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A Longitudinal Analysis of Memory in Patients with Schizophrenia

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Memory deficits are widely reported in patients with schizophrenia, but uncertainties remain about the extent and the longitudinal course of these deficits. Twenty-eight patients with a DSM-IV diagnosis of schizophrenia were tested on multiple aspects of memory at baseline, 9- and 18-month follow-up. Measures included: digit span, the Rivermead Behavioural Memory test (RBMT) battery, the Graded Naming Test (GNT) and several computerized memory tests from the Cambridge Automated Neuropsychological Testing Battery (CANTAB). A group of healthy controls (N=17) was tested on the CANTAB battery at baseline and 9-month follow up. The patients performed significantly poorer than controls on all CANTAB measures; however, there was no difference in change between groups over a 9-month period. Within-group patient comparisons revealed that symptoms reduced significantly over the study period, but had no association with memory. Significant improvements were observed for patients on two verbal memory tasks: the GNT and digit span, but not on any other measure. Interestingly, these were the only two tests on which patients were within normal limits at baseline. This study shows that patients with schizophrenia have deficits in multiple aspects of memory which remain stable over long periods of time. In addition, patients showed a tendency to improve on memory tasks which contained a verbal component.

Introduction

Little doubt remains that patients with schizophrenia have substantial memory deficits (e.g., Aleman Hijman, de Haan & Kahn, 1999), and these are often disproportionate to the general level of intellectual impairment and other aspects of cognitive function (Saykin et al., 1991; McKenna et al., 1990). It appears that multiple aspects of memory are affected because deficits have been reported in short term memory (e.g., Aleman et al., 1999; Conklin, Curtis, Katsanis & Iacono 2000), working memory (e.g., Minor & Park, 1999; Pukrop et al., 2003), semantic memory (e.g., Granholm, Chock & Morris 1998; Laws, Al-Uzri & Mortimer 2000), episodic memory (e.g., Cannon et al., 2000; Mellers, Toone & Lishman, 2000), recognition memory (e.g., Crespo-Facorro et al., 2001; Tracey et al., 2001) and recall (e.g., Paulsen et al., 1995; Putnam & Harvey, 1999).

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Nevertheless, an important and unresolved question relates to the longitudinal course of memory deficits. Are they stable? Do they fluctuate with symptom exacerbation and remediation or medication effects? Is there a progressive deterioration? An answer to these questions can shed light on 'trait' or 'state' theories of the origins of the memory deficits. Trait theories suggest that deficits are the result of structural abnormalities that are stable and largely unchanging. State theories suggest that memory deficits are unstable and result from neurochemical or neurophysiological disturbances which change over time in relation to medication effects and / or fluctuations in symptom profile. It is also plausible that memory dysfunction in schizophrenia involves both theories, with some functions being impaired and stable, whilst others fluctuate (Nopoulos, Flashman, Flaum, Arndt & Andreasen 1994). In addition, the possibility remains that some aspects of memory deteriorate over time. This suggestion is consistent with the classic Kraepelinian notion of 'dementia praecox'.

Previous investigations of the stability of memory function in patients with schizophrenia have produced mixed results, with about less than half reporting change in either direction (See Table 1). Of those studies that have reported change, some have reported improvements in verbal memory (Addington, Addington & Maticka-Tyndale 1991; Albus et al., 2002; Bilder et al., 1991; Gold et al., 1999; Sweeney, Haas, Keilp & Long 1991), visual memory (Addington et al., 1991; Albus et al., 2002); and short term memory (Rund, Landro & Orbeck, 1997). Conversely, others have reported deteriorations in visual memory and short term memory (Albus et al., 2002; Bilder et al., 1991). Such heterogeneity is underlined by the fact that all of those studies reporting some change(s) also reported no change on other memory tests. Moreover, the studies used a variety of methodologies that may also account for discrepant findings (e.g., differing lengths of illness, medication, symptom profiles and so on). Nevertheless, most of the previous studies have only focussed on two or three distinct aspects of memory and therefore the temporal stability of several important aspects of memory has not been previously investigated. These include pattern recognition, spatial recognition, spatial working memory, spatial short term memory and episodic memory.

