Psychological Medicine, 2001, **31**, 695–704. Printed in the United Kingdom

Verbal fluency in patients with schizophrenia and affective psychoses and their first-degree relatives

C. M. GILVARRY,[1] A. RUSSELL, P. JONES, P. SHAM, D. HEMSLEY AND R. M. MURRAY

From the Department of Psychological Medicine, Institute of Psychiatry, London

ABSTRACT

Background. Schizophrenic patients are known to have neuropsychological deficits including impaired verbal fluency, but it is not clear whether this latter deficit is: (*a*) a consequence of overall intellectual deficit; (*b*) shared with affective psychotic patients; or (*c*) shared by the relatives of schizophrenic patients; and (*d*) shared by the relatives of affective psychotic patients.

Methods. We administered Thurstone's Verbal Fluency Test to 45 schizophrenic patients and 72 of their relatives, and 30 affective psychotic patients and 53 of their relatives. Subjects were asked to generate as many words as possible beginning with the letters 'C' and 'S' and the total was taken as the dependent variable. Subjects also completed the National Adult Reading Test (NART) to provide a measure of (pre-morbid) IQ.

Results. Schizophrenic patients generated significantly fewer words than affective psychotic patients, however adjusting for NART this became non-significant. Schizophrenic (but not affective psychotic) patients generated significantly fewer words than their relatives; again adjusting for NART this became non-significant. Patients who had been exposed to obstetric complications (OC+) and those who had not (OC−) had similarly poor verbal fluency scores. Relatives of OC+ schizophrenic patients had superior verbal fluency than relatives of OC− schizophrenic patients and this remained significant after adjustment for NART.

Conclusions. The results suggest that some families transmit impairment in verbal fluency as part of a pattern of lower overall IQ. However, in other families, relatives show largely normal neuropsychological function, and the poorer verbal performance of the schizophrenic member appears to have arisen secondary to his/her exposure to OCs.

INTRODUCTION

There is an abundant literature indicating that patients with schizophrenia tend to have neuropsychological deficits (Saykin *et al.* 1991; Bilder, 1992; Hoff *et al.* 1992; Heaton *et al.* 1994; Gilvarry *et al.* 2000*a*). At least some of these deficits are present at the onset, or even prior to the onset, of the illness (Aylward *et al.* 1984; Hoff *et al.* 1992; Hutton *et al.* 1998), and often persist even after the florid manifestations of psychosis have remitted (Sweeney *et al.* 1991). There is considerable evidence that schizophrenic patients exhibit more neuropsychological impairment than affective psychotic patients (Kremen *et al.* 1998; Levy *et al.* 1983; Moldin *et al.* 1995). However, we (Gilvarry *et al.* 2000*b*) showed in a large sample of chronic community-care patients that schizophrenic and affective psychotic patients did not differ significantly in measures of pre-morbid IQ or executive ability. We concluded that among those patients who achieve the same level of chronicity, there are no significant differences in cognitive performance.

It is important therefore when seeking neuropsychological markers of genetic liability to

[1] Address for correspondence: Dr Catherine M. Gilvarry, Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London SE5 8AF.

schizophrenia, or affective psychosis, to rule out artefacts produced by failure to consider the possible impact of chronicity, stage of illness, age at onset and medication. Some researchers have attempted to avoid such potential confounding effects of the illness and its treatment by investigating the non-psychotic relatives of patients; any deficits found in relatives could be a reflection of a familial, possibly genetic, predisposition to schizophrenia. Subtle neuropsychological deficits have indeed been noted in relatives of schizophrenic patients (Cannon *et al*. 1994; Keefe *et al*. 1994; Kremen *et al*. 1994; Faraone *et al*. 1995). Furthermore, Moldin *et al*. (1995) and Kremen *et al*. (1998) showed relatives of schizophrenic patients to be significantly more neuropsychologically impaired than relatives of affective psychotic patients. However, while there have also been reports of neuropsychological deficits in the relatives of affective psychotic patients (Yurgelun-Todd, 1988; Morice, 1990) the evidence is conflicting.

Impairment of frontal lobe functioning is thought to be one of the characteristic features of schizophrenia (Gold & Harvey, 1993; Royall *et al*. 1993; Saykin *et al*. 1994). For example, patients with schizophrenia produce fewer words in verbal fluency tasks than control subjects (Allen & Frith, 1983; Kolb & Whishaw, 1983; Frith & Allen, 1988; Gruzelier *et al*. 1988; Crawford *et al*. 1993; Elliot & Shakian, 1995). The causes are uncertain, but might involve generation or initiation themselves, task specificity, novelty or the inability to inhibit perseverations (Stuss *et al*. 1994). If a subject produces only a few words, this could be a consequence of either a specific difficulty with a self-directed search process (impaired access) so that fewer words are retrieved, or corruption of semantic memory (degraded store) so that fewer words are available. Allen *et al*. (1993) concluded that schizophrenic patients have reduced access to semantic memory because of difficulties in organizing their search. Joyce *et al*. (1996) emphasized that verbal fluency is a test of both semantic memory and executive function, and concluded that impaired verbal fluency in schizophrenic patients is not secondary to an impoverished store of words, but rather reflects a failure to access the semantic store efficiently.

However, impaired verbal fluency could also be secondary to other features of schizophrenia or its treatment, i.e. chronicity, negative symptoms, neuroleptic medication. Furthermore, it is not known whether impaired verbal fluency is specific to schizophrenia or whether it is also found in affective psychosis. Finally, it remains unknown whether the impairment of verbal fluency found in people with schizophrenia is inherited, or is a consequence of some environmentally determined cerebral insult. Numerous reports have found an association between obstetric complications (OCs) and early onset of schizophrenia (Lewis & Murray, 1989; O'Callaghan *et al*. 1992; Geddes & Lawrie, 1995; Verdoux *et al*. 1997). In the general population, exposure to OCs and low birth weight are associated with compromised intellectual development (Aylward *et al*. 1989). In a previous study we showed that exposure to OCs did not have any significant impact on IQ in either schizophrenic or affective psychotic patients (Gilvarry *et al*. 2000*a*), however, to our knowledge, no investigations have been carried out into the effect of exposure to OCs on verbal fluency in schizophrenia.

