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Executive function in first-episode schizophrenia

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ABSTRACT

Background. We tested the hypothesis that schizophrenia is primarily a frontostriatal disorder by examining executive function in first-episode patients. Previous studies have shown either equal decrements in many cognitive domains or specific deficits in memory. Such studies have grouped test results or have used few executive measures, thus, possibly losing information. We, therefore, measured a range of executive ability with tests known to be sensitive to frontal lobe function.

Methods. Thirty first-episode schizophrenic patients and 30 normal volunteers, matched for age and NART IQ, were tested on computerized test of planning, spatial working memory and attentional set shifting from the Cambridge Automated Neuropsychological Test Battery. Computerized and traditional tests of memory were also administered for comparison.

Results. Patients were worse on all tests but the profile was non-uniform. A componential analysis indicated that the patients were characterized by a poor ability to think ahead and organize responses but an intact ability to switch attention and inhibit prepotent responses. Patients also demonstrated poor memory, especially for free recall of a story and associate learning of unrelated word pairs.

Conclusions. In contradistinction to previous studies, schizophrenic patients do have profound executive impairments at the beginning of the illness. However, these concern planning and strategy use rather than attentional set shifting, which is generally unimpaired. Previous findings in more chronic patients, of severe attentional set shifting impairment, suggest that executive cognitive deficits are progressive during the course of schizophrenia. The finding of severe mnemonic impairment at first episode suggests that cognitive deficits are not restricted to one cognitive domain.

INTRODUCTION

The precise characterization of the neuropsychological deficits associated with schizophrenia is important for both theoretical and clinical reasons. For example, the delineation of aberrant cognitive processes will contribute to an understanding of the neurobiological basis of the disorder and also to the planning of rehabilitation aimed at reducing the long-term

social consequences of the illness. Thus, the neuropsychological deficits associated with schizophrenia have been investigated extensively (see Levin *et al.* 1989; Elliott & Sahakian, 1995). Several studies have described global performance deficits (e.g. Kolb & Wishaw, 1983; Liddle & Crow, 1984; Braff *et al.* 1991). Others have shown selective deficits over and above general impairment but opinion is divided as to whether this concerns executive function (Shallice *et al.* 1991; Morrison-Stewart *et al.* 1992; Elliott *et al.* 1995) or memory (Saykin *et al.* 1991; Gold *et al.* 1992; Tamlyn *et al.* 1992). One possible reason for these discrepancies is the heterogeneity of

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chronic schizophrenic patients who vary in illness duration. To circumvent this possible confusion, studies have examined patients presenting with their first psychotic episode (Bilder *et al.* 1992; Hoff *et al.* 1992; Saykin *et al.* 1994; Rubin *et al.* 1995; Albus *et al.* 1996). Unfortunately, these results have mirrored those with chronic schizophrenia in that both uniform (Bilder *et al.* 1992; Hoff *et al.* 1992) and specific (Saykin *et al.* 1994; Rubin *et al.* 1995; Albus *et al.* 1996) deficits have been found. One explanation of why there is no consensus as to the critical cognitive deficits concerns the methodology employed in these studies. Large batteries of clinical tests measuring a wide range of neuropsychological functions have been used and many have additionally derived global indices of function thereby possibly losing important information. In the present study, we used a different approach by selecting only a few tests and decomposing performance to elucidate fundamental cognitive abnormalities. We adopted the hypothesis that cognitive deficits in schizophrenia are due to frontostriatal dysfunction (Robbins, 1990) and therefore focused on tests of executive function, although memory tests were included for comparison. Thirty first-episode schizophrenic patients who had been receiving medication for a few weeks only were studied. We chose to test the patients once the acute symptoms had abated with medication to allow testing of as representative a sample of the population as possible, including patients who were unable to cooperate when unmedicated due to the severity of their symptoms.

METHOD

Subjects

Thirty patients with DSM-IV schizophreniform disorder or schizophrenia presenting for the first time to the psychiatric services of two National Health Trusts in West London were studied. They were recruited during the first year of an ongoing longitudinal study into the neurobiology of first-episode schizophrenia. All but two patients were tested while taking antipsychotic medications at a time when they were able to cooperate with testing as judged by their clinician. Twenty-two patients were tested within 8 weeks of starting medication and six within 6

months. The 30 control subjects were healthy volunteers living in the same community.

Neuropsychological tests

All subjects were administered the National Adult Reading Test (NART, Nelson, 1976) to determine pre-morbid IQ for group matching. Several traditional neuropsychological tests were employed to enable direct comparison with other first-episode studies: letter (FAS) and category (animals, occupations, fruits) fluency in which words are produced for each exemplar in 60 seconds; two subtests of the Wechsler Memory Scale-Revised (Wechsler, 1987), Logical Memory, requiring recall of two short stories, and Paired Associate Learning, requiring the learning of eight word pairs—four easy (e.g. Baby-Cries) and four difficult (e.g. Crush-Dark). Subtests of the Cambridge Neuropsychological Test Automated Battery (CANTAB), a series of computerized tests run on an IBM compatible PC with a touch sensitive screen (Sahakian & Owen, 1992), were also administered.

Spatial span (Owen *et al.* 1990)

This is a measure of a subject's ability to remember the order in which a sequence of squares, increasing in number, are highlighted on the screen.

Spatial and pattern recognition memory (Sahakian *et al.* 1988)

In the spatial recognition task, five identical squares are presented in series each in a different location. One square is then presented at each target location along with a square at a novel location. Subjects are asked to touch the square at the location they recognize from the learning phase. There are three further trials at different locations. In the pattern recognition test, 12 abstract visual stimuli are presented sequentially on the screen. Each stimulus is then presented with a novel stimulus and the subject is asked to touch the familiar stimulus. This is repeated with 12 different stimuli.