Additionally, where different studies have assessed the same aspects of memory, the tests used have usually been different which limits the general conclusions that can be drawn. For example, of the six studies that have explored the temporal stability of verbal short term memory, three different types of tests have been used: two versions of the digit span test (Oltmanns & Neal, 1975; Wechsler, 1981), and the distractor technique (Peterson & Peterson, 1959). Another problem is that most studies have assessed patients only twice—at baseline and at follow-up. With this approach it is possible that short term fluctuations in performance at either time point—for example, reflecting motivational changes, the commencement or discontinuation of medications, or even regression to the mean might confound the results. To get a clearer and more definitive picture of the long term stability of memory function in schizophrenia, multiple follow-up assessments are needed.

Finally, additional important issues arise for longitudinal studies of cognitive performance in schizophrenics or any other group. Longitudinal studies are, by their very nature, suspect to a variety of problems that do not occur with snapshot studies and are different to those in cohort studies. Problems include patient drop-out, potentially reduced samples for follow-up examinations both of patients and of controls, length of follow-up that is practical, changes in medication, symptom status and so on. These problems are balanced, however, by the fact that some questions concerning the natural history of disorders cannot be definitively addressed using snapshot or cohort studies. This is especially true of

Table 1
Summary of previous investigations of the stability of memory function in schizophrenia[a]

Studies	N	Follow-up period	Aspect of memory measured and tests used	Outcome
Rund (1989)	14	48 Months	Short tem memory - Digit span (Oltmanns & Neale, 1975)	Paranoid schizophrenics not as stable as non paranoid schizophrenics
Bilder et al. (1991)	28	12 months	Verbal memory Visual memory - Wechsler Memory Scale Revised Short term memory (Wechsler, 1987) (verbal & visual)	Improvements in verbal and visual memory. Decline in digit span and visual span
Addington et al. (1991)	38	6 months	Verbal memory - Wechsler Memory scale (Wechsler, 1945) Visual memory - Rey-Osterrieth Figure (Rey, 1941)	Improvement on delayed visual memory and immediate verbal and visual memory
Sweeney et al. (1991)	39	12 Months	Short term memory - Digit span (Wechsler, 1981) Verbal memory - Rey Auditory Verbal Learning test (Rey, 1964) Visual memory - Wechsler Memory Scale Revised (Wechsler, 1987)	Significant improvement in recognition memory on the RAVLT. No change[b] on other measures
Hoff et al. (1992)	17	24 Months	Verbal memory - California Verbal Learning Test (Delis et al., 1983) Wechsler Memory Scale (Wechsler, 1945) Spatial memory - Benton Visual Retention test (Benton et al., 1974) Wechsler Memory Scale (Wechsler, 1945).	No change
Nopoulos et al. (1994)	35	12 or 24 Months	Verbal memory - Logical Memory Test (Wechsler, 1945) Rey Auditory Verbal Learning Test (Rey 1964) Paired Associates (test unspecified) Visual memory- Benton Visual Retention test (Benton et al., 1974)	No change

Continued

Table 1
(Continued)

Studies	N	Follow-up period	Aspect of memory measured and tests used	Outcome
Rund & Landro (1995)	22	12 Months	Short term memory - Distractor Technique (Peterson & Peterson, 1959) Long term memory - ContinuousDistractor Paradigm (Bjork & Whitten, 1974)	No change
Rund et al. (1997)	15	12 & 24 months	Short term memory - Distractor Technique (Peterson & Peterson, 1959) Long term memory - Continuous Distractor Paradigm (Bjork & Whitten, 1974)	Significant improvement in short term memory No change in long term memory
Censits et al. (1997)	60	19 Months	Verbal memory - Logical Memory Passages (Wechsler, 1945) California Verbal Learning test (Delis et al., 1983) Spatial memory - Design Reproduction (Wechsler, 1945)	No change
Gold et al. (1999)	54	60 Months	Delayed visual memory - Rey-Osterrieth Figure Delay (Rey,1941) Free recall verbal - Logical Memory Test (Wechsler, 1945)	Immediate recall improved on the Logical Memory Test. No change on other measures
Rosmark et al. (1999)	14	17 Months	Visuo-spatial STM - Memory for designs (Graham and Kendall, 1960) Verbal memory - Verbal learning test and retention test (Claeson et al., 1971)	No change
Heaton et al. (2001)	142	Annual assessment up to 10 years from baseline.	Short term memory - Digit span (Wechsler, 1981) Visual memory - Figural Memory (test unspecified) Verbal memory - California Verbal Learning Test (Delis et al., 1983) Story Recall (test unspecified).	No change

Continued

Table 1
(Continued)

