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Impaired generation and use of strategy in schizophrenia: evidence from visuospatial and verbal tasks

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ABSTRACT

Background. The aim of this study was to investigate mnemonic strategic deficits in schizophrenic patients.

Methods. Analogous tasks were used that required the self-generation of an efficient strategy and its implementation in two domains: visuospatial and verbal. The tasks were given to 20 IQ preserved schizophrenics and 20 matched normal controls. A number of different scores was derived from each task including strategy, short-term memory capacity and perseveration.

Results. Overall, the schizophrenic patients were significantly impaired in their ability to generate effective mnemonic strategies on both tasks. In addition, on the visuospatial task there was no difference between the groups on the memory scores, but the schizophrenic patients made significantly more perseverative errors than controls. They were disproportionately worse on the verbal strategy task, showing impairment on memory as well as on strategy scores and were also impaired at semantically classifying the words. Performance was similar to the deficit seen in patients with frontal lobe excisions and Parkinson's disease, in terms of the inability to generate an effective strategy. The deficit on the verbal task was similar to patients with temporal lobe excisions who show impaired verbal memory. However, the pattern differed in the sense that the temporal lobe patients were able to generate effective strategies, unlike the patients with schizophrenia.

Conclusions. High functioning schizophrenic patients are impaired in utilizing visuospatial and verbal mnemonic strategies. By comparing the results with those of neurosurgical excision patients, further evidence is provided for both frontal and temporal lobe involvement in schizophrenia.

INTRODUCTION

The use of strategies refers to the ability to generate efficient algorithms or procedures that facilitate complex task performance. The precise mechanisms underlying the use of strategies in problem solving are uncertain but in recent years some progress has been made in understanding first, its cognitive underpinnings and, secondly, the brain systems which subserve these functions. The use of strategy can be conceived as a prominent function of the so-called 'central executive' i.e. the co-ordination of cognitive abilities to optimize performance, which may at least partially be subserved by neural systems including the prefrontal cortex (Shallice, 1982; Baddeley, 1986; Passingham, 1993; Petrides, 1996). It has been suggested that schizophrenic subjects exhibit impaired executive function, including planning (Frith, 1992) and this has been linked to possible frontal lobe dysfunction (Weinberger *et al.* 1986). It follows that some of the cognitive impairment in schizophrenia may be secondary to the impaired use of strategies for optimal performance.

Robbins (1990) argued that frontostriatal dysfunction may be an important feature of

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schizophrenia, and that the heterogeneity of the disorder could be attributed in part to variations in the altered balance in the flow of information between different corticostriatal loops (Alexander *et al*. 1986), the output of each of which targets the frontal lobes. Jaskiw & Weinberger (1992) suggested that dysfunction of the prefrontal cortex may modulate subcortical dopamine release. At the neuropsychological level there is certainly considerable evidence that schizophrenic patients show poor performance on executive tasks (Shallice *et al*. 1991; Liddle & Morris, 1992; Elliott & Sahakian, 1995; Elliott *et al*. 1995, 1998; Morice & Delahunty, 1996; Pantelis *et al*. 1998). There are also a number of findings suggesting a working memory deficit in schizophrenia (Fleming *et al*. 1995; Gold *et al*. 1997). Dorsolateral prefrontal cortex dysfunction in schizophrenia has been implicated on developmental grounds (Weinberger *et al*. 1986), and in functional and structural imaging (but, see Chua & McKenna, 1995 for discussion).

In man, numerous neuropsychological and neuroimaging studies, both in normal volunteers and in patients with frontal lesions, have documented the role of the frontal lobes in high level decision making and memory tasks (among others: Luria, 1966; Shallice, 1982; Milner & Petrides, 1984; Fuster, 1993; Petrides, 1994; Owen *et al*. 1990, 1996*a*, *b*). Other studies have also found that patients with unilateral frontal lobe excisions perform poorly on tasks that depend on the development of strategies to maximize the efficiency of responding (Owen *et al*. 1990, 1996*a*; Shallice & Burgess, 1991*a*) and that this may be a specific cognitive deficit (Shallice & Burgess, 1991; Owen *et al*. 1996*a*, *b*). Owen *et al*. (1996*a*, *b*) used a graded, self-ordered spatial working memory task that required subjects to hold information 'on-line' about where they had found tokens in either 4, 6 or 8 boxes. They were told that returning to a box in which a token had previously been found would result in an error. When there are 6 or 8 boxes the subject is greatly aided if he or she can spontaneously generate a search strategy, although this is not a direct requirement of the task. On the basis of psychometric and neuroimaging evidence, Robbins (1996) hypothesized that the different subcomponents of this task, i.e. short-term memory capacity and strategy use, may depend on different parts of the prefrontal cortex. Two previous studies have used the same spatial working memory task with schizophrenics (Pantelis *et al*. 1998; Elliott *et al*. 1998) and found that they exhibited a similar pattern of impairment to patients with frontal lobe excisions: although they made more errors, this was primarily due to their inability to spontaneously generate a search strategy to facilitate task performance.

In order to analyse further the role of strategies in mnemonic performance in patients with schizophrenia, two main questions arise. First, to what extent are apparent deficits in the use of strategies described above dependent on the spontaneity of the strategy in question, and the degree to which strategy use can be cued or trained in such subjects? Secondly, to what extent do these impairments generalize to other types of task, such as those involving verbal processing? To address the former question we modified another spatial working memory task used previously by Owen *et al*. (1995) to test patients with Parkinson's disease or frontal lobe damage. In this task, subjects originally had to generate as many novel sequences as they could from an array of four touch sensitive boxes arranged symmetrically around the screen, trying not to repeat sequences already made. We extended this task by adding two further stages, a training state, which was designed to introduce or cue a strategy, followed by a repeat of the first stage. The training stage, interposed between the first and second exposure to the test paradigm, was designed to facilitate task reconfiguration. Omission of the training stage leads to no improvement at stage 2 in normal controls (Iddon *et al*. 1998). A recent study by Iddon *et al*. (1996, 1998) found that patients with frontal lobe excisions and patients with Parkinson's disease were impaired in their ability to generate an effective mnemonic strategy to complete this test of visuospatial working memory. In contrast however, patients with temporal lobe excisions are unimpaired on the same task. Taken together, these findings further suggest that both the prefrontal cortex and the basal ganglia may be implicated in frontostriatal circuitry that helps to subserve strategy generation.