Spatial working memory (Owen *et al.* 1990)

Subjects are required to search through a number of boxes for hidden tokens. Trials differ in difficulty according to the number of boxes (3, 4,

6 and 8). On each trial only one box contains a token. The key instruction is that once a token has been found, that box will not be used to hide a token again. There are two types of error. A subject might return to open a box in which a token has already been found – a between-search error reflecting memory for token location. A subject might also return to a box already opened in the same search sequence – a within-search error reflecting memory for recent responses. An efficient strategy for performing this task is to follow a predetermined search sequence, beginning with one box and returning to start each new search with that box after a token has been found. A measure was taken of the use of this strategy by counting the number of search sequences starting with the same box at the 6- and 8-box stages.

Planning (Owen *et al.* 1990)

This is a modification of the Tower of London task (Shallice, 1982). Subjects are required to move coloured 'balls' in an arrangement displayed on the bottom half of the screen to match a goal arrangement displayed on the top half of the screen. Problems differ in difficulty by requiring a minimum of 2, 3, 4 or 5 moves. Subjects are asked to study the position of the balls and attempt the solution in the minimum number of moves. For each problem a yoked control condition is employed to provide measures of motor initiation and motor execution times. Here subjects follow a sequence of single moves executed by the computer in the top half of the screen, by moving the corresponding ball in the bottom half of the screen. Accuracy measures were: (i) problems solved in the minimum number of moves (perfect solutions); (ii) mean number of moves above the minimum possible (excess moves); and (iii) problems solved within the maximum permitted number of moves. Performance latency measures were: (i) initial thinking time, derived by subtracting the time taken to complete the first move of each problem during the control phase from that of the planning phase; and (ii) subsequent thinking time per move, derived by subtracting the time to complete the task after the first move during the control phase from that of the planning phase, divided by the number of moves taken for each problem. In the

rare cases where the calculations resulted in negative values, they were replaced by zero.

Attentional set shifting (Owen *et al.* 1991)

Using feedback provided by the computer, subjects are required to learn a series of visual discriminations in which one of two stimulus dimensions is correct or relevant and the other is not. At two critical points subjects are required first to maintain attention to different examples within the same dimension (intradimensional shift – IDS) and then to shift attention to the previously irrelevant dimension (extra-dimensional shift – EDS). For each stage, continuation on to the next stage is dependent on six successive correct responses being made. If this criterion is not reached after 50 trials the test is terminated automatically by the computer.

Statistical analysis

Latency data were log transformed to reduce skew. Analysis of variance (ANOVA) was performed using the Statistical Program for Social Sciences (SPSS). For most of the test variables the ANOVA model was a mixed two-factor design, with group as the between-subject factor, and difficulty level as the within-subject factor. For the attentional set shifting task, the numbers of subjects and controls passing or failing each stage were cast into contingency tables, and analysed using a likelihood ratio method (Kullback, 1959; Robbins, 1977). The resulting *2i* statistic is distributed as chi-squared.

RESULTS

Subjects

Table 1 shows the characteristics of the two groups. As the gender distribution was not even, preliminary analyses were performed on the

Table 1. Group number, gender ratio and group means (range) for age and NART IQ

	Schizophrenic patients	Normal volunteers
<i>N</i>	30	30
Gender (M/F)	23/7	15/15
Age (years)	27.77 (17–47)	26.1 (19–37)
Verbal IQ (NART)	109.53 (99–123)	110.87 (99–121)

control data to determine whether there were any detectable gender differences in performance. This was negative in line with other reports of no, or relatively few, gender effects on

neuropsychological performance (Lezak, 1983; Robbins *et al.* 1994; Anon, 1996). Fourteen patients were receiving regular anticholinergics (13) or benzodiazepines (1) in addition to antipsychotics. Since these drugs can affect cognitive function (see King & Green, 1996), these patients were compared with the rest on test performance. No differences were found and the patient data were pooled.

Table 2. Group means (standard error of mean) and significance of difference for neuropsychological variables

Neuropsychological test	Normal volunteers	Schizophrenic patients	P
Recognition memory			
Pattern recognition (prop. correct)	0.92 (0.02)	0.83 (0.03)	< 0.05
Spatial recognition (prop. correct)	0.75 (0.02)	0.67 (0.03)	< 0.01
Latency for correct resps (ms)	2415.07 (6.60)	2556.12 (9.34)	NS
Spatial span	6.37 (1.16)	5.43 (0.99)	< 0.01
Spatial working memory			
Strategy score	29.70 (0.98)	36.60 (0.85)	< 0.001
Planning			
Perfect solutions	9.40 (0.32)	7.03 (0.34)	< 0.0001
Total solutions	11.17 (0.15)	10.30 (0.29)	< 0.01
Attentional set shift			
Trials to criterion at IDS + EDS	11.23 (1.14)	12.73 (1.86)	< 0.05
Verbal fluency			
Category	69.33 (2.63)	53.08 (2.20)	< 0.001
Letter	46.58 (2.39)	36.79 (2.14)	< 0.001
Wechsler Memory Scale - R			
Logical memory	24.88 (1.20)	15.15 (1.18)	< 0.0001
Paired associates - easy	11.32 (0.18)	9.52 (0.32)	< 0.01
Paired associates - difficult	10.48 (0.27)	6.19 (0.65)	< 0.0001

Spatial span, pattern and spatial recognition memory

Spatial span was mildly but significantly reduced in the schizophrenic group (Table 2, $t(58) = 2.67$, $P = 0.01$). For pattern and spatial recognition memory, scores were available for 27 controls and 29 patients. Table 2 shows that schizophrenic patients were significantly worse than controls for both pattern ($t(54) = 2.16$, $P < 0.05$), and spatial ($t(54) = 3.16$, $P < 0.01$) recognition. There were no differences in latency.