We therefore set out to study verbal fluency in patients with schizophrenia and affective psychosis and their relatives. We hypothesized that: (1) schizophrenic patients would show a deficit in verbal fluency compared with affective psychotic patients; (2) both patient groups would show deficits compared with their relatives; (3) those patients exposed to OCs (OC+) would show greater deficits in verbal fluency than those not exposed to OCs (OC−); (4) the relatives of OC+ patients would show fewer deficits in verbal fluency than the relatives of OC− patients.

METHOD

Subjects

Patients

The patient sample comprised those patients recruited for the Camberwell Collaborative Psychosis Study (Jones *et al*. 1993; Sham *et al*. 1994; Van Os *et al*. 1994; Gilvarry *et al*. 1996; 2000*a*, *c*; Wright *et al*. 1996; Davies *et al*. 1997; Cannon *et al*. 1997; Marcelis *et al*. 1998). These patients were admitted to the Bethlem Royal and Maudsley Hospitals and Dulwich North Hospital with delusions, hallucinations or thought disorder according the definitions of the

https://doi.org/10.1017/S0033291701003816 Published online by Cambridge University Press

Research Diagnostic Criteria (RDC) (Spitzer *et al*. 1978*a*). Patients were interviewed within days of their admission using: the Present State Examination (PSE, 9th edition) (Wing *et al*. 1974) and diagnostic classification was made according to the RDC; and, the Negative Symptom Rating Scale (NSRS) (Iager *et al*. 1985) to assess negative symptoms. Patients were also asked to complete the National Adult Reading Test (NART) (Nelson, 1982) to provide a measure of pre-morbid IQ, and Thurstone's Verbal Fluency Test (TVFT) (Thurstone, 1938; Thurstone & Thurstone, 1949). Patients were divided into two groups: schizophrenic patients; and, affective psychotic patients (schizoaffective and manic/depressed). While schizoaffective patients are often categorized with both schizophrenic and manic/depressed patients, we categorized them with manic/depressed patients as they consistently show less cognitive abnormality than schizophrenic patients (Lindenmayer *et al*. 1989).

All patients recruited into the study were under 50 years of age and had to have a mother who was available for interview. Two of the patients recruited, both with a diagnosis of schizophrenia, came from the same family; the remaining patients came from different families. A measure of social class was derived from the Office of Population Consensus and Surveys (1991) *Classification of Occupations*. Subjects currently unemployed were coded by their previous occupation. All subjects were coded in a similar way: i.e. 1, professional; 2, intermediate; 3, skilled; 4, semiskilled; 5, unskilled/long-term unemployed.

Relatives

After discussion with the patients, permission was sought to contact other family members with a view to meeting with and also testing them. Where a contact address was available, we wrote to all relatives, explaining the study and requesting their participation. If permission was granted, a researcher met with the relatives at their own homes. The interviewer remained blind to proband diagnosis. Demographic data was collected from each relative and interviews consisted of a clinical assessment using the Schedule for Affective Disorders and Schizophrenia (SADS-L) (Spitzer *et al*. 1978*b*). Relatives were asked to complete the NART and the TVFT. In addition, details of obstetric complications (OCs) in the patients were collected from patients' mothers using the scale of Lewis *et al*. (1989).

We eliminated a total of 34 relatives who met the criteria for a psychotic illness (schizophrenia, bipolar disorder, psychotic depression, schizoaffective disorder and unspecified functional psychosis) either currently or at some time in the past. Thus, a total of 295 relatives were eligible to participate, of whom 125 completed the neuropsychological tests. Where English was not the first language, patients and relatives were not asked to complete the neuropsychological tests, otherwise the attrition rate was due to refusal on the part of subjects to complete the tests.

Thurstone world fluency test

Subjects were given 5 min to produce as many words as they could think of beginning with the letter 'S' and then 4 min to produce as many words as possible beginning with the letter 'C'. Words beginning with 'S' could be of any length, words beginning with 'C' were to be four letter words only. Subjects were asked to write down on paper the words they produced. Subjects were asked to exclude proper nouns, numbers and the same word with a different suffix (e.g. sit, sitting, sits) and were reminded of instructions when an error was made.

Analysis

Demographic characteristics were compared between patient and relative groups using χ^2 tests for categorical variables and analysis of variance (ANOVA) for continuous variables. For continuous outcomes, means and standard deviations summarize the data in each group. For categorical variables, proportions of subjects in each group with the particular characteristic are reported. Adjusted analyses were carried out using analysis of covariance (ANCOVA) and multiple regression models. The dependent variable was total words produced, i.e. 'C' words and 'S' words combined. We identified age at testing, age at first contact with psychiatric services, ethnicity, IQ and negative symptoms as potential confounding factors in the patient sample and the data were analysed adjusting for these variables. We did not identify any potential confounding factors

in the relatives sample apart from measures of IQ; however we adjusted for age at testing when analysing patient and relative groups together. We grouped patients into two categories according to whether they had or had not suffered OCs; (1) OC+(definite OCs) and (2) OC− (no OCs). Subjects with equivocal OC ratings were eliminated from the analyses as the number was so small. Subjects with missing data on any particular variable were omitted from analyses involving that variable.