In the light of these findings, the present study assessed the ability of schizophrenic patients to generate and use cognitive strategies using the new, three-stage task. An analogous verbal strategy task was also used to assess the domain specificity of any impairment found. The term 'analogous' as used here refers to the common way in which the tasks were administered, i.e. an initial phase, followed by training and a second phase, and also their common capacities to use as organizational principles for enhancing memory for spatial sequences and word lists in retrieval. However, 'analogous' does not imply that the types of strategy used in visuospatial and verbal tasks are exactly the same.

Based on the previous findings by Iddon *et al.* (1996), performance on the visuospatial task, which is largely non-verbal, is likely to be mediated in part by neural networks including prefrontal cortex and its subcortical connections. But the integrity of the temporal lobes has been shown not to be essential for performing the task well (Iddon *et al.* 1998). The verbal task also requires strategy generation and as such, success on it is also likely to be reliant on intact frontostriatal functioning. However, another component of the task, namely the memory and recall of semantically related words, would be expected to depend primarily on left temporal lobe structures which have been implicated in schizophrenia (Crow, 1990; Kerwin *et al.* 1992; Goldberg *et al.* 1995). Our hypothesis, therefore, is that both the visuospatial and verbal tasks may be impaired in schizophrenia as a result of impaired strategy use but that performance on the verbal task may be further impaired as a result of basic deficits in encoding and recalling semantically related words.

METHOD

Sample

Twenty patients (16 male and 4 female) meeting Research Diagnostic Criteria for schizophrenia (Spitzer *et al.* 1978) were included in the study. All the patients met standard exclusion criteria, including neurological and other concomitant disorder, history of alcohol or drug abuse and mental handicap. All patients had chronic illness, and as a group were relatively severely ill, as determined by the consultant psychiatrist (P.J.M.). None was in a state of active psychotic relapse at the time of examination. All were taking neuroleptic medication (clozapine).

The patients were selected partly on the basis of their being non-elderly, as it has been found that ageing affects the ability to generate effective cognitive strategies to complete these memory tasks (Iddon *et al.* 1996, 1998). Their mean age was 39·1 (S.D. = 8·4). Because schizophrenia is commonly associated with evidence of general intellectual impairment, the patients were also selected to be IQ preserved in order to minimize the confounding effect of generally poor performance as far as possible. Thus, they all had Mini-Mental State (MMSE, Folstein *et al.* 1975) scores above the cut-off of 23/30 for mild dementia. Patients with a discrepancy of more than 15 points between their pre-morbid and current IQ were excluded: the mean pre-morbid verbal IQ, as estimated using the National Adult Reading Test (NART) (Nelson, 1982) was 107·5 (S.D. = 8·4) and the mean current Verbal IQ as measured using the WAIS was 102·9 (S.D. = 12·3).

Twenty healthy control volunteers (14 male and 6 female) were matched to the patient group by age and NART estimated verbal intelligence. Their mean age was 40·7 (S.D. = 9·6) and their mean NART IQ was 110·45 (S.D. = 9·0). Any control subject taking medication that could affect their results was excluded from the study.

The study was approved by the Local Research Ethics Committee. All patients and controls gave their informed consent to take part in the study and were paid £4 for their participation.

Procedure

Two tasks were given in a counterbalanced order in a quiet room.

Visuospatial Strategy Task (see Fig. 1)

This task was performed in three stages on a portable touch sensitive computer screen, comprising a 9·5 inch Datalux touch sensitive screen and a CarryI portable hard disk. The computer was controlled by the tester who gave verbal instructions to the patients for each part of the test. The patient sat directly in front of the screen with comfortable reaching distance. No time limit was imposed for the completion of this task.

Stage 1

Four individual red squares were arranged symmetrically on the computer screen in the same positions as the numbers 3, 6, 9 and 12 would be organized on a clockface. The subject was instructed to try to generate as many new sequences as possible, using all four boxes each time, without touching one more than once. The requirement, therefore, was not to repeat a sequence that had already been made, and hence relied heavily on spatial working memory capacity. Subjects were informed that there was a total of 24 possible sequences and that 24 trials would be allowed to achieve this. There was no time limit. A score out of 24 was displayed in the centre of the screen and informed the subject of how many trials had occurred and how many correct sequences had been made. Feedback was given after each sequence had been attempted: repeat sequences were signified by a low, unpleasant tone and no increase in the number of novel sequences as represented by the displayed score whereas new sequences were signified by a high tone and an increment in the score.

Training stage

After the completion of stage 1, the screen cleared, re-appearing with the same four red boxes, but this time with the addition of a white outline around the '12 o'clock position' red box. The subjects were then asked to start at that white-outlined box each time and told that there were six possible different sequences that could be generated from there alone. This training, thus, cues the subject into perceiving that the task can be approached more efficiently by breaking it down into four simpler subtasks ('subgoals' in a problem-solving context). After six attempts the white outline moved anticlockwise to the next red box and the subject repeated the exercise again. This sequence continued until the outline had moved around to each of the four boxes in turn. Again feedback information was given in the form of a displayed score and a tone. This part of the task assessed the subject's ability to generate the most efficient strategy having been cued as to which strategy was most effective. They were, thus, not told explicitly what the most effective strategy was but the format of the training cued the subject to restructure the task in this way. There was a total of 24 sequences possible and, therefore, to obtain the full number, each box had to be started from six times (because $4 \times 6 = 24$).