Studies	N	Follow-up period	Aspect of memory measured and tests used	Outcome
Albus et al. (2002)	50	24 Months	Semantic memory – WMS-R (Wechsler, 1987) Visual memory - Verbal memory - California Verbal Learning Test (Delis et al., 1987)	Improvement on the CVLT. Deterioration on visual reproduction. No change on logical memory

[a] The studies included explicitly investigated the longitudinal stability of cognitive deficits in schizophrenia. Other longitudinal investigations of cognition, such as those exploring medication effects or the effects of cognitive remediation therapy, were not included.
[b] 'No change' denotes that either there were no significant differences in performance between baseline and follow-up, or that any changes observed were comparable to changes in control performance.

cohort studies when one considers the degree of cognitive and symptomatic heterogeneity in samples of schizophrenics.

Some problems associated with past studies may, however, be readily addressed. The first concerns the reliability of memory tests themselves. Obviously if tests have low reliability this can lead to apparent change in cognitive function. In this case, it is notable that the reliabilities of the memory scores are often poorer than for other cognitive skills especially for delayed retention measures (Goldstein & Watson, 1989; McCaffrey & Westervelt, 1995; Mitrushina & Satz, 1991). Indeed, the longitudinal stability of memory in patients with schizophrenia has been investigated using various subscales of the Wechsler memory test and other standardised memory measures (see Table 1); however, some have quite low reliability (see Dikmen, Heaton, Grant & Temkin, 1999). For example, the paired associates test has a test-retest reliability of .58; visual reproduction .62; logical memory is better at .70). A second major issue concerns separating practice effects from genuine change. Obviously when retested, some change may reflect practice. To address this, it is necessary to include a control sample to determine the degree of practice effect that may exist on tests. Examining the studies of memory in schizophrenia in Table 1, a minority (6/13) included controls (Albus et al., 2002; Censits, Ragland, Gur & Gur, 1997; Heaton et al., 2001; Rund, 1989; Rund and Landro, 1995; Rund et al., 1997). Given the normal impact of aging on memory, it is also necessary to match controls with the patients on such relevant variables.

The aim of the following study is to provide a comprehensive investigation of the stability of memory function in schizophrenia. The study details the longitudinal course of aspects of memory that have not been previously investigated and attempts to address some of the flaws in previous studies by choosing memory tests with higher reliability and by examining the influence of practice by including a matched control comparison group tested at the first two time points. The patients were selected for testing to fit a variety of criteria, including that they: met all of the usual exclusion criteria (history of head injury or other neurological problem, evidence of drug or alcohol abuse); had normal estimated premorbid intellectual functioning; no sign of dementia; were similar in age to patients in previous studies; and displayed a wide range of length of illness. Given the variability in previous studies, we attempted to select a group that was relatively comparable with most previous studies. A secondary aim of this study is to investigate associations between memory function and I.Q., symptoms and medication.

Materials and Methods

Patients

Twenty-eight patients (18 males; 10 females) with a DSM-IV diagnosis of schizophrenia were recruited from inpatient and outpatient units in East Yorkshire, UK. DSM-IV diagnosis was made using both a clinical interview and a review of the patient's history. This was completed by AMM, Professor of Psychiatry at the University of Hull. Patient selection was also based on the following criteria: age between 18 and 60; no history of neurological disease or head trauma; no history of drug or alcohol abuse. All were screened for global cognitive impairment using the Mini Mental State Examination (MMSE: Folstein, Folstein & McHugh 1975) and their mean of 27 (SD= 2; range 22-30) indicates that the majority of the group are functioning within the normal cognitive range (one patient

scored below the 24 cut-off). The Brief Psychiatric Scale (BPRS) was used to assess symptom type and severity (Hedlund & Vieweg, 1980).