Spatial working memory

Within-search errors were negligible. The patient group made significantly more between-search errors than controls (Fig. 1, $F(1, 58) = 19.34$, $P < 0.001$). There was a significant interaction between difficulty and group ($F(3, 174) = 10.28$, $P < 0.01$) patients making more errors only at 6 and 8 box levels ($F(1, 58) = 17.41$ and 12.91 , $P < 0.001$). Table 2 shows the strategy scores; a higher score represents poorer strategy use. Patients used this strategy less than controls

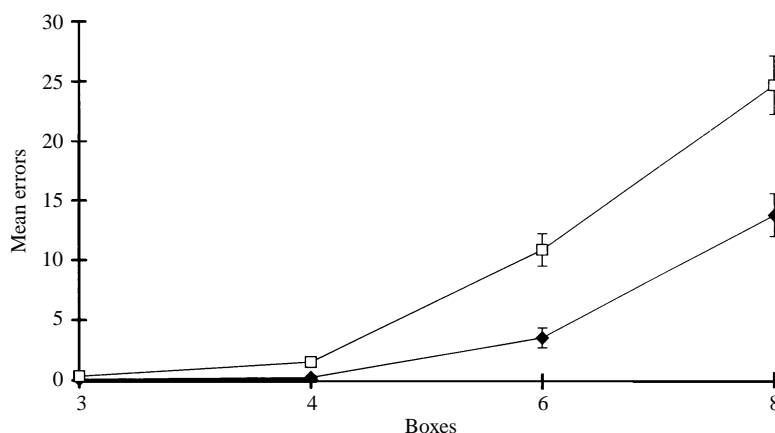


Fig. 1. Mean between-search errors on the spatial working memory task for schizophrenic patients (□) and controls (◆) for each level of difficulty (boxes). Error bars represent standard error of the mean (S.E.M.).

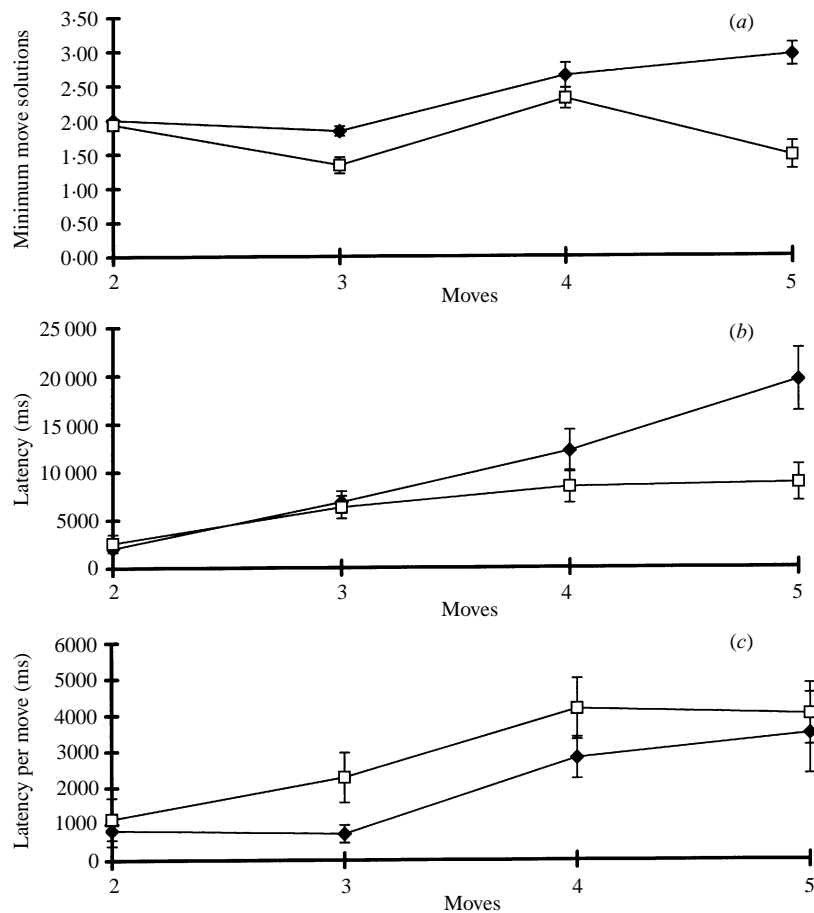


FIG. 2. Planning task: (a) number of perfect solutions; (b) initial thinking time; and (c) subsequent thinking time for each level of difficulty (stage) for correct solutions for schizophrenic patients (\square) and controls (\blacklozenge). Error bars represent S.E.M.

($t(58) = -5.32$, $P < 0.001$). For both groups, strategy score correlated with the number of errors combined for 6- and 8-box stages (patients, $r = 0.73$, $P < 0.01$; controls, $r = 0.68$, $P < 0.01$). The contribution of memory span to performance was assessed by correlating spatial span score with between-search errors. This was significant only for the patient group (patients, $r = -0.44$, $P < 0.05$; controls, $r = 0.05$, NS). The relative contribution of spatial span and strategy score to performance was assessed with analyses of covariance. Covarying strategy, there was no significant difference in errors between the two groups ($F(1, 57) = 0.35$). Covarying span, the main effect of group remained ($F(1, 57) = 12.37$, $P < 0.05$). In other words, the differences in errors are accounted for by the

differences between the two groups in their use of the search strategy rather than their short-term memory capacity as measured by spatial span.