RESULTS

Characteristics of patients and their relatives

Forty-five subjects fulfilled RDC criteria for schizophrenia (33 men and 12 women); 30 patients (20 male and 10 female) were given a diagnosis of affective psychosis i.e. schizo-affective disorder ($N = 10$, 8 male and 2 female) and manic/depressed patients ($N = 20$, 12 male and 8 female). Table 1 gives demographic details for both patient groups. There were significant differences between groups in age at testing, age at first contact with psychiatric services, ethnicity, pre-morbid IQ and negative symptoms. These were therefore adjusted for throughout in the analyses. Table 2 gives demographic details of the relative groups. There were no significant differences between relatives of schizophrenic and affective psychotic patients in proportions of mothers, fathers and siblings participating, ethnicity, social class or age at interview. However, relatives of affective psychotic patients had significantly higher IQ than relatives of schizophrenic patients ($P = 0{\cdot}004$).

Characteristics of patients – participants and non-participants

There was no significant difference in the proportion of schizophrenic (43%) or affective psychotic (39%) patients completing the tests ($P = 0{\cdot}57$). In addition, there was no significant differences between groups of participants and non-participants in age at first contact with psychiatric services, age at interview, ethnicity, social class, sex, negative symptoms or years of education. There was, however, a significant difference between groups in NART estimated pre-morbid IQ ($P = 0{\cdot}05$) with non-participants having significantly higher pre-morbid IQ (107·70) than participants (104·48). This difference was accounted for by the schizophrenic patient group among whom non-participants had a higher pre-morbid IQ (105·26) than participants (100·25) ($P = 0{\cdot}02$). There was no significant difference in pre-morbid IQ between affective psychotic participants (110·30) and non-participants (111·61).

Characteristics of relatives – participants and non-participants

Seventy-two relatives of schizophrenic patients (15·3%) and 53 relatives of affective psychotic patients (15·5%) completed the verbal fluency tests. A χ^2 test showed no significant difference in the proportion of relatives of schizophrenics and affective psychotic patients participating or not participating in the study ($P = 0{\cdot}02$). White relatives were more likely to complete the verbal fluency tests than non-white relatives ($P < 0{\cdot}0001$); this may be due in part to English

Table 1. *Demographic details of patients*

	Schizophrenic patients ($N = 45$)	Affective psychotic patients ($N = 30$)	P
Sex, Male:Female, N (%)	33:12 (73·3:26·7)	20:10 (66·7:33·3)	0·53
Age at testing, mean (S.D.)	25·97 (6·54)	30·93 (7·60)	0·004
Age at first contact, mean (S.D.)	21·35 (6·51)	24·70 (7·60)	0·04
Number of hospital admissions, mean (S.D.)	3·38 (3·58)	3·17 (3·23)	0·89
Ethnicity, N (%)			
Black	19 (42·2)	2 (6·7)	0·0007
White and Other	26 (57·8)	28 (93·3)	
Social class, N (%)			
1, 2 and 3	28 (62·2)	21 (75)	0·25
4 and 5	17 (37·8)	7 (25)	
Years of educational, mean (S.D.)	12·11 (2·59)	12·50 (2·96)	0·55
NART-based IQ, mean (S.D.)	100·25 (9·46)	110·30 (7·81)	< 0·0001
Negative symptoms, mean (S.D.)	20·02 (7·36)	14·00 (8·86)	0·002

https://doi.org/10.1017/S0033291701003816 Published online by Cambridge University Press

Table 2. *Demographic details of relatives*

	Relatives of		
	Schizophrenic patients ($N = 72$)	Affective psychotic patients ($N = 53$)	P
Sex, Male:Female, N (%)	29:43 (40·3:59·7)	24:29 (45·3:54·7)	0·57
Mothers, N (%)	25 (34·7)	18 (34·0)	0·99
Fathers, N (%)	17 (23·6)	13 (24·5)	
Siblings, N (%)	30 (41·7)	22 (41·5)	
Sex siblings, Male:Female, N (%)	12:18 (40:60)	11:11 (50:50)	0·47
Ethnicity, N (%)			
Black	10 (13·9)	4 (7·7)	0·28
White and Other	62 (86·1)	48 (92·3)	
Social class, N (%)			
1, 2 and 3	55 (87·3)	37 (78·7)	0·22
4 and 5	8 (12·7)	10 (21·3)	
Age at interview, mean (S.D.)	47·54 (15·78)	46·22 (18·49)	0·72
NART-based IQ, mean (S.D.)	110·60 (8·41)	115·19 (8·72)	0·004

Table 3. *Unadjusted Verbal Fluency Scores (with S.D. in parentheses) for patients and their relatives*

	Patients			Relatives of		
Words	Schizophrenic ($N = 45$)	Affective psychotic ($N = 30$)	P	Schizophrenic patients ($N = 72$)	Affective patients ($N = 53$)	P
'C'	8·64 (7·19)	14·00 (9·51)	0·007	12·91 (7·23)	15·32 (8·66)	0·09
'S'	27·51 (17·86)	39·96 (19·20)	0·005	35·18 (13·57)	38·84 (15·26)	0·15
Total	36·17 (24·23)	53·96 (27·79)	0·004	48·08 (19·27)	54·16 (22·46)	0·10

Table 4. *Unadjusted Verbal Fluency Scores (with S.D. in parentheses) for affective psychotic patients and their relatives*

	Patients			Relatives of		
Words	Schizoaffective ($N = 10$)	Manic/Dep. ($N = 20$)	P	Schizoaffective patients ($N = 22$)	Manic/Dep. patients ($N = 31$)	P
'C'	14·50 (8·43)	13·75 (10·20)	0·84	13·81 (8·09)	16·38 (9·02)	0·29
'S'	39·90 (17·86)	40·00 (20·29)	0·99	37·18 (14·82)	40·03 (15·69)	0·50
Total	54·40 (24·71)	53·75 (29·83)	0·95	51·00 (21·30)	56·41 (23·34)	0·39

not being the first language of some of the non-white group. Relatives from social classes 1, 2 and 3 were more likely to complete the tests than those from classes 4 and 5 ($P = 0·0003$). Significantly more women completed the tests than men ($P = 0·02$). Participating relatives of schizophrenics had significantly lower IQ (110·60) than non-participating (116·50) relatives ($P = 0·01$), but there was no significant difference in IQ between participating and non-participating relatives of affective psychotics. Finally, there was no significant difference in age at interview ($P = 0·57$) between participating and non-participating relatives.