The average age of the sample was 34 years (SD = 10; range 18–54) and so comparable with similar longitudinal studies (mean age in Table 1 was 33.5). At the time of their inclusion in the study, the patients had an average length of illness of 8 years; however, we selected a wide range of illness length: from 3 weeks to 38 years (SD = 9 years). The mean score on the BPRS was 15 although there was considerable variance in symptom presence, with patients scoring between 2 and 28. When the BPRS score was broken down according to the four symptom dimensions identified by Overall (1976), the ratings were: thinking disturbance (mean = 5.9, SD 3.4, range 0–12); withdrawal/retardation (mean = 2.7, SD 3.5, range 0–13); hostility/suspiciousness (mean = 2.4. SD 2.0, range 0–9), and anxiety/depression (mean = 7.0, SD 3.2, range 1–14). Patients were on the following antipsychotic medications for the duration of the study (patient numbers and mean daily dose at baseline in brackets); Chlorpromazine (N–1; 200 mg), Olanzapine (N = 4; 10mg), Clozapine (N = 8; 209mg), Quetiapine (N = 5; 330 mg) Risperidone (N = 6; 4mg), Amisulpride (N = 4; 550mg). Only one patient was on typical neuroleptics and anticholinergics[1]. Antipsychotic dosages were converted to the Percentage of Maximum Dose (PMD) according to the British National Formulary (BNF, 2004) in order to investigate associations between dosage and neuropsychological test performance. This method of comparing antipsychotic potency is considered more reliable than using chlorpromazine equivalents (Yortson & Pinney, 2000). There was minimal change in medication dosage over the study period.

Controls

Seventeen non-psychiatric controls who were sampled from non-academic staff at the University of Hull and who were demographically similar to the patient group were included in the study. The controls were matched with the patients for age (39.4 vs. 33.85: $t_{43} = -1.69$, $p > .05$) and estimated premorbid IQ (106.17 vs. 101.17: $t_{43} = -1.29$, $p > .05$) as measured by the National Adult Reading test (NART: Nelson, 1982).

Tests and Procedure

Patients were assessed on all memory measures at baseline, 9-month and 18-month follow-up. These time intervals were set in order to get a long-term picture of memory function in schizophrenia. Indeed, many previous follow-up studies of cognition in schizophrenia have been criticised for their short-term focus (Keefe, Silva, Perkins & Lieberman, 1999). Memory tests were chosen to reflect a full range of memory abilities and to include tests that have good reliability (see below).

Digit span test (DS: Wechsler, 1981)

This test is considered to reflect short-term auditory memory and requires a subject to repeat an increasing sequence of numbers in the same order as they have been read to them. The reliability for the DS tests is high (.88: Wechsler 1987).

[1] The performance of this patient was not different from those not taking anticholinergics.

Rivermead Behavioural Memory Test (RBMT: Wilson, Cockburn & Baddeley, 1985)

This test provides an ecologically valid assessment of everyday memory function. This battery comprises the following subtests:

- Remembering a name (given the photograph of a face)
- Remembering a belonging (a belonging of the subject is concealed and the subject has to remember to ask for it back at the end of the session)
- Remembering a message after a delay (the subject is told to say some key words when an alarm rings after 20 minutes)
- An object recognition task (10 pictures of objects are shown, and the subject then has to recognize these out of a set of 20 pictures shown after a delay)
- A face recognition task (similar to object recognition, but using five faces to be recognized amongst five distracters)
- A task requiring the subject to remember and follow a route around the room both immediately and after a delay
- Delivering a message—whilst retracing the route around the room the subject has to remember to place a message envelope in a specific place
- Recall of a short story both immediately and after a delay
- Orientation and date questions

The RBMT test-retest reliability for the profile score (combining all subtests) used here is .85

Graded Naming Test (GNT: McKenna & Warrington, 1983)

This test of naming to picture taps aspects of lexical/semantic memory. There is no reliability data for the GNT; however, as a test of lexical-semantic ability, rather than episodic memory it should have high reliability. For example, the highly comparable Boston Naming Test has a test-retest reliability of .92 (Dikmen et al., 1999).

Cambridge Automated Neuropsychological Testing Battery (CANTAB)

The remaining tests were taken from the Cambridge Automated Neuropsychological Testing Battery (CANTAB: Morris, Evenden, Sahakian & Robbins 1987). This is a computerized battery of tests that are presented on a touch screen computer:

Pattern and Spatial Recognition

These tests follow the traditional structure of recognition memory tests where subjects have to pick out items they have previously seen. The pattern recognition test utilizes colored, nonverbalizable patterns that are displayed individually during the presentation stage of the task, and with a distracter during the recognition stage. The same procedure is utilized for the spatial recognition task except that the stimuli are white squares appearing at random locations on the computer screen. Recognition scores for both tests are converted to a percentage of the total correct responses made.

Spatial Span

This is a computerised analogue of the Corsi block-tapping test (Milner, 1971) and requires the subject to observe and remember the sequence and location of a series of

boxes changing color. Scoring on this test is in terms of the maximum sequence of squares changing color that the subject could successfully follow (between 2 and 9).

