	27.11	0.0000

although this has never been claimed with conviction. Previous studies based on known lesions and using the WCST have failed to differentiate between left- and right-sided lesions (Milner, 1963). While there is no incontrovertible evidence for a focal right-hemisphere dysfunction in bipolar illness, some persuasive findings were offered by Flor-Henry & Yeudall (1979). The results from this current study would support a speculative interpretation that schizophrenia could be related to left pre-frontal dysfunction and bipolar illness (mania) to right pre-frontal dysfunction.

Perhaps even more surprising than the results for bipolar patients were those for non-psychiatric control subjects. While the mean score for the group was significantly below both the schizophrenic and manic groups, 18 (52.9%) scored above the cut-off of 13 perseverative errors suggested by Heaton (1981) as predictive of 'brain damage', and 16 (47.1%) scored above 16, suggested as predictive of 'focal frontal involvement'.

Heaton based his normative data on results from 150 paid volunteers. They recorded a mean perseverative error score of 12.6 (s.d. = 10.2). From these figures, obviously many of his normal subjects would have been above his cut-off scores.

Could general cognitive ability (intelligence) have influenced the WCST results? Certainly, there were IQ differences between the groups. However, manic subjects, with significantly higher IQs than schizophrenic subjects, recorded equivalently poor WCST results. And the lower-IQ control subgroup recorded WCST results similar to those for the higher-IQ control subgroup. General intelligence differences alone did not seem to explain the WCST differences.

Nor could they be understood in terms of medication effects. Manic subjects were receiving substantially lower doses of antipsychotic medication compared with schizophrenic subjects. If anything, especially in active psychosis, antipsychotic medication might be expected to improve neuropsychological test performance (Hymowitz & Spohn, 1980).

Conclusions

In summary, significant problems with respect to cognitive flexibility (the ability to shift cognitive set) existed in schizophrenic and bipolar (manic) patients. This psychological dysfunction potentially could have profound effects on the daily functioning of patients. There is substantial evidence from previous research that the ability to shift cognitive set is subserved, at least in part, by the pre-frontal cortex. Therefore, problems with cognitive flexibility suggest some level of dysfunction of the pre-frontal cortex in schizophrenia and bipolar illness. It is interesting to speculate that schizophrenia could be associated with dysfunction of the left pre-frontal cortex, and bipolar illness with dysfunction of the right pre-frontal cortex.

https://doi.org/10.1192/bjp.157.1.50 Published online by Cambridge University Press

The actual prevalence of dysfunction (either of the psychological process or of the pre-frontal cortex) must remain unresolved. If the currently recommended cut-off figures for the WCST are used (Heaton, 1981), high prevalence rates occur in schizophrenia and mania, but moderate rates also occur in non-psychiatric controls. More realistic cut-off figures may be obtained by adding one standard deviation to the mean scores obtained for the controls. In this study, the cut-off score for perseverative errors would thus become 24 (note that Heaton's equivalent cut-off would become 23). Using a cut-off of 24, two-thirds (67% and 65%) of schizophrenic and manic subjects and one-fifth (21%) of non-psychiatric controls could be regarded as demonstrating 'significant' cognitive inflexibility (and, putatively, pre-frontal dysfunction). Obviously, aetiology of the dysfunction may differ between groups.

The assessment of specific cognitive functions in schizophrenia and bipolar illness is assuming greater salience in treatment, as the roles of these functions in the tasks of daily living are being recognised, and, more particularly, as cognitive rehabilitation begins to form a therapeutic component in the management of the major psychoses (Brenner, 1987).

Acknowledgements

This study was supported by a grant from National Health and Medical Research Council of Australia. I am grateful to Sally Gulliver, Doreen Murrie, Melissa Monfries and Angela Cowan for data collection, and to Sally Gulliver, Mark Ryan and especially Barry Frost for constructive comments on earlier drafts of this paper.

References

American Psychiatric Association (1980) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn) (DSM-III). Washington, DC: APA.

Berg, E. A. (1948) A simple objective technique for measuring flexibility in thinking. *Journal of General Psychology*, **39**, 15–22.

Berman, K. F., Zec, R. F. & Weinberger, D. R. (1986) Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. II. Role of neuroleptic treatment, attention, and mental effort. *Archives of General Psychiatry*, **43**, 126–135.