Planning

The patients achieved fewer perfect solutions (Fig. 2a) than controls ($F(1, 58) = 25.9$, $P < 0.01$). A significant interaction ($F(3, 174) = 12.1$, $P < 0.01$) and main effects analysis revealed that this was specifically at the 3- and 5-move stages ($F(1, 58) = 12.92$ and 31.54 , $P < 0.01$). The patients also solved fewer problems within the maximum permitted moves (Table 2, $F(1, 58) = 7.07$, $P < 0.05$). A significant interaction ($F(3, 174) = 2.91$, $P < 0.05$), and main effects analysis showed that they were

specifically impaired at the 4- and 5-move stages ($F(1, 58) = 4.18$ and 8.17 , $P < 0.05$). The patients made more excess moves per solution ($F(1, 58) = 19.41$, $P < 0.01$). A significant interaction ($F(3, 174) = 9.01$, $P < 0.01$) and main effects analysis showed that this was also at the 3- and 5-move stages ($F(1, 58) = 14.3$ and 17.5 , $P < 0.01$). These findings remained when analysed for only problems solved correctly (group, $F(1, 58) = 17.63$, $P < 0.01$; group by difficulty, $F(3, 174) = 12.93$, $P < 0.01$). In summary patients were impaired on each performance measure: they solved fewer problems and even when they solved the problem, they took more moves to do so. Correlations performed to examine the relationship between spatial span and planning (excess moves) were not significant (patients, $r = -0.30$, NS; controls, $r = 0.12$, NS).

Schizophrenic patients were significantly slower than controls for both motor initiation times and motor execution times ($F(1, 58) = 11.1$ and 5.64 , $P < 0.05$). Taking these into account, the patients spent less time planning solutions for the problems requiring 4 or 5 moves than controls (Fig. 2*b*: group, $F(1, 58) = 14.63$, $P < 0.01$; group \times difficulty, $F(3, 174) = 2.89$, $P < 0.05$; level 4 main effect, $F(1, 58) = 4.11$, $P < 0.05$; level 5 main effect, $F(1, 58) = 8.12$, $P < 0.05$). Fig. 2*c* shows that subsequent thinking times per move were slower in the patients than in the control group across all levels of difficulty ($F(1, 58) = 4.37$, $P < 0.05$).

To investigate the relationship between latency and accuracy, initial and subsequent thinking times were calculated only for those problems solved perfectly, and for all problems solved within the maximum number of moves. The patients still showed decreased initial thinking times for problems solved perfectly ($F(1, 47) = 19.58$, $P < 0.01$) and all problems solved ($F(1, 58) = 13.59$, $P < 0.01$). Subsequent thinking times were increased for solutions made within the maximum number of moves ($F(1, 58) = 4.11$, $P < 0.05$) but not for perfect solutions ($F(1, 47) = 0.88$, NS).

Attentional set shifting test

The percentage of patients and controls passing each stage is shown in Fig. 3. The control subjects completed all stages. Only at the EDS stage did more schizophrenic patients fail than controls ($2i = 5.85$, $P < 0.05$). For subjects who

completed all stages, the number of errors made at the IDS and EDS stages were compared with an ANOVA (factors: group, stage). The patients made more errors before reaching criterion than controls (group, $F(1, 52) = 5.33$, $P < 0.05$). The interaction was not significant ($F(1, 52) = 0.41$) indicating that there was no disproportional impairment at the EDS stage. Comparisons between the six schizophrenic patients who failed the test and the successful 24 revealed no differences on the other tests.

Verbal fluency

Data were available from 25 patients and 25 controls. The patients were impaired on both letter and category fluency (Table 2, $t(48) = 5.40$ and 6.56 , $P < 0.001$).

Weschler Memory Scale Revised subtests

Data were available from 27 patients and 27 controls. The patients were impaired on logical memory and paired associate learning (Table 2) but were more impaired on difficult than easy paired associates (group, $F(1, 50) = 20.07$, $P < 0.01$; group by difficulty, $F(1, 50) = 17.02$, $P < 0.01$).

Profile of neuropsychological impairment

To examine whether there were any specific cognitive deficits within this general pattern of poor performance, the scores of the schizophrenic patients were converted into standardized Z scores based on the performance of the control group (Fig. 4). The following measures were used: spatial span; pattern and spatial recognition memory; planning – number of minimum move solutions; spatial working memory – combined number of between-search errors at the 6- and 8-box stages; attentional set shifting – combined average number of errors to criterion at IDS and EDS stages for subjects passing the stage; logical memory score; associate learning scores for easy and difficult pairs; combined score for letter and category fluency.

The mean performance of the schizophrenic group fell below that of control performance on every measure. An ANOVA was used with group as a between-subjects factor and test score as a within-subjects factor, to determine whether there were significant differences in performance across the tests (Saykin *et al.* 1991).