Stage 2

The final stage of this task repeated stage 1 so that the subject was required for a second time to generate as many new sequences as they could out of a possible 24. They were asked to try to improve on their original score. Improvement on this part of the task, thus, relied heavily on the ability to implement an effective strategy, so reducing the working memory load.

Indices of performance for the visuospatial strategy task

(1) *Sequence generation scores*

The number of novel sequences generated at stage 1 and stage 2 of the task (repeated sequences were not included), at each stage there was a possible total score of 24. Each box could only be used once within a sequence and therefore it was not possible to make 'repeat box' errors.

(2) *Training stage score*

The number of sequences generated from boxes 1–4 added together to obtain a total score out of 24.

(3) *Span score*

A working memory capacity score calculated on stage 1 of the task. The score is the number of sequences made from the start of the block before a repeated sequence (i.e. an error) is made. It is important to note that a pure span score such as this could not be calculated at stage 2 of the task because trained use, or attempted use, of a strategy was likely to contaminate such a score.

(4) *Strategy score*

A score derived at stages 1 and 2 to assess whether the subject has generated and is implementing the strategy. It was measured by calculating the number of blocks of five or more consecutive sequences starting with the same box. This was considered to be the definitive strategy to use for two main reasons: (1) this strategy was the one that subjects were alerted to during the training block; and (2) this is the most logical mathematical algorithm that can be used to complete this task. Other strategies can be used but are not likely to be as efficient as the one described, trained and assessed here. It

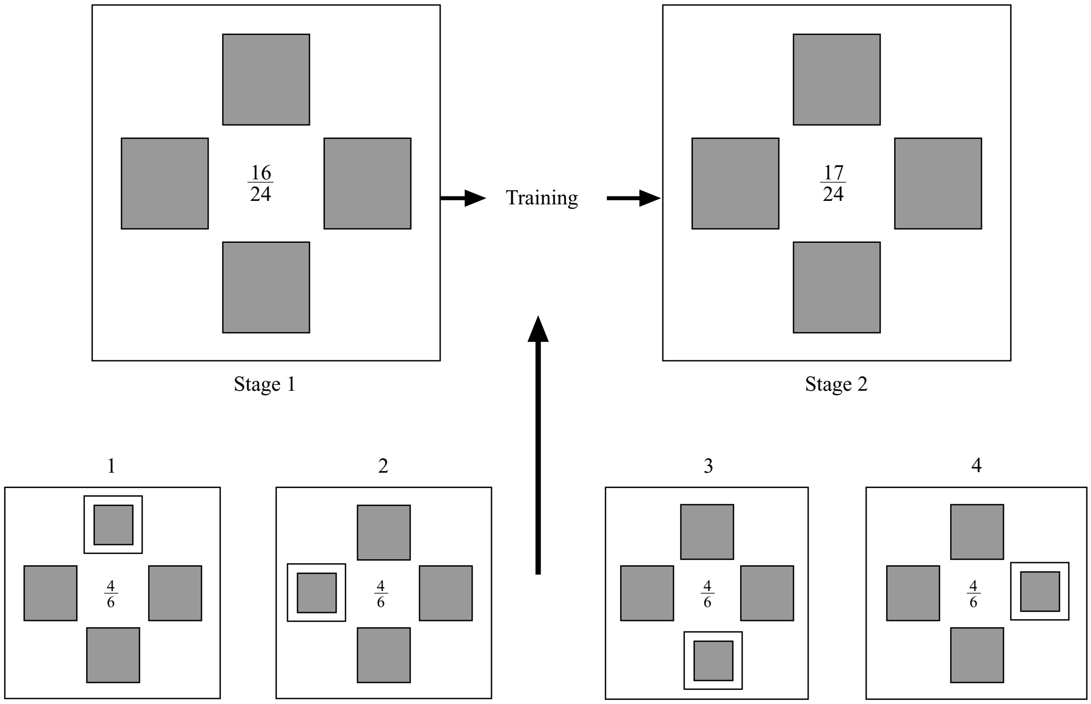

FIG. 1. The Visuospatial Strategy Task. This task is performed on a touch sensitive computer screen over three stages. The instructions are as follows: Stage 1, try to generate as many sequences as you can out of 24 trying not to repeat ones already made; Training, try to make six new sequences from each of the four highlighted boxes in turn; Stage 2, try to generate as many sequences as you can out of 24 trying not to repeat ones already made, but trying to beat your stage 1 score; Feedback, this is given via a fraction in the middle of the screen. After each sequence a tone is heard, a high tone indicates a new sequence and a low tone indicates a repeat sequence.

should also be noted that this was deliberately not the most stringent criterion. This scoring scheme thus had a range from 0–4 with the optimum score being 4.

(5) *Perseveration score*

This was calculated on stages 1 and 2 of the task. A perseveration is any repetition of a complete sequence of four responses on the next trial (non-immediate repeats were not considered to be perseverations).

Verbal Strategy Task

This task was also performed in three stages.

Stage 1

Subjects were presented with a list of sixteen words for 1 min. These were taken from four inanimate semantic categories (e.g. clothing, kitchen utensils, musical instruments, vehicles) matched for word frequency from the Battig & Montague norms (1969). The words were presented in a random order and the subject was not made aware of the categories. As far as they were concerned it was simply a list of unrelated words. The only instruction they had to follow was to try to memorize as many of the words as they could in the time allowed.

After the minute had passed the words were taken away from the subject so that he/she could no longer see them, and then he/she was asked to recall verbally as many as possible. Responses were reported verbatim and no time limit was imposed.