Spatial Working Memory

This test requires the subject to search through an increasing number of boxes on the computer screen in order to locate tokens. Once a token has been found in a particular box, another will not appear in the same box and therefore the subject has to keep track of the locations where they have previously found tokens and remember not to re-search that box. The main type of error that is recorded on this test is a *between–search error* when the subject returns to a box where a token was previously found. In addition, a score representing the strategy used to complete the task is also recorded. An optimum strategy would be for the subjects to follow a pre-planned search sequence, starting with one box and returning to that box at the beginning of a new search after a token has been found. A high strategy score would be obtained if the subject used the same starting location for the search within each of the six and eight box problem. A low score represents random starting positions for each search. The range of strategy score is between 1 (optimum) and 37 (very poor).

As noted above, memory tests often have low reliability. In a recent review of the Test Retest Reliability (TRR) of memory tests, Paolo (1998) introduced a categorical system of TRR coefficients, declaring >0.8 to be 'good', 0.6–0.8 to be 'fair' and scores of <0.6 to be 'poor'. As noted by Paolo, the application of this system to the TRR of a number of well-known memory tests shows that the majority of tests fall within the fair category, though some are clearly poor. Two studies (CeNeS, 2000; Lowe and Rabbitt, 1998) have examined the TRR reliability for the CANTAB battery. According to the Paolo criteria, the Pattern Recognition test (.72, .84) has good reliability; the Spatial Working Memory test (.70, 68) and the Spatial Span task (.60, .64) are fair; however, the Spatial Recognition test (.48, .57), has poor reliability (although the reasons for these lower reliabilities are unclear).

Results

Between-groups (Baseline to 9 Months)

There was no evidence of either floor or ceiling effects in the data for patients or controls. Separate two-way ANOVAs with time (baseline and 9 months) and group (patients and controls) as factors were used to analyze data from the CANTAB tests. In each case, the patients performed significantly worse than controls, but the main effect for time and the interaction for group-by-time were not significant. Hence, although showing worse memory, there was no evidence of greater change in the schizophrenic patients than controls over 9 months.

Memory scores for patients correlated widely and significantly with NART IQ at most time points (baseline correlations are in Table 2); however, covarying for baseline IQ made no difference to the results.

Within Patient Comparisons Over 18 Months

Further data was available for the patients at an 18 month follow-up and this was analyzed using a within-patient ANOVA to analyze patient change (see Table 3). Except for a trend

Table 2
Correlations between baseline memory tests and NART IQ in schizophrenic patients

Baseline memory scores	NART IQ
Spatial span	.36
Pattern recognition	.38
Spatial recognition	.51
Spatial working memory strategy	−.29
Spatial working memory error	−.67
GNT	.42
RBMT	.46
Digit span	.36

* Except for digit span and SPWMS, all $p < .05$.

Table 3
Longitudinal performance of schizophrenics on the CANTAB memory tests

Memory scores	Baseline Mean[SD]	9 months Mean[SD]	18 months Mean [SD]	Time difference
Spatial span	4.89 [1.70]	4.86 [1.76]	5.39 [1.31]	$F_{2, 54} = 2.77$, $p = .07$
Pattern recognition	77.63 [13.78]	77.77 [14.38]	80.55 [15.10]	$F_{2, 52} = 0.58$, $p = .56$
Spatial recognition	71.29 [13.56]	67.96 [14.29]	70.18 [13.19]	$F_{2, 52} = 0.51$, $p = .60$
Spatial working memory strategy	36.77 [5.25]	34.46 [5.51]	35.15 [5.02]	$F_{2, 50} = 2.19$, $p = .12$
Spatial working memory error	45.08 [25.74]	40.15 [21.92]	38.96 [22.26]	$F_{2, 50} = 1.22$, $p = .30$

for spatial span to improve (reflecting a significant 9 to 18 month improvement: $t_{27} = 2.3$, $p = .03$), there were no significant effects of time on the memory performance in the patients and so, accords well with the control-based comparisons.

Additionally, patient data for the three times was available for the Graded Naming Test, Rivermead Behavioural Memory Test battery and forward digit span. On the GNT and digit span, the patients showed significant improvement and were within the low-average normal range at baseline (see Table 4); in both cases this reflected an improvement between baseline and 18 months ($t_{25} = 2.7$, $p = .01$ and $t_{26} = 3.7$, $p = .005$). Critically, the GNT scores did not differ from those predicted by their NART IQ scores ($t_{25} = 0.11$, $p = 0.88$). By contrast, compared to test norms, their RBMT scores indicated poor memory and this did not change significantly across time. Finally, we combined the visual and verbal subtests of the RBMT into a visual and a verbal memory score—neither revealed changes across time (both $F < 1$).