Comparision of verbal fluency between patient groups

Unadjusted verbal fluency mean scores for schizophrenic and affective psychotic patients and their relatives are presented in Table 3, and for schizoaffective and manic/depressed patients and their relatives in Table 4. Schizophrenic

https://doi.org/10.1017/S0033291701003816 Published online by Cambridge University Press

Table 5. *Unadjusted Verbal Fluency Scores (with S.D. in parentheses) for OC− and OC+ schizophrenic patients and their relatives*

	Schizophrenic patients			Rels. of schizophrenic patients		
Words	OC− ($N = 19$)	OC+ ($N = 9$)	P	OC− ($N = 43$)	OC+ ($N = 9$)	P
'C'	8·57 (6·52)	8·33 (6·34)	0·92	11·83 (7·33)	18·33 (6·92)	0·01
'S'	29·47 (18·75)	23·44 (14·59)	0·40	33·18 (13·53)	52·77 (7·41)	< 0·0001
Total	38·05 (24·24)	31·77 (20·81)	0·51	45·00 (19·39)	71·11 (10·83)	< 0·0001

patients differed significantly from affective psychotic patients in verbal fluency ($F = 4·92$, df $= 1,68$, $P = 0·03$); parameter estimates obtained from the subsequent multiple regression analysis showed the adjusted estimated difference to be 14·60 (95% CI 1·47, 27·73). Repeating the analysis adjusting for IQ removed any significant difference between the groups ($F = 0·08$, df $= 1,65$, $P = 0·77$). Furthermore, when we repeated the analyses adjusting for negative symptoms there was no significant difference between patient groups ($F = 2·54$, df $= 1,65$, $P = 0·11$).

Comparison of verbal fluency between relative groups

A total of 72 relatives of schizophrenic patients (25 mothers, 17 fathers and 30 siblings), and 53 relatives of affective psychotic patients (18 mothers, 13 fathers and 22 siblings) completed the verbal fluency tests. There was no significant difference between relatives of schizophrenics and relatives of affective psychotic patients in verbal fluency ($F = 2·60$, df $= 1,104$, $P = 0·11$). There was, however, a significant difference between relatives of schizophrenics and relatives of manic/depressed patients ($F = 3·93$, df $= 1,85$, $P = 0·05$), estimated size of difference being 9·68 (95% CI 0·03, 19·39), but this difference did not survive adjustment for IQ. There was no significant difference between relatives of schizophrenics and schizoaffective patients ($F = 3·03$, df $= 1,82$, $P = 0·92$); nor was there any significant difference between relatives of schizoaffective and manic/depressed patients ($F = 0·20$, df $= 1,41$, $P = 0·65$).

Comparison of verbal fluency between patients and their relatives

Schizophrenic patients differed significantly from their relatives in verbal fluency ($F = 6·20$, df $= 1,101$, $P = 0·01$), estimated difference being 12·02 (95% CI 2·44, 21·60), but when we controlled for the potential confounding effects of IQ, this difference became non-significant. There was no significant difference between schizoaffective patients and their relatives ($F = 0·03$, df $= 1,25$, $P = 0·86$), or between manic/depressed patients and their relatives ($F = 3·31$, df $= 1,41$, $P = 0·71$).

Obstetric complications and verbal fluency in patients

Tables 5 and 6 show unadjusted mean verbal fluency scores for OC− and OC+ schizophrenic and affective psychotic patients and their relatives. Combining both patient groups there was no significant difference between OC+ and OC− patients ($F = 0·10$, df $= 1,40$, $P = 0·75$), further adjusting for IQ did not alter the non-significance of this finding ($F = 0·16$, df $= 1,36$, $P = 0·69$). There was no significant difference between OC+ and OC− schizophrenic patients before ($F = 0·03$, df $= 1,23$, $P = 0·85$), or after adjusting for IQ ($F = 0·15$, df $= 1,21$, $P = 0·70$). Finally, there was no significant difference between OC+ and OC− affective psychotic patients before ($F = 0·01$, df $= 1,14$, $P = 0·91$), or after ($F = 0·46$, df $= 1,13$, $P = 0·50$) adjusting for IQ.

Relatives of patients with and without obstetric complications

We then compared measures of verbal fluency among all relatives subdivided according to whether the proband was OC+ or OC−, and found no significant difference ($F = 1·02$, df $= 1,78$, $P = 0·31$). However, there was a significant difference between relatives of OC+ and OC− schizophrenic patients ($F = 13·10$, df $= 1,42$, $P < 0·001$), estimated difference being 26·54 (95% CI 11·74, 41·34), with relatives of OC+ patients generating more words. Furthermore, when we controlled for the potential confounding effect of IQ, differences remained

https://doi.org/10.1017/S0033291701003816 Published online by Cambridge University Press

Table 6. *Unadjusted Verbal Fluency Scores* (*with* S.D. *in parentheses*) *for OC− and OC+ affective psychotic patients and their relatives*

	Affective patients			Rels. of affective patients		
Words	OC− ($N = 10$)	OC+ ($N = 8$)	*P*	OC− ($N = 19$)	OC+ ($N = 14$)	*P*
'C'	15·90 (8·92)	12·87 (9·53)	0·49	18·05 (8·77)	13·85 (8·34)	0·17
'S'	40·20 (16·42)	43·87 (17·18)	0·65	44·42 (15·51)	37·21 (15·51)	0·19
Total	56·10 (24·63)	56·75 (25·16)	0·95	62·47 (23·02)	51·07 (22·74)	0·16

significant ($F = 4·73$, df = 1,40, $P = 0·03$), estimated differences being 14·48 (95% CI 1·02, 27·94). There was no significant difference between relatives of OC+ and OC− affective psychotic patients ($F = 2·58$, df = 1,26, $P = 0·12$).