Training phase

The same list of words was then given back to the subject together with a second sheet identifying the four semantic categories from which the words in the list were derived. The subject was asked to write down each word according to its correct semantic category and informed that there were four words per category. The subject was asked to work as fast as they could as they would be timed. This was to assess how quickly they were able to select the correct semantic category for each word. This portion of the task was designed to show that the words in the list were from different semantic categories although the subjects were not told this explicitly.

Stage 2

The subjects were given a new list of sixteen words to memorize for 1 min. These were taken from four new semantic categories (e.g. furniture, toys, sports, reading material), although they were not made aware of these. At the end of the time allowed the list was taken away and the subject was asked to recall as many words as possible, again with the experimenter recording their responses.

Two different lists of words were counter-balanced i.e. half of the subjects were given one list of words first and the other list second, the other half were given the two lists in the reverse order.

Indices of performance for the Verbal Strategy Task

(1) *Recall scores for stages* 1 *and* 2

The total words recalled from each of the two stages. Total possible score for each stage = 16. It should be noted that the visuospatial and verbal tasks, although analogous in certain ways (see Introduction) were not designed to be directly cross-compared, and therefore the scoring systems were not the same for the two tasks. However, despite this it was considered that general conclusions from patterns of strategy performance could be drawn if necessary, e.g. by converting the scores to a standardized metric.

(2) '*Serial strategy*' *score for stages* 1 *and* 2

Number of words recalled from the top of the list in descending order that follows in serial order. Total possible score for each stage = 16.

(3) '*Semantic strategy*' *score for stages* 1 *and* 2

One point was scored for each word that was recalled directly after a word from the same semantic category. Total possible score for each of the two stages = 12.

(4) *Semantic categorization time*

The time to place the words from the first list into four defined semantic categories.

No measures of immediate perseverations (to parallel the perseveration measure used in the visuospatial task) was included, as immediate verbal perseverations were never in fact, made.

Statistic analysis

Two-way Analysis of Variance (ANOVA) was performed on the data designed in each case to include 1 between subject variable (group) and 1 within subject variable (stage). Simple effects were calculated when a significant interaction was found. Student's unmatched *t* tests were performed on single measure scores. Other types of analysis are described where appropriate.

RESULTS

Visuospatial Strategy Task

Sequence generation scores (see Fig. 2*a*)

From Fig. 2*a* it can be seen that schizophrenic patients generated significantly fewer sequences than controls at stage 2 but not at stage 1 of the task. This was confirmed by a highly significant interaction between group and stage ($F(1,38) = 21{\cdot}2$, $P < 0{\cdot}001$). When the simple main effects were calculated the patients with schizophrenia were no different to controls at stage 1 of the task ($F(1,38) = 0{\cdot}15$, $P = 0{\cdot}7$) but there was a highly significant difference at stage 2 ($F(1,38) = 14{\cdot}02$, $P < 0{\cdot}001$) with the schizophrenic group failing to generate as many sequences as controls. The controls improved significantly between stages 1 and 2 ($F(1,38) = 21{\cdot}7$, $P < 0{\cdot}001$). However, if anything, the schizophrenic group were worse on stage 2($F(1,38) = 3{\cdot}6$, $P = 0{\cdot}07$).

Training score

The two groups were significantly different on the training score of the task ($t(1,38) = 4{\cdot}47$, $P < 0{\cdot}001$) with the schizophrenics performing worse than controls. (Mean scores: controls = 21·3, S.E. = 0·4; schizophrenic patients = 17·85, S.E. = 0·7).

Span score

The two groups did not differ from each other on the memory span score for stage 1 ($t(1,38) =$

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0·25, $P = 0·8$). (Mean scores: controls = 7·65, S.E. = 0·7; schizophrenic patients = 7·7, S.E. = 0·9.)

Strategy score (see Fig. 2*b*)

As seen in Fig. 2*b* the schizophrenics used the strategy (as defined in the method section) significantly less than controls at stage 2 of the task. This was confirmed statistically by a highly significant interaction between group and stage ($F(1, 38) = 22·1$, $P < 0·001$). When the simple main effects were calculated the groups were not different at stage 1 ($F(1, 38) = 2·53$, $P = 0·12$) but they were at stage 2 ($F(1, 38) = 26·9$, $P < 0·001$) with the schizophrenics performing worse than controls. Both groups improved significantly on the strategy score from stage 1 to stage 2 although the controls clearly to a much greater degree: schizophrenics ($F(1, 38) = 4·92$, $P < 0·05$), controls ($F(1, 38) = 78·7$, $P < 0·001$).

Perseveration score (see Fig. 2*c*)

As can be seen from Fig. 2*c*, schizophrenic patients made significantly more perseverative responses than controls, irrespective of stage, as confirmed by a significant group effect ($F(1, 38) = 3·8$, $P < 0·05$). Perseveration did not alter between the stages ($F(1,38) = 0·02$, $P = 0·88$) and there was no significant interaction between group and stage ($F(1, 38) = 0·09$, $P = 0·75$).

Multiple regression analysis

(*a*) *Patients with schizophrenia*

The above analysis reveals that schizophrenic patients are impaired on the Visuospatial Strategy Task. However, it does not reveal the relative contributions of working memory capacity, strategy use and perseverations to overall scores on the task. To clarify the contributions of these variables multiple regression equations were constructed, each one for the pre- and post-training stages of the task. The order of entry of predictor variables was determined by the programme.

For stage 1 of the task, memory span and perseveration scores were entered into a multiple regression analysis, with total number of novel sequences generated as the dependent variable. A stepwise-entry method was used as recommended by Howell (1992). On the first pass, memory span at stage 1 was entered ($F(1, 18) = 8·77$, $P < 0·01$) and accounted for 29% of the variance. No further variables reached the required significance for entry into the regression equation.