Symptoms and Medication

Analysis of BPRS scores over 18 months revealed a significant decrease in symptoms ($F_{1, 27} = 37.5$, $p = .000$: baseline 15.29 ± 7.12; 9 months 9.75 ± 7.38; and 18 months

Table 4
Longitudinal performance of schizophrenics on tests tapping verbal memory

Test scores	Baseline Mean [SD]	9 months Mean [SD]	18 months Mean [SD]	Baseline comparison with Normative data and Effect Size (d)	Time difference
Graded Naming Test	18.88 [4.58]	19.46 [5.02]	19.96 [5.13]	25-50th percentile n = 710: Warrington 1997 d = .56	$F_{2, 50}$ = 3.77, p = .03
Rivermead Behavioural Memory Test	16.88 [5.56]	17.92 [4.76]	17.88 [4.51]	<5th percentile n = 118: Wilson et al., 1991 Indicates moderate to poor memory d = 1.76	$F_{2, 52}$ = 1.13, p = .33
Digit Span	6.04 [0.84]	6.28 [0.79]	6.44 [0.82]	Within normal range 7 ± 2	$F_{2, 48}$ = 4.32, p = .02

8.61 ± 5.48). Indeed, only 3/28 (<10%) patients failed to show improvement. The reduction reflected a significant decrease in symptoms from baseline to 9 months (t_{27} = 5.02, p = .000); the change between 9 and 18 months was nonsignificant (t_{27} = 1.2, p = .23).

Despite the change in symptoms, there were no significant correlations between the BPRS change scores (baseline to 9 months; 9 months to 18 months) and changes in memory or memory at baseline (the vast majority of correlations were between zero and .1). Finally, turning to potential medication effects, there were no significant correlations between the percentage of maximum dose and any test at any time point.

Discussion

The aim of this study was to examine various aspects of memory in patients with schizophrenia and to determine which areas of memory are impaired, whether they are stable across time and how (if at all) they might relate to factors such as IQ, symptoms and medication. The current study used a large battery of memory tests to examine a wide range of memory abilities, including: visual and verbal, short-term and long-term, episodic and semantic, recall and recognition. Patients with schizophrenia consistently performed worse than controls (and/or below normative levels) on the tests. Although IQ correlated with memory performance in patients (as expected), covarying for IQ made no difference to the outcome of analyses. Hence, the memory problems are not attributable to any general intellectual deficit and would appear to be stable across time (at least for 18 months) for most aspects of memory. Nevertheless, it should be noted that the measure of IQ was an estimate of *premorbid* functioning and the patients were relatively normal on this measure. Hence, the results could be different for premorbidly less capable individuals or if a measure of current IQ (such as the WAIS) were used.

The patients did show a relatively more intact performance on some more verbally-based tasks and this was accompanied by significant improvement across time for 2 of 3 verbal tasks (digit span and picture naming). These positive changes may be due to the effects of the atypical antipsychotics used in the current study, as several of these have been shown to enhance verbal functioning in patients with schizophrenia (Green et al., 1997; Keefe et al., 1999). All aspects of memory performance were independent of symptom ratings and level of medication.

Given our largely null result, it is, of course, feasible that our study lacked power because of the sample size[2]. Nevertheless, our sample size was comparable with the average in past studies (see Table 1); and if anything, past positive findings emerged in studies using smaller or comparable sample sizes (and most null results have emerged in the larger studies). This suggests that change (across comparable or shorter periods) should be detected with samples of this size. Along with the fact that we used a large memory battery and our inclusion of memory tests with higher reliabilities (than those typically used in previous studies) also leads us to believe that our null findings should not be dismissed as a product of a small sample and any consequent power problems. Despite this, the test-retest reliability coefficients were somewhat lower for two tests: spatial span and spatial recognition (though comparable to some previously used memory measures). If anything, the finding of impaired memory in patients on tests with both high (digit span, RBMT, spatial recognition, pattern recognition) and low reliability (spatial span and

[2] A post hoc power analysis showed that for the smallest effect size obtained (.5), the power to detect group differences was .7.

spatial recognition) indicates that the failure to find time related changes is not attributable to reliability issues.