DISCUSSION

Methodological issues

Before we discuss our findings, we must first address some methodological issues.

Our sample of psychotic patients had a relatively early onset. This was a direct consequence of our selection criteria which required that: (*a*) patients had to be less than 50 years of age; and, (*b*) have a mother available for interview. This early age of onset inevitably skewed the sample towards a higher male to female ratio, and it may also have selected a series of patients in whom neurodevelopmental factors were of particular importance. We included patients whose relatives did not participate in the study and this might have affected our results. However, when we compared patients whose relatives completed the verbal fluency tests with patients for whom we have no relative data, there was no significant difference in verbal fluency; furthermore, our results remained unchanged after patients for whom we have no relative data were eliminated.

Predictably, not all patients gave permission for us to interview their relatives, and not all relatives agreed to participate. Females, relatives from higher social classes, and white relatives were more likely to complete the verbal fluency tests. However, it is unlikely that these differences confounded our results since they were adjusted for throughout in the analyses.

Overall, the participating schizophrenic patients and their relatives had lower NART scores than non-participating schizophrenic patients and their relatives. It is difficult to account for this, as this pattern was not apparent in affective psychotic patients or their relatives. Plainly, as we have NART scores for these relatives, English was their first language, so this can only be accounted for by refusal of the relatives to participate. Again, it is difficult to interpret why those relatives with higher NART scores should refuse to complete the verbal fluency tests. The interview with both patients and their relatives was quite lengthy, it may be that those with higher NART scores felt more confident to terminate the interview early, although this can only be speculation. However, we did control for NART scores, and in so doing differences in verbal fluency between groups, almost without exception, became non-significant.

Interpretation

It is widely accepted that as a group, schizophrenic patients perform more poorly than normal individuals on virtually any neuropsychological task that is set for them. There is good evidence that schizophrenia is associated with intellectual deficit (Aylward *et al.* 1984; Nelson *et al.* 1990; Gilvarry *et al.* 2000*a*), and in some chronic cases this attains the level of severity seen in organic dementia (Owens & Johnstone, 1980). Therefore, care needs to be taken to ensure that when a particular neuropsychological impairment is found in schizophrenia, it is not merely a function of the overall tendency to poor performance, but it is present over and above any wider pattern of impairment.

It is clear that performance on verbal fluency tests is influenced by other variables such as verbal IQ, but Crawford *et al.* (1993) and Joyce *et al.* (1996) found that verbal fluency scores for schizophrenic patients were poorer than those predicted by their verbal intelligence, indicating a specific deficit in verbal fluency. Miller (1984)

https://doi.org/10.1017/S0033291701003816 Published online by Cambridge University Press

found that when they controlled for verbal intelligence, fluency still remained depressed in subjects with frontal lesions, but in patients with dementia, fluency scores were similar to those predicted from measures of verbal intelligence. This suggests that impaired fluency is a specific phenomenon following frontal lesions, but is merely a consequence of intellectual deterioration in dementia. In a previous study, using the same sample, (Gilvarry *et al.* 2000*a*) we showed that schizophrenic patients had lower IQ than both their relatives, and affective psychotic patients and the evidence here does not suggest that verbal fluency in schizophrenia is selectively impaired, as in patients with frontal lesions, but merely reflects a general intellectual deterioration. This pattern was reflected also in the relative groups i.e. relatives of manic/depressed patients generated significantly more words than relatives of schizophrenic patients, but after adjusting for IQ this became non-significant.

It is well established that negative symptoms are associated with poorer performance of patients on a variety of neuropsychological tests (Andreasen & Olsen, 1982; Roy & Devriendt, 1994; Capleton, 1996; Gilvarry *et al.* 2000*b*). Indeed, Hawkins *et al.* (1997) showed that while bipolar patients performed better than schizophrenic patients on cognitive tasks, this effect was much less marked when they were compared with schizophrenic patients without negative symptoms. Pantelis *et al.* (1989, 1992) suggested that slowness of thought processing may be part of a subcortical syndrome characterizing a subgroup of schizophrenic patients who exhibit negative symptoms. On the other hand, the presence of positive symptoms does not appear to correlate with neuropsychological deficits (Bilder *et al.* 1985; Liddle, 1987); indeed Nelson *et al.* (1990) found that patients with the lowest pre-morbid IQ had the least severe positive symptoms. Similarly, in our study controlling for the potential confounding effects of negative symptoms made the difference in verbal fluency between schizophrenic and affective psychotic patients become non-significant.

Faraone *et al.* (1999) showed that impairments in episodic memory and executive functioning are stable among the relatives of patients with schizophrenia, and this stability of neuropsychological impairment is consistent with reports of structural brain anomalies among the non-psychotic relatives of patients with schizophrenia (Seidman *et al.* 1997; Sharma *et al.* 1998), and suggests that both neuropsychological and brain structural findings are manifestations of the familial, presumed genetic, predisposition to schizophrenia. Our evidence supports this view at least for the families of OC− schizophrenic patients and we have previously shown that relatives of OC+ schizophrenic patients have significantly higher IQ than relatives of OC− schizophrenic patients (Gilvarry *et al.* 2000*a*). In fact relatives of OC+ schizophrenic patients do not have significantly different IQ than relatives of affective psychotic patients. We suggest, therefore, that relatives of OC− schizophrenic patients transmit slightly reduced general intellectual functioning including verbal fluency, and the impairment of premorbid IQ and verbal fluency which we found in the OC− schizophrenic patients appear to be a manifestation of this.