A similar regression analysis was constructed for stage 2 of the task, with strategy score, training and perseverations as predictor variables. On first pass, training phase score was entered into the regression equation ($F(1, 18) = 31·9$, $P < 0·001$) and accounted for 62% of the variance. Perseveration score was entered on the second pass ($F(1, 18) = 24·9$, $P < 0·001$) and accounted for an additional 10% of the variance. On the third pass, strategy score at stage 2 was entered ($F(1, 18) = 22·8$, $P < 0·001$) accounting for an additional 5% of the variance. Thus, these three variables accounted for a total of 78% of the variance in scores for stage 2.

(*b*) *Control subjects*

A similar analysis was carried out for control performance. For stage 1 no single factor emerged as accounting for the variance. For stage 2 only training score entered the equation ($F(1, 18) = 8·5$, $P < 0·01$) and accounted for 72% of the variance.

Verbal Strategy Task

Total stages 1 *and* 2 (see Fig. 3*a*)

When the schizophrenic group were compared to the controls on the total number of words recalled from stages 1 and 2 the schizophrenic group was significantly worse at both stages of the task ($F(1, 38) = 56·55$, $P < 0·001$), although the deficits were greater on stage 2 ($F(1, 38) = 17·3$, $P < 0·001$). Simple main effects showed that the schizophrenics recalled significantly fewer words both at stage 1 ($F(1, 38) = 24·6$, $P < 0·001$) and at stage 2 ($F(1, 38) = 61·1$, $P < 0·001$). The schizophrenics failed to improve significantly between stages 1 and 2 ($F(1, 38) = 0·5$, $P = 0·48$), unlike the controls who did improve ($F(1, 38) = 25·5$, $P < 0·001$).

Serial strategy score

There was an evident failure for the control group to show use of a serial strategy for recall, whereas the schizophrenic group maintained their serial strategy. However, the ANOVA revealed only a significant main effect of group ($F(1, 38) = 3·9$, $P < 0·05$) with the schizophrenic group showing significantly enhanced serial

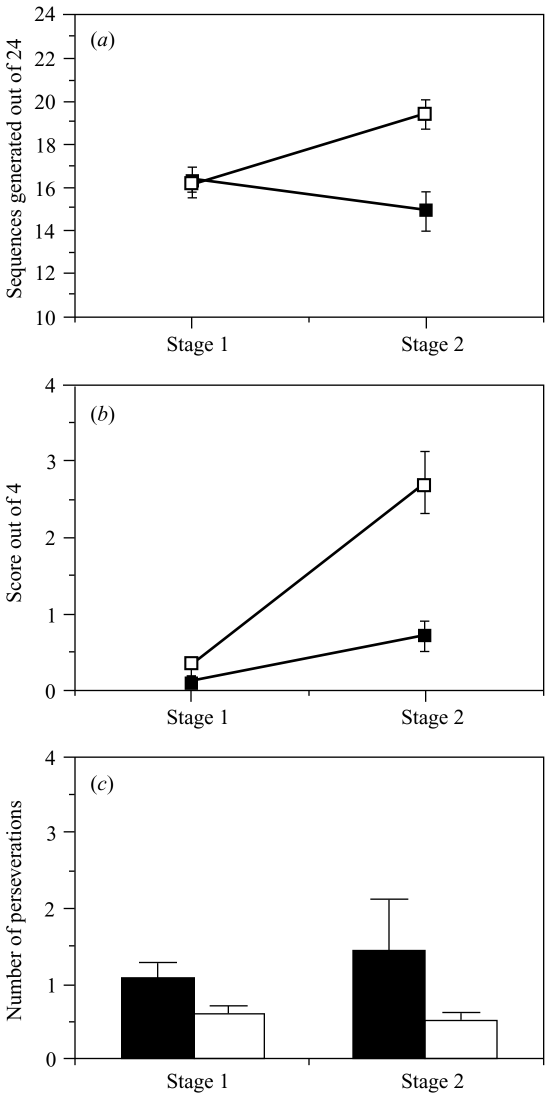

FIG. 2. Performance of schizophrenics (■) and controls (□) on the Visuospatial Strategy Task: (*a*) total sequences generated at stages 1 and 2, scores out of a total of 24; (*b*) strategy score for stages 1 and 2, scores out of 4; (*c*) perseveration score for stages 1 and 2.

strategy use. The interaction between group and stage failed to reach significance ($F(1, 38) = 1·15$, $P < 0·29$).

Semantic strategy score (see Fig. 3*b*)

As can be seen from Fig. 3*b*, the schizophrenic group, unlike controls, did not use a semantic strategy as confirmed by a main effect of group ($F(1, 38) = 56·11$, $P < 0·001$), stage ($F(1, 38) = 32·51$, $P < 0·001$) and a significant interaction between the two ($F(1, 38) = 24·2$, $P < 0·001$). When simple main effects were calculated this showed that controls used a semantic strategy significantly more than the schizophrenic group both at stage 1 of the task ($F(1, 38) = 11·52$, $P < 0·01$) and at stage 2 ($F(1, 38) = 62·3$, $P < 0·001$). The schizophrenic group failed to utilize a semantic strategy at stage 2 after training ($F(1, 38) = 0·32$, $P = 0·57$), whereas the controls showed an increased use of the strategy at stage 2 after training ($F(1, 38) = 53·44$, $P < 0·001$).

Semantic categorization time (see Fig. 3*c*)

As can be seen from Fig. 3*c*, the schizophrenic patients were substantially slower at sorting the words according to their correct semantic categories in the training phase of the task ($t(1, 38) = 7·12$, $P < 0·0001$). (Mean scores: controls = 65·9 s, S.E. = 2·6; schizophrenic patients = 149·8 s, S.E. = 11·5.)