Previous research in this area has yielded conflicting results which is perhaps unsurprising given the differences in: medications prescribed (typicals vs. atypicals), methodologies employed, tests used, number of patients recruited, length of follow-up period and the poor reliability of many memory tests. Nevertheless, some consistent findings have emerged. Only 2 of 13 studies, that have explored the temporal stability of memory function in schizophrenia, have found that aspects of memory worsen over time. Although Bilder et al. (1991) reported that digit span and visual span declined over 12 months, these findings were not replicated in several other studies that also measured the same abilities (Addington et al., 1991; Heaton et al., 2001; Hoff et al., 1992; Rosmark et al., 1999; Rund & Landro, 1995; Rund et al., 1997; Sweeney et al., 1991). In addition, the finding by Albus et al. (2002) that visual reproduction declined over a 24-month period is also not consistent with previous research (Gold et al. 1999; Heaton et al. 2001; Hoff et al., 1992; Nopopolous, 1994; Sweeney et al., 1991). Hence, as with the majority of previous studies, the current study accords with the notion that memory function is substantially impaired, but does not progressively deteriorate in schizophrenia; and may improve in some cases for some aspects of memory (principally verbal in this study).

In the current study, we found no association between memory and medication dosage at any time point. Although a link between memory changes and medication has been reported (Albus et al., 2002; Rund et al., 1997; Sweeney et al., 1991), others have found no link (Censits et al., 1997; Nopoulus et al., 1994; Saykin et al., 1994) and the recent meta-analysis by Aleman et al. (1999) indicates that medication dosage is not a moderator of memory function in schizophrenia. Another unresolved and related issue concerns any association between memory changes and psychotic symptoms. Although several studies, including the current one, have found no association (Addington et al., 1991; Albus et al., 2002; Gold et al., 1999; Heaton et al., 2001; Nopoulus et al., 1994), others have reported an association (Censits et al., 1997; Hoff et al., 1992; Rund et al., 1989; Sweeney et al., 1991). As noted, schizophrenic patients are quite heterogenous in their cognitive performance and symptom profiles and so our results may reflect certain characteristics of this cohort, e.g., their tendency to show symptom improvement across time. Unfortunately, we could not compare a set of patients who did and did not improve because only 3/28 failed to improve during the study. Nevertheless, the current results do accord with the meta-analysis of Aleman et al. (1999) who showed that neither severity of symptoms nor illness duration moderate memory performance. Significant improvements were observed in short-term memory and semantic memory. Clearly, these tests are different from the rest of the battery because both are verbally based, and several previous studies have reported improvements in verbal memory (Addington et al., 1991; Albus et al., 2002; Bilder et al., 1991; Gold et al., 1999; Rund et al., 1997; Sweeney et al., 1991). Digit span does usually provide a lower effect size than other aspects of memory generally (.71 vs. 1.21: Aleman et al., 1999). With regard to the GNT, this is intriguing because severe deficits have been documented in patients with schizophrenia (e.g., Garbrovska, Laws, Sinclair, McKenna, 2000; Laws, Al-Uzri and Mortimer 2000). The patients in the current study were, however, younger than those tested by Laws et al. and Gabrovska et al. (33 vs. 46 and 42 years) and had been ill for much less time (8 vs. 23 and 20 years). It is therefore feasible that protracted illness leads to greater deficits in semantic and lexical memory. While length of illness may not directly relate to degree of memory impairment, it may be that different types of memory impairment occur at different points during the course of the illness. For example, semantic memory impairment may occur after episodic

impairment. Indeed, Al-Uzri, Laws and Mortimer (in press) have also recently shown that picture naming is intact in younger schizophrenic patients (mean age = 34, illness duration 11 years).

To return to our empirical questions, it seems that many memory functions are impaired quite early in the course of illness and remain quite stable (at least over 18 months). Nevertheless, one novel finding from this study concerns semantic lexical memory and how that remains intact even in patients with quite severe episodic memory deficits (both for verbal and nonverbal material). Similarly, digit span remained well within the normal range and even showed a tendency to improve (as did name GNT performance). The intriguing aspect of these findings is that we know from other studies that performance on these tasks is impaired (and very severely) in older patients with more chronic length of illness. This suggests that in schizophrenic patients, lexical semantics may hold up better and for longer than their episodic memory which shows substantive but stable impairments.

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