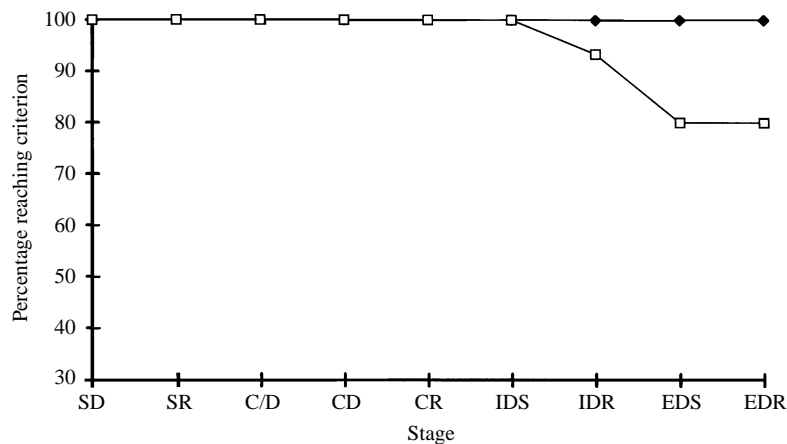


FIG. 3. The percentage of subjects reaching criterion at each test stage for controls (◆) and schizophrenic patients (□) on the attentional set shifting test. Stages are simple discrimination (SD), simple discrimination reversal (SDR), compound discrimination (exemplars separated, compound discrimination C-D; exemplars superimposed, compound discrimination CD), compound discrimination reversal (CDR), intra-dimensional shift (IDS), intra-dimensional shift reversal (IDR), extra-dimensional shift (EDS) and extra-dimensional shift reversal (EDR).

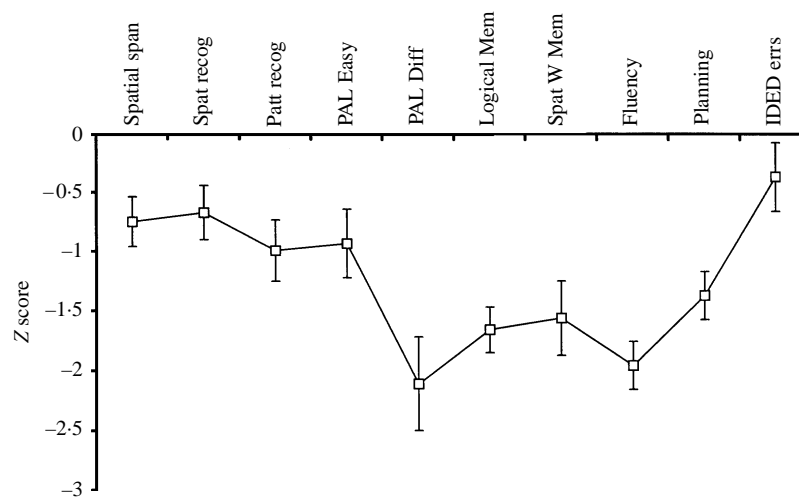


FIG. 4. Performance of schizophrenic patients expressed in terms of Z scores (control standard deviations). Error bars represent S.E.M. Spat recog = spatial recognition memory; Patt recog = pattern recognition memory; PAL = paired associate learning; Diff = difficult; Spat W Mem = spatial working memory; IDED errs = attentional set shifting errors at IDS and EDS.

A significant main effect of group ($F(1, 41) = 40.97$, $P < 0.001$) confirmed that the patients were generally impaired relative to controls. Performance on five tasks fell within one standard deviation of control performance: spatial span, pattern and spatial recognition memory, easy paired associate learning and attentional set shift errors. Performance on the remaining five tasks was 1.5 or more standard deviation from control performance. A sig-

nificant interaction confirmed that the degree of impairment was not uniform across tests ($F(9, 369) = 3.77$, $P < 0.001$). Within-subject contrasts were used to compare each neuropsychological function with the mean of the remaining functions to determine the degree of impairment on each test. With type I errors controlled by the Bonferroni procedure, performance on the difficult paired associate learning was significantly more impaired than per-

performance generally ($t = -3.44$, $P < 0.001$) and performance on the attentional set shifting task was less impaired ($t = 3.25$, $P < 0.001$).

DISCUSSION

We compared 30 first-episode schizophrenic patients with 30 normal volunteers matched for age and pre-morbid IQ on tests selected primarily to assess executive function, although memory tests were also included for comparison. The finding of impaired performance on all tests has been reported in previous first-episode studies (Bilder *et al.* 1992; Hoff *et al.* 1992; Saykin *et al.* 1994; Rubin *et al.* 1995; Albus *et al.* 1996). However, in contradistinction to these studies, we found that schizophrenic patients have severe impairments of executive function at the onset of the illness. Further, executive impairment was not uniform across all measures and was particularly evident for planning ability and strategy use.

On the planning test, the patients were impaired on all performance measures: total solutions, perfect solutions and excess moves. In addition, after the slower initial and subsequent movement times were taken into account to yield measures of thinking time, the patients were faster than controls to initiate the harder problems but slower to complete the problems. One interpretation is that the patients failed to consider the solutions sufficiently before attempting them and thus made more mistakes. However, this cannot be the sole explanation since they still failed more problems than controls despite spending longer completing the problems suggesting that, in addition to impulsivity, they had difficulty in monitoring their moves and redressing their errors.

In this task subjects need to retain a planned sequence of moves in memory while executing the task – an attribute of working memory. Schizophrenic subjects had shorter spatial spans suggesting that they have difficulty in maintaining a sequence of moves in memory over a short period of time. However, there was no evidence that this contributed to poor performance on the planning task. First, the correlation between spatial span and excess moves was not significant. Secondly, the deficit on spatial span was not marked and the patients were able to remember a sequence of five moves, which is the

maximum required for the planning task. Thus, it appears that the deficit on this task was the inability to plan a correct sequence of moves.