Analysis of covariance

Further analysis was carried out on the data in the form of analysis of covariance (ANCOVA) to assess the contribution of certain factors on this test. When semantic strategy score was used as a covariate for performance at stage 1 the group difference remained significant ($F(1, 38) = 11·28$, $P < 0·01$). When performance at stage 1 was used as a covariate for performance at stage 2 of the task the difference also remained significant ($F(1, 38) = 10·8$, $P < 0·01$). However, this difference at stage 2 became non-significant when the semantic strategy score was used as a covariate ($F(1, 38) = 3·41$, $P = 0·07$). When semantic categorization time was used as a covariate for performance at stage 2 the difference between the groups remained significant ($F(1, 38) = 50·7$, $P < 0·001$). This implies that the differences between the groups at stage 2 did not arise simply from a failure of the schizophrenic patients to encode words at a semantic level, but suggests an additional difficulty in the generation and implementation of an organizational strategy.

Multiple regression analysis

(*a*) *Patients with schizophrenia*

The above analysis reveals that patients with schizophrenia are profoundly impaired on the verbal strategy task. However, it does not reveal

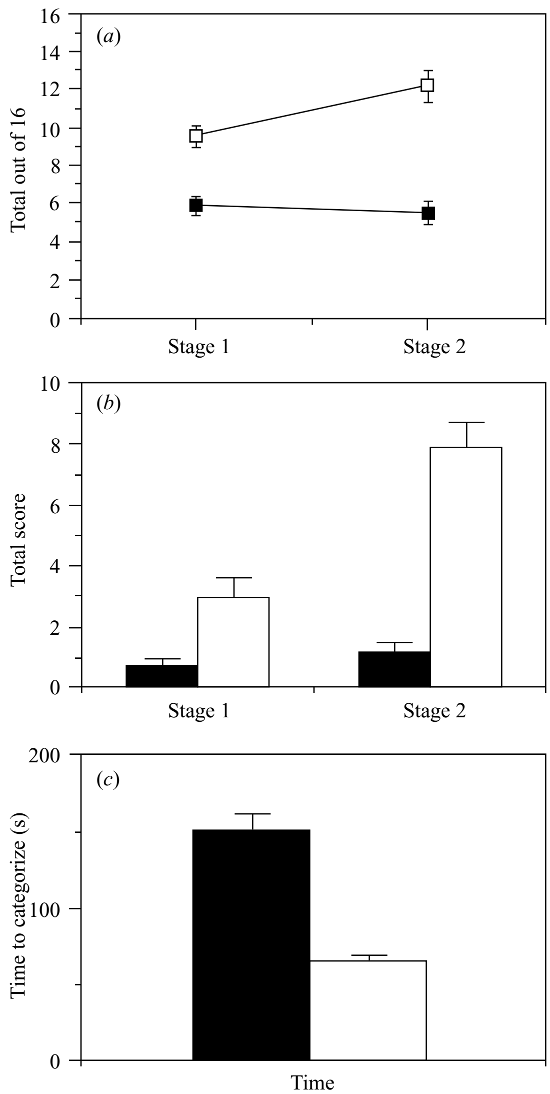

FIG. 3. Performance of schizophrenics (■) and controls (□) on the Verbal Strategy Task: (*a*) total words recalled at stages 1 and 2, scores out of 16; (*b*) semantic strategy score for stages 1 and 2, scores out of 12; (*c*) time taken to semantically categorize between stages 1 and 2.

the relative contributions of the different types of strategy scores to overall performance at different stages of the task. To clarify the contributions of these variables to impaired recall ability, two multiple regression equations were constructed, each one for the pre- and post-training stages of the task. The order of entry of the predictor variables was determined by the programme.

For stage 1 of the task serial and semantic strategy scores for stage 1 were entered into a multiple regression analysis, with total words recalled as the dependent variable. A stepwise-entry method was used as recommended by Howell (1992). No single factor accounted for a significant amount of variance at this stage, presumably because neither type of strategy was used significantly.

A similar regression equation was constructed for stage 2 of the task. On the first pass, semantic score was entered into the equation ($F(1, 18) = 24{\cdot}7$, $P < 0{\cdot}001$) accounting for 55% of the variance. Serial score was entered on the second pass ($F(1, 18) = 19{\cdot}3$, $P < 0{\cdot}001$) and accounted for a further 11% of the variance. Thus, these two variables accounted for 66% of the overall variance in scores for stage 2.

(*b*) *Control subjects*

A similar analysis was carried out for control performance. For stage 1 on the first pass semantic score entered into the regression equation ($F(1, 18) = 6{\cdot}6$, $P < 0{\cdot}05$) and accounted for 23% of the variance. On the second pass serial strategy was entered ($F(1, 18) = 6{\cdot}8$, $P < 0{\cdot}01$) and accounted for a further 14% of the variance. Thus these two variables together accounted for 37% of the variance in scores for total words recalled at stage 1.

For stage 2 only semantic score at stage 2 entered the equation ($F(1, 18) = 101{\cdot}5$, $P < 0{\cdot}001$) and accounted for 84% of the variance, consistent with the recruitment of the semantic strategy by the control subjects.

DISCUSSION

The central finding of this study is that schizophrenic patients were impaired in their ability to generate and learn explicit mnemonic strategies to complete effectively either a visuospatial or a verbal memory task. The use of strategies is a high-level cognitive function that engages working memory consistent with Baddeley's (1986) and Shallice's (1988) respective models of executive function, and thus with the view that schizophrenics exhibit executive impairments. This study employed parallel visuospatial and verbal tasks, performance on both of which could be improved by the use of defined strategies. Although the tasks were parallel in the sense that defined strategies could be employed to improve performance, they did differ in a number of respects other than simply modality. For example, the verbal task involved the learning of different word lists whereas the visuospatial task consisted of generating response sequences from the same set of response locations. Nevertheless, control subjects performed equivalently (in terms of percentage correct) on both tasks and benefited to a similar degree from the use of a cued strategy in each test. For control subjects the two tasks were roughly equivalent in difficulty on a percentage correct basis at both stages. In contrast, the schizophrenic patient group was much more impaired on the verbal as compared to the visuospatial task, at stage 1. However, this study has demonstrated a failure by patients with schizophrenia to use strategies to enhance performance in either of these two different tasks at stage 2, even when training in the use of an effective strategy was given.