Brenner, H. D. (1987) On the importance of cognitive disorders in treatment and rehabilitation. In *Psychosocial Treatment of Schizophrenia* (eds J. S. Strauss, W. Boker & H. D. Brenner). Bern: Hans Huber Publications.

Drewe, E. A. (1974) The effect of type and area of brain lesion on Wisconsin Card Sorting Test performance. *Cortex*, **10**, 159–170.

Fey, E. T. (1951) The performance of young schizophrenics and young normals on the Wisconsin Card Sorting Test. *Journal of Consulting Psychology*, **15**, 311–319.

Flor-Henry, P. & Yeudall, L. T. (1979) Neuropsychological investigations of schizophrenia and manic–depressive psychoses. In *Hemispheric Asymmetries of Function in Psychopathology* (eds J. H. Gruzelier & P. Flor-Henry). Amsterdam: Elsevier.

Fuster, J. M. (1989) *The Prefrontal Cortex* (2nd edn). New York: Raven Press.

Godfrey, K. (1985) Comparing the means of several groups. *New England Journal of Medicine*, **313**, 1450–1456.

Goldberg, T. E., Weinberger, D. R., Berman, K. F., *et al* (1987) Further evidence for dementia of the prefrontal type in schizophrenia? *Archives of General Psychiatry*, **44**, 1008–1014.

Heaton, R. K. (1981) *A Manual for the Wisconsin Card Sorting Test*. Odessa, Florida: Psychological Assessment Resources.

Hymowitz, P. & Spohn, H. (1980) The effects of anti-psychotic medication on the linguistic ability of schizophrenics. *Journal of Nervous and Mental Disease*, **168**, 287–296.

Kolb, B. & Whishaw, I. R. (1983) Performance of schizophrenic patients on tests sensitive to left or right frontal temporal, or parietal function in neurological patients. *Journal of Nervous and Mental Disease*, **171**, 435–443.

Lukoff, D., Nuechterlein, K. H. & Ventura, J. (1986) Manual for expanded Brief Psychiatric Rating Scale (BPRS). *Schizophrenia Bulletin*, **12**, 594–602.

Malmo, H. P. (1974) On frontal lobe functions: psychiatric patient controls. *Cortex*, **10**, 231–237.

Milner, B. (1963) Effects of different brain lesions on card sorting. *Archives of Neurology*, **9**, 90–100.

Nelson, H. E. (1976) A modified card sorting test sensitive to frontal lobe defects. *Cortex*, **12**, 313–324.

Robinson, A. L., Heaton, R. K., Lehman, R. A. W., *et al* (1980) The utility of the Wisconsin Card Sorting Test in detecting and localizing frontal lobe lesions. *Journal of Consulting and Clinical Psychology*, **48**, 605–614.

Robins, L. N., Helzer, J. E., Croughan, J., *et al* (1981) National Institute of Mental Health Diagnostic Interview Schedule (DIS). *Archives of General Psychiatry*, **38**, 381–389.

Tarter, R. E. & Parsons, O. A. (1971) Conceptual shifting in chronic alcoholics. *Journal of Abnormal Psychology*, **77**, 71–75.

Wechsler, D. (1981) *Wechsler Adult Intelligence Scale – Revised*. New York: Psychological Corporation.

Weinberger, D. R. (1987) Implications of normal brain development for the pathogenesis of schizophrenia. *Archives of General Psychiatry*, **44**, 660–669.

——, Berman, K. F. & Zec, R. F. (1986) Physiological dysfunction of dorsolateral prefrontal cortex in schizophrenia. I. Regional cerebral blood flow evidence. *Archives of General Psychiatry*, **43**, 114–124.

——, —— & Illowsky, B. P. (1988) Physiological dysfunction of dorsolateral prefrontal cortex in schizophrenia. III. A new cohort and evidence for a monoaminergic mechanism. *Archives of General Psychiatry*, **45**, 609–615.

*Rodney Morice, MD, FRANZCP, *Director, Hunter Area Mental Health Services, and Clinical Professor of Psychiatry, University of Newcastle*

*Correspondence: *c/o James Fletcher Hospital, PO Box 833, Newcastle, NSW, 2300, Australia*

https://doi.org/10.1192/bjp.157.1.50 Published online by Cambridge University Press