It is unlikely that these results reflect anti-psychotic medication because patients with mild Parkinson's disease, whose primary deficit is dopaminergic underactivity, show normal accuracy, increased initial thinking times and normal subsequent thinking times (Owen *et al.* 1992). Rather, schizophrenic group performance is a more extreme version of patients with frontal lobe resections (Owen *et al.* 1990), who show increased subsequent thinking times, obtain fewer perfect solutions and make more excess moves suggesting that they also attempt the problems before they have been fully planned. The conclusion that our results may reflect a specific abnormality of frontal lobe function is supported by the finding that patients with temporal lobe resections are unimpaired on this task (Owen *et al.* 1995). The slow movement times in the patient group is a non-specific finding because patients with frontal lobe resections, temporal lobe resections and Parkinson's disease also show this despite having different profiles of performance.

The patients were also impaired on the spatial working memory test. They made more between-search errors, indicating that they had difficulty keeping track of the boxes which had already contained a token while they searched for a new token. The use of a search strategy has been shown to aid performance on this task (Robbins, 1996). Indeed, a measure of strategy correlated highly with between-search errors for both groups. However, the patients were markedly deficient in their use of this strategy, suggesting that this resulted in their poor performance. This is supported by the finding that the difference between the groups disappeared when strategy score was covaried with errors. Perhaps because they were unable to adopt a strategy, the schizophrenic group appeared to rely more on spatial short-term memory than controls, since spatial span correlated with errors in patients but not controls. The performance of the schizophrenic group resembles that of frontal lobe resection patients who also fail the task because they do not adequately utilize a search strategy (Owen *et al.* 1990). The neuroanatomical specificity of this performance profile is also demonstrated by the fact that patients with

temporal lobe excisions, Parkinson's disease and Alzheimer's disease also make more between-search errors but only frontal patients have a deficiency in strategy use (Owen *et al.* 1990, 1992, 1995, 1996; Sahgal *et al.* 1992).

The attentional set-shifting task also measures executive function, mainly at the extradimensional shift (EDS) stage which is analogous to the attentional shift involved in the Wisconsin Card Sorting Task (WCST). At this stage, subjects must inhibit a previously reinforced response to one dimension and switch attention to a newly reinforced dimension. While significantly more patients failed at this stage than controls, the surprising thing was that most patients (80%) completed the entire task. An analysis of trials to criterion for those successfully completing both intradimensional shift (IDS) and EDS stages showed that the schizophrenic patients took more trials at each stage but were not more impaired at the EDS stage. Thus, the patients had difficulty adjusting to novel exemplars but were able to learn both shifts of rule equally, although one required an attentional shift in dimension and the other did not. Thus, it cannot be concluded that patients in the early stages of schizophrenia have an executive dysfunction of the type measured by this test. The Z score comparison confirmed that performance on the attentional set shifting task was relatively preserved in the schizophrenic group.

Patients with frontal resections (but not temporal resections) are impaired on the attentional set shifting task specifically at the EDS stage (Owen *et al.* 1991). Thus, the executive dysfunction of first-episode schizophrenic patients is more specific than that of patients with frontal lobe lesions: they are more impaired on the planning task, similarly impaired on the spatial working memory task because of poor strategy use and less impaired on the attentional set shifting task. The differential performance on these frontal tasks in the schizophrenic patients can be explained by the different demands of the tests. The common requirement of the planning and spatial working memory tasks is the ability to initiate and monitor plans and strategies. The set shifting task requires the ability to inhibit a prepotent response and shift attention with little requirement for planning and response sequencing. Thus, it appears that

patients early in the course of schizophrenia have particular executive difficulties in planning and strategy use. This specific type of executive dysfunction might also explain the poor performance of the patient group on the verbal fluency tasks since the verbal fluency impairment in schizophrenia is also due to an inability to initiate a strategic search of semantic store (Allen *et al.* 1993; McKenna *et al.* 1994; Joyce *et al.* 1996).

These findings are important for the current understanding of cognitive dysfunction in schizophrenia for several reasons. First, they distinguish first-episode patients from chronic schizophrenic patients since the latter have difficulties with the WCST (see Levin *et al.* 1989; Elliott & Sahakian, 1995) and are more impaired on the CANTAB attentional set shifting task than on the planning and spatial working memory tasks (Elliott *et al.* 1995, 1997; Pantelis *et al.* 1997). Thus, it appears that the nature of the executive impairment changes over the course of the illness. Secondly, they explain why the previous first-episode studies have failed to demonstrate significant executive dysfunction. These studies have employed the WCST as the test of executive function and, on the basis of our attentional set shifting results, we would not expect performance on this test to be severely impaired. Thus, these studies are not strictly comparable to ours as they did not use tests of executive function which measure planning ability and strategy use. Thirdly, they may have implications for the neuropathological specificity of frontal lobe dysfunction at the onset of schizophrenia. For example, functional imaging studies have shown that a neural network involving the dorsolateral prefrontal cortex and parietal cortex mediates the planning task (Baker *et al.* 1996) whereas additional areas, including orbitofrontal and temporal cortex, are activated during WCST performance (Berman *et al.* 1995), suggesting that planning and set shifting are mediated by different neural networks, perhaps involving different frontal areas.