It is important to note that we cannot at this stage distinguish between the capacity of the schizophrenic patients to generate or implement strategies. We have already shown that explicit training of the strategy employed in the visuospatial task improves performance in similarly aged patients with frontal lobe lesions or early onset Parkinson's disease (Iddon *et al*. 1998), however, schizophrenic patients have not yet been tested under this condition.

The failure of schizophrenic patients to capitalize on organizational saltrategies to enhance performance adds to early research on this topic. Thus, Cutting (1985) concluded that schizophrenic patients generally failed to show improvement in memory performance even when they were provided with mnemonic strategies such as pointing out that the initial letters of a sequence of to-be-remembered trigams were arranged alphabetically, or in a sequence, or in terms of semantic organization in lists of words. This latter finding, of failure to benefit from semantic organization in verbal recall tasks, has been reported in a number of studies (Calev *et al*. 1983; McClain, 1983; Delis *et al*. 1987; Gold *et al*. 1992; Kareken *et al*. 1996; Brébion *et al*. 1997). However, the specific novel contribution of this study has been to show impairments in generation of strategies in the visuospatial, as well as the verbal domain.

By themselves, however, these earlier findings did not establish that there is a specific deficit in the use of strategy by patients with schizophrenia, since such patients perform poorly on virtually any cognitive task (e.g. Chapman & Chapman, 1973) and commonly show some degree of general intellectual impairment (e.g. McKenna *et al*. 1994). This study has attempted to avoid this difficulty of interpretation by selecting the schizophrenic patients on the basis of their having preserved general intellectual function, in the sense that they were in the normal range on the MMSE and showed an estimated – current IQ decline from estimated pre-morbid levels of less than 15 points. However, despite being a generally intellectually well-preserved group, they failed to show any benefit whatsoever from training in the use of strategy on both tasks, still showing significant impairment over and above their preserved IQ. This adds to demonstrations of other selective cognitive impairments in similarly intellectually well-preserved subjects (e.g. Elliott *et al*. 1998).

A further requirement for demonstrating specificity of the strategy deficit in schizophrenia is to show that such impairment cannot be reduced to more fundamental aspects of performance. On the visuospatial task, which requires generation of a strategy and its holding in working memory, the strategy deficit was present in the context of unimpaired performance on other aspects of the task: these high functioning schizophrenic patients generated as many sequences as controls at stage one of the task, when a strategy was not explicitly required, and they also had an intact memory span score on this task. In the case of the verbal memory task it was significant that the schizophrenics tended to organize the words serially on both stages of the task, whereas controls resorted to a more efficient semantic strategy. A similar finding has been shown with Parkinson's disease patients (Buytenhuijs *et al*. 1994) and frontal lobe excision patients (Stuss *et al*. 1994) and it was suggested in the paper by Buytenhuijs *et al*. (1994) that this may reflect a distinction between externally (serial strategy) *v*. internally (semantic strategy) guided strategies with the latter proving to be significantly more efficient.

In the present study, the apparent semantic strategic impairment was accompanied by overall poorer verbal recall performance. An analysis of covariance using total words recalled at stage 1 as a covariate, showed that the stage 2 score was indeed dependent on the score at stage 1. However, further analysis showed that recall performance at stage 2 of the task was no longer significantly different between controls and schizophrenics when semantic strategy at stage 2 was used as a covariate. This was not the case when semantic score was used as a covariate for performance at stage 1 where the group difference remained significant. Therefore, it would appear that impaired performance on this task was due to two main factors, poor verbal memory and an inability to generate and use a semantic strategy. It also suggests that schizophrenic patients were disproportionately worse on verbal as compared to spatial memory tasks, a finding which gives further credence to the notion that schizophrenia is associated with changes in left temporal lobe structures (Crow, 1990; Kerwin *et al.* 1992; Goldberg *et al.* 1995). However, firm conclusions on this point may be unwarranted in the view of other differences in the task requirements.

To clarify the contributions that different processes made to performance on the two tasks, multiple regression analysis was also performed on the data. For both the schizophrenics and the control group it was shown on the visuospatial task that not generating a strategy during the training sequences was the main contributor to impaired sequence generation at stage 2. The same was also true for the verbal strategy task where the main influence on performance on stage 2 was whether a semantic strategy score was used, i.e. that the strategy had indeed been formulated during the training stage. So for both tasks multiple regression analysis confirmed that not generating an effective strategy was the major cause for overall impairment.

In fact, although the strategy deficit was not present in complete isolation from other cognitive impairments, the findings of this study are generally consistent with the emergent view of the pattern of neuropsychological impairment in schizophrenia, of deficits in executive function and memory that are disproportionate to the background level of general intellectual impairment/general poor performance (Shallice *et al.* 1991; McKenna *et al.* 1994; Elliott & Sahakian, 1995; Pantelis *et al.* 1998; Elliott *et al.* 1998). The patients in the present study, in whom general intellectual impairment was at a minimum, showed evidence of executive impairment (making the assumption that the generation of strategy is an executive function), and long-term memory impairment (in word list recall). In this study, the patients showed no impairment on a measure of working memory from the spatial task that taps the 'visuospatial sketch pad' (Baddeley, 1986). It is, however, controversial whether there is an impairment, or at any rate a disproportionate impairment, in working memory. Poor performance on working memory tasks has been found in some studies (Goldman-Rakic, 1991, 1996; Park & Holzman, 1992; Fleming *et al.* 1995; Javitt *et al.* 1995; Gold *et al.* 1997). For example, Park & Holzman (1992) compared schizophrenics and controls on spatial delayed-response tasks and found them to be impaired. Fleming *et al.* (1995) used a modified Brown-Peterson paradigm to compare working memory in the verbal domain and concluded that schizophrenic patients exhibit dysfunction of this system due to a dimunition in overall processing resources. Other studies, though, have not found clear evidence of impairment: Goldberg *et al.* (1993) compared reverse digit span between schizophrenic patients and their non-schizophrenic monozygotic co-twins and found only a trend to impairment.