What then is the role of exposure to OCs? We found no significant difference in either NART scores (Gilvarry *et al.* 2000*a*) or in verbal fluency between schizophrenic patients who were exposed to OCs and those not exposed to OCs. Both groups showed similar deficits suggesting that these increase risk of schizophrenia no matter how they arise. However, there was a significant difference between the relatives of OC+ and OC− schizophrenic patients on measures of verbal fluency such that relatives of OC+ patients produced significantly more words than the relatives of OC− patients; this difference remained significant when we controlled for NART. Thus, it appears that the families of OC+ schizophrenic patients do not transmit any impairment of IQ or verbal fluency. Rather the neuropsychological deficits we found in the OC+ schizophrenic patients are a consequence of their exposure to OCs.

REFERENCES

Allen, H. A. & Frith, C. D. (1983). Selective retrieval and free emission of category exemplars in schizophrenia. *British Journal of Psychology* **74**, 481–490.

Allen, H. A., Liddle, P. F. & Frith, C. D. (1993). Negative features, retrieval processes and verbal fluency in schizophrenia. *British Journal of Psychiatry* **163**, 769–775.

Andreasen, N. C. & Olsen, S. (1982). Negative v. positive schizophrenia. *Archives of General Psychiatry* **39**, 789–794.

Aylward, E., Walker, E. & Bettes, B. (1984). Intelligence in schizophrenia: meta-analysis of the research. *Schizophrenia Bulletin* **10**, 430–459.

Aylward, G. P., Pfeiffer, S. L., Wright, A. & Verhulst, S. J. (1989). Outcome of studies of low birth weight infants published in the last decade: a meta-analysis. *Journal of Pediatrics* **115**, 515–520.

Bilder, R. M. (1992). Structure-function relations in schizophrenia: brain morphology and neuropsychology. In *Progress in Experimental Personality and Psychopathology Research. Vol. 15* (ed. E. F. Walker, R. H. Dworkin and B. A. Cornblatt), pp. 183–251. Springer: New York.

Bilder, R. M., Mukherjee, S., Rieder, R. O. & Pandurangi, A. K. (1985). Symptomatic and neuropsychological components of defect states. *Schizophrenia Bulletin* **11**, 409–419.

Cannon, M., Jones, P., Gilvarry, C., Rifkin, L., McKenzie, K., Foerster, A. & Murray, R. M. (1997). Premorbid social functioning in schizophrenia and bipolar disorder. Similarities and differences. *American Journal of Psychiatry* **154**, 1544–1550.

Cannon, T. D., Zorrilla, L. E., Shtasel, D., Gur, R. E., Gur, R. C., Marco, E. J., Moberg, P. & Price, A. (1994). Neuropsychological functioning in siblings discordant for schizophrenia and healthy volunteers. *Archives of General Psychiatry* **51**, 651–661.

Capleton, R. A. (1996). Cognitive function in schizophrenia: association with negative and positive symptoms. *Psychological Reports* **78**, 123–128.

Crawford, J. R., Obonsawin, M. C. & Bremner, M. (1993). Frontal lobe impairment in schizophrenia: relationship to intellectual functioning. *Psychological Medicine* **23**, 787–790.

Davies, N. J., Sham, P. C., Gilvarry, C., Jones, P. B. & Murray, R. M. (1997). Comparison of the family history with the family study method: report from the Camberwell Collaborative Psychosis Study. *American Journal of Medical Genetics and Neuropsychiatry Genetics* **74**, 12–17.

Elliot, R. & Shakian, B. (1995). The neuropsychology of schizophrenia: relations with clinical and neurobiological dimensions. *Psychological Medicine* **25**, 581–594.

Faraone, S. V., Seidman, L. J., Kremen, W. S., Pepple, J. R., Lyons, M. J. & Tsuang, M. T. (1995). Neuropsychological functioning among the non-psychotic relatives of schizophrenic patients: a diagnostic efficiency analysis. *Journal of Abnormal Psychology* **104**, 286–304.

Faraone, S. V., Seidman, L. J., Kremen, W. S., Toomey, R., Pepple, J. R. & Tsuang, M. T. (1999). Neuropsychological functioning among the nonpsychotic relatives of schizophrenic patients: a 4 year follow up study. *Journal of Abnormal Psychology* **108**, 176–181.

Frith, C. D. & Allen, H. A. (1988). Language disorders in schizophrenia and their implications for neuropsychology. In *Schizophrenia: The Major Issues* (ed. P. Bebbington and P. McGuffin), pp. 172–186. Heinemann Medical: Oxford.

Geddes, J. R. & Lawrie, S. M. (1995). Obstetric complications and schizophrenia: a meta-analysis. *British Journal of Psychiatry* **167**, 786–793.

Gilvarry, C. M., Sham, P. C., Jones, P. B., Cannon, M., Wright, P., Lewis, S. W., Bebbington, P., Toone, B. & Murray, R. M. (1996). Family history of autoimmune diseases in psychosis. *Schizophrenia Research* **19**, 33–40.

Gilvarry, C. M., Takei, N., Russell, A., Rushe, T., Hemsley, D. & Murray, R. M. (2000*a*). Premorbid IQ in patients with functional psychosis and their first-degree relatives. *Schizophrenia Research* **41**, 417–429.

Gilvarry, C. M., Barber, J. A. & Murray, R. M. (2000*b*). Neuropsychological performance of psychotic patients in community care: Results from the UK700 Study. *Acta Psychiatrica Scandinavica* (in the press).

Gilvarry, C. M., Russell, A., Hemsley, D. & Murray, R. M. (2000*c*). Trail making test performance in the first degree relatives of schizophrenic and affective psychotic patients. *Cognitive Neuropsychiatry* **5**, 219–234.