Our patients also failed on memory tests, suggesting that their deficits are not restricted to planning and strategy formation. This finding accords with other studies of schizophrenia which have demonstrated memory deficits in both chronic (e.g. Gold *et al.* 1992; Tamlyn *et al.* 1992) and first episode (Saykin *et al.* 1994)

schizophrenia. However, as with the executive tests, performance was not uniform. The patients were much less impaired on recognition memory and easy paired associate learning, scoring within one standard deviation of control performance, than free recall of a story and difficult paired-associate learning. Indeed, the latter was the most severely affected measure on the Z score analysis. Superior recognition than free recall can be attributed to executive dysfunction rather than to a fundamental memory problem since free recall requires more strategic processing to aid learning and recall (see Parkin & Leng, 1993). This may also explain the discrepant performance on easy and difficult paired-associate learning. Furthermore, studies which have manipulated encoding and recall strategies suggest that schizophrenic patients do not routinely implement efficient encoding and retrieval strategies (Koh, 1978; Traupman, 1980; McClain, 1983; Goldberg *et al.* 1989). A different explanation is that the tests vary in the amount of cognitive effort required, and the schizophrenic group simply performed better on the easier tasks. Our current data do not permit an analysis to distinguish these possibilities. It is unlikely, however, that differences in task difficulty explain our executive data. The attentional set shifting task is not an inherently easier task than the planning or spatial working memory task. Further, studies of different patients have shown that performance of the attentional set shifting task can be more impaired than that of the other executive tasks (Lawrence *et al.* 1996) suggesting that it is the nature of the task in relation to the underlying neuropathology which determines performance.

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REFERENCES

- Albus, M., Hubman, W., Ehrenberg, C., Forcht, U., Mohr, F., Sobizack, N., Wahlheim, C. & Hecht, S. (1996). Neuropsychological impairment in first episode and chronic schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience* **246**, 249–255.
- 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.
- Anon (1996). *CANTAB Norms*. Cambridge Cognition: Cambridge.
- Baker, S. C., Rogers, R. D., Owen, A. M., Frith, C. D., Dolan, R. J., Frackowiak, R. S. J. & Robbins, T. W. (1996). Neural systems engaged by planning: a PET study of the Tower of London task. *Neuropsychologia* **34**, 515–526.
- Benton, A. & Hamsher, K. (1976). *Multilingual Aphasia Examination*. University of Iowa: Iowa City.
- Berman, K. F., Ostrem, J. L., Randolph, C., Gold, J., Goldberg, T. E., Coppola, R., Carson, R. E., Herscovitch, P. & Weinberger, D. R. (1995). Physiological activation of a cortical network during performance of the Wisconsin Card Sort Task: a positron emission tomography study. *Neuropsychologia* **33**, 1027–1046.
- Bilder, R. M., Lipschutz-Broch, L., Reiter, G., Geisler, S., Mayerhoff, D. & Lieberman, J. A. (1992). Neuropsychological deficits in the early course of first episode schizophrenia. *Schizophrenia Research* **5**, 198–199.
- Braff, D., Heaton, R., Kuck, J., Cullum, M., Moranville, J., Grant, I. & Zisook, S. (1991). The generalized pattern of neuropsychological deficits in outpatients with chronic schizophrenia with heterogeneous Wisconsin Card Sorting Test results. *Archives of General Psychiatry* **48**, 891–898.
- Elliott, R. & Sahakian, B. J. (1995). The neuropsychology of schizophrenia: relations with clinical and neurobiological dimensions. *Psychological Medicine* **25**, 581–594.
- Elliott, R., McKenna, P. J., Robbins, T. W. & Sahakian, B. J. (1995). Neuropsychological evidence for frontostriatal dysfunction in schizophrenia. *Psychological Medicine* **25**, 619–630.
- Elliott, R., McKenna, P. J., Robbins, T. W. & Sahakian, B. J. (1997). Specific neuropsychological deficits in schizophrenic patients with preserved intellectual function. *Cognitive Neuropsychiatry* (in the press).
- Gold, J., Randolph, C., Carpenter, C., Goldberg, T. & Weinberger, D. (1992). Forms of memory failure in schizophrenia. *Journal of Abnormal Psychology* **101**, 487–494.
- Goldberg, T. E., Weinberger, D. R., Pliskin, N. H., Berman, K. B. & Podd, M. H. (1989). Recall memory deficit in schizophrenia: a positive manifestation of prefrontal function? *Schizophrenia Research* **2**, 251–257.
- Hoff, A., Riordan, H., O'Donnell, M., Morris, L. & DeLisi, L. (1992). Neuropsychological functioning of first-episode schizophreniform patients. *American Journal of Psychiatry* **149**, 898–903.
- 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.
- King, D. J. & Green, J. F. (1996). Medication and cognitive functioning in schizophrenia. In *Schizophrenia: A Neuropsychological Perspective* (ed. C. Pantelis, H. E. Nelson and T. R. E. Barnes), pp. 419–446. John Wiley and Sons: Chichester.
- Koh, S. D. (1978). Remembering of verbal materials by schizophrenic young adults. In *Language and Cognition in Schizophrenia* (ed. S. Schwartz), pp. 55–99. Lawrence Erlbaum Associates: Hillsdale, NJ.
- Kolb, B. & Whishaw, I. Q. (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 Diseases* **171**, 435–443.
- Kullback, S. (1959). *Information Theory and Statistics*. John Wiley: New York.
- Lawrence, A. D., Sahakian, B. J., Hodges, J. R., Rosser, A. E., Lange, K. W. & Robbins, T. W. (1996). Executive and mnemonic functions in early Huntington's disease. *Brain* **119**, 1633–1645.
- Levin, S., Yurgelun-Todd, D. & Craft, S. (1989). Contribution of clinical neuropsychology to the study of schizophrenia. *Journal of Abnormal Psychology* **98**, 341–356.
- Lezak, M. (1983). *Neuropsychological Assessment*, 2nd edn. Oxford University Press: New York.
- Liddle, P. F. & Crow, T. J. (1984). Age disorientation in chronic schizophrenia is associated with global intellectual impairment. *British Journal of Psychiatry* **144**, 193–199.
- McClain, L. (1983). Encoding and retrieval in schizophrenic's free recall. *Journal of Nervous and Mental Diseases* **171**, 471–479.
- McKenna, P. J., Mortimer, A. M. & Hodges, J. R. (1994). Semantic memory and schizophrenia. In *Neuropsychology of Schizophrenia* (ed. J. Cutting and A. David), pp. 163–178. Lawrence Erlbaum: Hove.