The results of this study are consistent with deficits in those aspects of working memory that emphasize the central executive (Baddeley, 1986). This is especially the case for the visuospatial task. In neural terms the results support a neural theory of working memory processes that separate short term memory processes that 'hold stimuli on-line' (Goldman-Rakic, 1991) from processes which manipulate the information and which Petrides (1996) attributes to ventrolateral and dorsolateral prefrontal cortex, respectively. Specifically, it is hypothesized that the manipulation of information includes the processes that govern the formulation and possibly the implementation of encoding and retrieval strategies (Robbins, 1996; Shallice & Burgess, 1996).

The results add to recent findings of apparent deficits in different samples of schizophrenic patients on a self-ordered, spatial working memory task in which a consistent effective strategy is spontaneously generated by normal subjects, but to a much less successful degree in the patient groups (chronic schizophrenia, Pantelis *et al*. 1998; intellectually preserved schizophrenia, Elliott *et al*. 1998; first episode schizophrenia, Hutton *et al*. 1998). The present study has extended these observations by the demonstration of impairment in the generation of non-spontaneous, semi-cued strategies, in the verbal as well as the non-verbal, domains in a similar group of intellectually preserved schizophrenic patients as studied by Elliott *et al*. (1998).

The apparent deficits in strategic thinking are in keeping with a breakdown in functioning in schizophrenia in Shallice's (1988, Shallice & Burgess, 1996) Supervisory Attentional System, specifically affecting the higher level system which modulates contention scheduling. If indeed the contention scheduling system is forced to work alone in activating or inhibiting particular schema when the frontal system is dysfunctional, this would account for why schizophrenics are unable to develop strategies to cope with novel situations. The results were clearest in the spatial strategy task; here it was only when the executive process of strategy generation came into play that performance was impaired. Indeed, both the stage 1 score and the memory span scores did not differ from controls. On the verbal task, the strategic deficit was present against a background of poor memory although performance at stage 2 could not be entirely explained by this.

A lack of executive control in the schizophrenic group was also evident from the increases in perseverative responding in both stages of the visuospatial task, that are expressed as repetition of the entire four-element sequences. This perseveration can be seen as a hall-mark of a dysregulated contention scheduling system, and, almost certainly as a distinct deficit in executive control for strategy generation and implementation. The perseveration cannot be secondary to the loss of strategy because it occurred on the first stage of the task when in fact performance was not significantly worse than in controls – and patients with Parkinson's disease, who also exhibit a lack of utilization of strategy, nevertheless show no perseveration of the type observed here (Iddon *et al*. 1998).

The findings may also be relevant more widely to general theories of psychological deficit in schizophrenia. For example, Hemsley (1992 for review) suggested that the chief cognitive deficit in schizophrenia is a failure to use information about past regularities to inform current perception. A similar failure to use previously acquired information has also been proposed to underlie some of the socio-cognitive deficits seen in schizophrenia (Corcoran *et al*. 1995). Frith (1987, 1992) has proposed that defective central monitoring may underlie a range of key symptoms in schizophrenia. His hypothesis, supported by direct experimental evidence (Malenka *et al*. 1982; Frith & Done, 1989; Mlakar *et al*. 1994), is that patients may be unable to reflect (consciously) upon their own mental activity, and suggests that problems will be especially prominent on tasks where continuous monitoring of action is an important component and where the actions are generated in response to wishes, plans and intentions rather than in response to environmental stimuli. There are obvious homologies between Frith's account and the notion of breakdown in the Shallice's supervisory attentional system. It could also be argued that concepts of self-generation and monitoring of intentions is not so very different from the strategic generation and use of algorithms or rules for guiding behaviour that are required for the present tasks.

In terms of brain localization, the pattern of poor performance by schizophrenic patients on the visuospatial strategy task in the present study is similar to that seen in patients with frontal lobe excisions and patients with Parkinson's disease but differs from that of patients with temporal lobe excisions who were unimpaired overall (Iddon *et al*. 1996, 1998). The picture was slightly different on the verbal task: whereas the schizophrenic patients were poor at recalling words and unable to generate a strategy, frontal excision and patients with Parkinson's disease were unimpaired on part 1 of the task (Iddon *et al*. 1998), recalling as many words as controls. However, they were impaired in the generation of a semantic strategy and subsequently in their recall of the second set of words, subsequent to training. Patients with either left or right temporal lobectomy showed a different pattern: they were impaired in terms of memory recall, but unimpaired at generating a semantic strategy (Iddon *et al*. 1998). Therefore, these findings further implicate dorsolateral prefrontal and fronto-subcortical structures as well as temporal lobe involvement in the neuropsychology of schizophrenia.

In conclusion, the data presented here provide perhaps the first clear demonstration that schizophrenic patients are unable to generate effective strategies to complete difficult cognitive tasks, and that this deficit is not domain specific. These results cannot be attributed to a general intellectual decline or to normal ageing effects. They suggest that both frontostriatal and temporal regions of the brain are malfunctioning in the schizophrenia syndrome. These results are also interesting in terms of our understanding of the 'core' cognitive deficits that may have implications for everyday life.

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