Gold, J. M. & Harvey, P. D. (1993). Cognitive deficits in schizophrenia. *Psychiatric Clinics of North America* **16**, 295–312.

Gruzelier, J., Seymour, K., Wilson, L., Jolley, A. & Hirsch, S. (1988). Impairments of neuropsychological tests of temporohippocampal and frontohippocampal functions and word fluency in remitting schizophrenia and affective disorders. *Archives of General Psychiatry* **45**, 623–629.

Hawkins, K. A., Hoffman, R. E., Quinlan, D. M., Rakfeldt, J., Docherty, N. M. & Sledge, W. H. (1997). Cognition, negative symptoms and diagnosis: a comparison of schizophrenic, bipolar and control samples. *Journal of Neuropsychiatry and Clinical Neurosciences* **9**, 81–89.

Heaton, R., Paulsen, J. S., McAdams, L. A., Kuck, J., Zosook, S., Braff, D., Harris, J. J. & Jeste, D. V. (1994). Neuropsychological deficits in schizophrenics. Relationship to age, chronicity and dementia. *Archives of General Psychiatry* **51**, 469–476.

Hoff, A. L., Riordan, H., O'Donnell, D., Stritzke, P., Neale, C., Boccio, A., Anand, A. K. & DeLisi, L. E. (1992). Anomalous lateral sulcus asymmetry and cognitive function in first-episode schizophrenia. *Schizophrenia Bulletin* **18**, 257–270.

Hutton, S. B., Puri, B. K., Duncan, L-J., Robbins, T. W., Barnes, T. R. E. & Joyce, E. M. (1998). Executive function in first episode schizophrenia. *Psychological Medicine* **28**, 463–473.

Iager, A. C., Kirch, D. G. & Wyatt, R. J. (1985). A negative symptom rating scale. *Psychiatry Research* **16**, 27–36.

Jones, P. B., Bebbington, P., Forester, A., Lewis, S. W., Murray, R. M., Russell, A., Sham, P., Toone, B. K. & Wilkins, S. (1993). Premorbid social underachievement in schizophrenia. Results from the Camberwell Collaborative Psychosis Study. *British Journal of Psychiatry* **162**, 65–71.

Joyce, E. M., Collinson, S. L. & Crichton, P. (1996). Verbal fluency in schizophrenia: relationship with executive function, semantic memory and clinical alogia. *Psychological Medicine* **26**, 39–49.

Keefe, R. S., Silverman, J. M., Lees Roitman, S. E., Harvey, P. D., Duncan, M. A., Alroy, D., Siever, L. J., Davis, K. L. & Mohs, R. C. (1994). Performance of non-psychotic relatives of schizophrenics on cognitive tests. *Psychiatry Research* **53**, 1–12.

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

Kremen, W. S., Seidman, L. J., Pepple, J. R., Lyons, M. J., Tsuang, M. T. & Faraone, S. V. (1994). Neuropsychological risk indicators for schizophrenia: a review of family studies. *Schizophrenia Bulletin* **20**, 103–119.

Kremen, W. S., Faraone, S. V., Seidman, L. J., Pepple, J. R. & Tsuang, M. T. (1998). Neuropsychological risk indicators for schizophrenia: a preliminary study of female relatives of schizophrenic and bipolar probands. *Psychiatry Research* **79**, 227–240.

Levy, D. L., Yasiollo, N. J., Janicak, P. G., Gaviria, M. & Dais, J. M. (1983). Relatives of unipolar and bipolar patients have normal pursuit. *Psychiatry Research* **10**, 285–293.

Lewis, S. W. & Murray, R. M. (1989). Obstetric complications, neurodevelopmental deviance, and risk of schizophrenia. *Journal of Psychiatric Research* **21**, 413–421.

Lewis, S. W. Owens, M. J. & Murray, R. M. (1989). Obstetric complications and schizophrenia: methodology and mechanisms. In *Schizophrenia: Scientific Progress* (ed. S. C. Schulz and C. A. Tamminga), pp. 56–68. Oxford University Press: New York.

Liddle, P. F. (1987). Schizophrenic syndromes, cognitive performance and neurological dysfunction. *Psychological Medicine* **16**, 49–57.

Lindenmayer, J-P., Kay, S. R. & Van Pragg, H. (1989). Distinction of schizoaffective from schizophrenic profile: independent validation. *Schizophrenia Research* **2**, 423–424.

Marcelis, M., Van Os, J., Sham, P., Jones, P., Gilvarry, C., Cannon, M., McKenzie, K. & Murray, R. M. (1998). Obstetric complications and familial morbid risk of psychiatric disorders. *American Journal of Medical Genetics and Neuropsychiatry Genetics* **82**, 29–36.

Miller, E. (1984). Verbal fluency as a function of a measure of verbal intelligence and in relation to different types of cerebral pathology. *British Journal of Clinical Psychology* **23**, 53–57.

Moldin, S. O., Newcomer, J. W., Richter, J. S. & Boyd, D. C. (1995). Familial aggregation of memory and attentional deficits in schizophrenia. *Schizophrenia Research* **15**, 43.

Morice, R. (1990). Cognitive inflexibility and pre-frontal dysfunction in schizophrenia and mania. *British Journal of Psychiatry* **157**, 50–54.

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

Nelson, H. E., Pantelis, C., Carruthers, K., Speller, J., Baxendale, S. & Barnes, T. (1990). Cognitive functioning and symptomatology in chronic schizophrenia. *Psychological Medicine* **20**, 357–365.

O'Callaghan, E., Gibson, T., Cohohan, H. A., Buckley, P., Walsh, D. G., Larkin, C. & Waddington, J. L. (1992). Risk of schizophrenia in adults born after obstetric complications and their association with early onset of illness: a controlled study. *British Medical Journal* **21**, 1256–1259.