- Morrison-Stewart, S., Williamson, P., Corning, W., Kutcher, S., Snow, W. & Merskey, H. (1992). Frontal and non-frontal neuropsychological test performance and clinical symptomatology in schizophrenia. *Psychological Medicine* **22**, 353–359.
- Nelson, H. (1976). *The National Adult Reading Test*. NFER-Nelson: Windsor.
- Owen, A., Downes, J., Sahakian, B., Polkey, C. & Robbins, T. (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia* **28**, 1021–1034.
- Owen, A., Roberts, A., Polkey, C., Sahakian, B. & Robbins, T. (1991). Extra-dimensional versus intra-dimensional set shifting performance following frontal lobe excisions, temporal lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia* **29**, 991–1006.
- Owen, A., James, M., Leigh, P., Summers, B., Marsden, C., Quinn, N., Lamge, K. & Robbins, T. (1992). Fronto-striatal cognitive deficits at different stages of Parkinson's disease. *Brain* **115**, 1727–1751.
- Owen, A. M., Sahakian, B. J., Semple, J., Polkey, C. E. & Robbins, T. W. (1995). Visuospatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia* **33**, 1–24.
- Owen, A. M., Morris, R. G., Sahakian, B. J., Polkey, C. E. & Robbins, T. W. (1996). Double dissociation of memory and executive functions in working memory tasks following frontal lobe excisions, temporal lobe excisions or amygdalo-hippocampectomy in man. *Brain* **119**, 1597–1615.
- Pantelis, C., Barnes, T. R. E., Nelson, H. E., Tanner, S., Weatherley, L., Owen, A. M. & Robbins, T. W. (1997). Frontal-striatal cognitive deficits in patients with chronic schizophrenia. *Brain* **120**, 1823–1843.
- Parkin, A. J. & Leng, N. R. C. (1993). *Neuropsychology of the Amnesic Syndrome*. Lawrence Erlbaum Associates: Hove.
- Robbins, T. (1990). The case for frontostriatal dysfunction in schizophrenia. *Schizophrenia Bulletin* **16**, 391–401.
- Robbins, T. W. (1997). A critique of the methods available for the measurement of spontaneous motor activity. In *Handbook of Psychopharmacology*, Vol. 7 (ed. L. L. Iversen, S. D. Iversen and S. H. Snyder), pp. 37–82. Plenum Press: New York.
- Robbins, T. W. (1996). Dissociating executive functions of the prefrontal cortex. *Philosophical Transactions of the Royal Society of London*, B **351**, 1463–1471.
- Robbins, T. W., James, M., Owen, A. M., McKinnes, L. & Rabbitt, P. (1994). Cambridge Automated Neuropsychological Test Battery (CANTAB). A factor analytic study in a large sample of normal volunteers. *Dementia* **5**, 266–281.
- Rubin, P., Holm, A., Moller-Madsen, S., Videbech, P., Hertel, C., Povlsen, U. J. & Hemmingsen, R. (1995). Neuropsychological deficit in newly diagnosed patients with schizophrenia or schizophreniform disorder. *Acta Psychiatrica Scandinavica* **92**, 35–43.
- Sahakian, B., Morris, R., Evenden, J., Heald, A., Levy, R., Philpot, M. & Robbins, T. (1988). A comparative study of visuospatial memory and learning in Alzheimer-type dementia and Parkinson's disease. *Brain* **111**, 695–718.
- Sahakian, B. & Owen, A. (1992). Computerised assessment in neuropsychiatry using CANTAB. *Journal of the Royal Society of Medicine* **85**, 399–402.
- Sahgal, A., Lloyd, S., Wray, C. J., Galloway, P. H., Robbins, T. W., Sahakian, B. J., McKeith, I. J. & Cook, J. H. (1992). Does visuospatial memory in Alzheimer's disease depend on the severity of the disorder? *International Journal of Geriatric Psychiatry* **7**, 427–436.
- Saykin, A., Gur, R., Gur, R., Mozley, D., Mozley, L., Resnick, S., Kester, D. & Stafiniak, P. (1991). Neuropsychological function in schizophrenia. *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. (1994). Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. *Archives of General Psychiatry* **51**, 124–131.
- Shallice, T. (1982). Specific impairments in planning. *Philosophical Transactions of the Royal Society of London B* **298**, 199–209.
- Shallice, T., Burgess, P. & Frith, C. (1991). Can the neuropsychological case study approach be applied to schizophrenia? *Psychological Medicine* **21**, 661–673.
- Tamlyn, D., McKenna, P., Mortimer, A., Lund, C., Hammond, S. & Baddeley, A. (1992). Memory impairment in schizophrenia: its extent, affiliations and neuropsychological character. *Psychological Medicine* **22**, 101–115.
- Traupman, K. L. (1980). Encoding processes and memory for categorically related words by schizophrenic patients. *Journal of Abnormal Psychology* **89**, 704–716.
- Wechsler, D. (1987). *Wechsler Memory Scale Revised*. The Psychological Corporation: London.