Office of Population Consensus and Surveys (1991). *Classification of Occupations. Standard Occupational Classification* (*SOC*). HMSO: London.

Owens, D. G. C. & Johnson, E. C. (1980). The disabilities of chronic schizophrenia: their nature and the factors contributing to their development. *British Journal of Psychiatry* **136**, 384–393.

Pantelis, C., Barnes, T. R. & Nelson, H. E. (1989). A pilot study of subcortical dementia in schizophrenia. *Schizophrenia Research* **2**, 69.

Pantelis, C., Barnes, T. R. & Nelson, H. E. (1992). Is the concept of subcortical dementia relevant to schizophrenia? *British Journal of Psychiatry* **160**, 442–460.

Roy, M. A. & Devriendt, X. (1994). Positive and negative symptoms in schizophrenia: a current overview. *Canadian Journal of Psychiatry* **39**, 407–414.

Royall, D. R., Mahurin, R. K., True, J. E., Anderson, B., Brock, I. P., Freeburger, L. & Miller, A. (1993). Executive impairments among the functionally dependent: comparisons between schizophrenic and elderly subjects. *American Journal of Psychiatry* **150**, 1813–1819.

Saykin, A. J., Gur, R. C., Gur, R. E., Mozley, P. D., Mozley, L. H., Resnick, S. M., Kester, B. & Stafiniak, P. (1991). Neuropsychological function in schizophrenia; selective impairment in memory and learning. *Archives of General Psychiatry* **48**, 618–624.

Saykin, A. J., Shtasel, D. L., Gur, R. E., Kester, D. B., Mozley, L. H., Stafiniak, P. & Gur, R. C. (1994). Neuropsychological deficits in neuroleptic naïve patients with first-episode schizophrenia. *Archives of General Psychiatry* **51**, 124–131.

Seidman, L. J., Faraone, S. V., Goldstein, J. M., Goodman, J. M., Kremen, W. S., Matsuda, G., Hoge, E. A., Kennedy, D. N., Makris, N., Caviness, V. S. & Tsuang, M. T. (1997). Reduced subcortical brain volumes in nonpsychotic siblings of schizophrenic patients: a pilot MRI study. *American Journal of Medical Genetics and Neuropsychiatric Genetics* **74**, 507–514.

Sham, P. C., Jones, P., Russell, A., Gilvarry, C., Bebbington, P., Lewis, S., Toone, B. & Murray, R. M. (1994). Age at onset, sex, and familial psychiatric morbidity in schizophrenia. Camberwell Collaborative Psychosis Study. *British Journal of Psychiatry* **165**, 466–473.

Sharma, T., Lancaster, E., Lee, D., Lewis, S., Sigmundsson, T., Takei, N., Gurling, H., Barta, P., Pearlson, G. & Murray, R. (1998). Brain changes in schizophrenia. Volumetric MRI study of families multiply affected with schizophrenia – The Maudsley Family Study 5. *British Journal of Psychiatry* **173**, 132–138.

Spitzer, R. L., Endicott, J. & Robins, E. (1978*a*). *Research Diagnostic Criteria* (*RDC*) *for a Selected Group of Functional Disorders*, *3rd edn*. Biometrics Research Division, New York State Psychiatric Institute: New York.

Spitzer, R. L., Endicott, J. & Robins, E. (1978*b*). *Schedule for Affective Disorders and Schizophrenia – Lifetime Version* (*SADS-L*). New York State Psychiatric Institute: New York.

Stuss, D. T., Eskes, G. A. & Foster, J. K. (1994). Experimental neuropsychological studies of frontal lobe functions. In *Handbook of Neuropsychology* (ed. F. Boller and J. Grafman, J.), pp. 149–185. Elsevier Science: Amsterdam.

Sweeney, J. A., Hass, G. L., Keilp, J. G. & Long, M. (1991). Evaluation of the stability of neuropsychological functioning after acute episodes of schizophrenia: one-year follow-up study. *Psychiatry Research* **38**, 63–76.

Thurstone, L. L. (1938). *Primary Mental Abilities*. University of Chicago Press: Chicago.

Thurstone, L. L. & Thurstone, T. (1949). *Examiner Manual for the SRA Primary Mental Abilities Test*. Science Research Associates: Chicago.

Van Os, J., Fahy, T. A., Bebbington, P., Lewis, S., Toone, B. & Murray, R. M. (1994). The influence of life events on the subsequent course of psychotic illness. A prospective follow-up of the Camberwell Collaborative Psychosis Study. *Psychological Medicine* **24**, 503–513.

Verdoux, H., Geddes, J. R., Takei, N., Lawrie, S. M., Bovet, P., Eagles, J. M., Heun, R., McCreadie, R. G., McNeil, T. F., O'Callaghan, E., Stober, G., Willinger, U., Wright, P. & Murray, R. M. (1997). OCs and age at onset in schizophrenia: an international collaborative meta-analysis of individual patient data. *American Journal of Psychiatry* **154**, 1220–1227.

Wing, J. K., Cooper, J. E. & Sartorius, N. (1974). *Measurement and Classification of Psychiatric Symptoms*. Cambridge University Press: Cambridge.

Wright, P., Sham, P. C., Gilvarry, C. M., Jones, P. B., Cannon, M., Sharma, T. & Murray, R. M. (1996). Autoimmune disease in the pedigrees of schizophrenic and control subjects. *Schizophrenia Research* **20**, 261–267.

Yurgelun-Todd, D., Craft, S., O'Brian, C., Kaplan, E. & Levin, S. (1988). Wisconsin Card Sort in schizophrenia and manic depressive illness. *Journal of Clinical and Experimental Neuropsychology* **10**, 71.