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Visuospatial learning and executive function are independently impaired in first-episode psychosis

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ABSTRACT

Background. Demonstrating specific cognitive impairments in psychotic disorders is difficult. However, specific deficits in memory and executive functions have often been claimed. The Cambridge Neuropsychological Test Automated Battery (CANTAB) tasks of IDED attention-shifting (an executive task) and visuospatial paired associates learning (PAL, a memory task) require intact frontal and temporo-hippocampal functioning, respectively; both have been suggested as markers of disease progress in psychosis.

Method. Seventy-one subjects with a first-episode psychosis or at-risk mental state were assessed on these two tasks during referral to a specialist service, the Cambridge-based CAMEO early intervention team.

Results. Performance on the two tasks was dissociated. Poor performance on the PAL test was associated with increased symptom levels and poorer global function, while failure on the IDED executive test was not found to have significant clinical associations. Duration of illness was not associated with performance on either task.

Conclusions. Visuospatial PAL failure may be a marker of clinical severity at the onset of psychosis while IDED performance may reflect a more stable, trait-like impairment. Dissociated performance on the executive and associative learning tasks may reflect independent, neurally dissociated impairments that do not arise in a fixed order. This may explain some of the heterogeneity of cognitive function seen in early psychosis.

INTRODUCTION

There is a long-standing debate concerning the extent to which the cognitive impairment seen in schizophrenia consists of domain-specific impairments such as memory or executive function, and the extent to which it is a generalized impairment (Blanchard & Neale, 1994; Mohamed *et al*. 1999). This is theoretically important since it implies whether hypothesized structural or functional brain abnormalities will be global or localized in nature.

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Neuropsychological testing is increasingly common in psychosis clinics but there are methodological problems in determining specific impairments using standard neuropsychological batteries. First, even well-validated tests differ in terms of discrimination, so a person with general cognitive impairment may pass one test but fail another simply because the second was more discriminative. This has been the subject of much psychometric debate (see Chapman & Chapman, 2001) but is largely ignored by non-psychometric researchers, including those arguing for specific deficits on the basis of greater impairment on one test than another (e.g. Riley *et al*. 2000). Secondly, most neuropsychological

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tests are polyfactorial, requiring intact processing in more than one cognitive domain.

Two of the most striking cognitive impairments in psychotic disorders are in memory and executive functions. Despite suggestions of extreme memory impairment in schizophrenia (McKenna *et al.* 1990), much recent research has focused on executive deficits. It is not clear, however, that executive deficits are more severe than memory deficits. A meta-analysis of neurocognitive performance in schizophrenia (Heinrichs & Zakzanis, 1998) found the largest effect sizes in 'global verbal memory', with less impairment on executive measures such as the Wisconsin Card Sort Test (WCST). Nor do executive deficits impair functioning more; associations between cognition and functional outcome are greater for memory domains than for card-sorting (Green *et al.* 2000).

One reason executive deficits in schizophrenia have captured research interest is their potential as trait markers of genetic risk for psychosis. Impaired executive function is found in the healthy relatives of people with schizophrenia (Cannon *et al.* 1994; Kremen *et al.* 1994; Byrne *et al.* 1999; Egan *et al.* 2001; Wolf *et al.* 2002). However, in psychotic disorders executive deficits may reflect disease progression. The Intradimensional-Extradimensional (IDED) attention-shifting task from the Cambridge Neuropsychological Test Automated Battery (CANTAB) is a measure of executive functioning; the 'extra-dimensional' shift (EDS) stage of the task is conceptually akin to the WCST. Performance at the EDS is worse in chronic schizophrenia than in first-episode patients (Elliott *et al.* 1995; Hutton *et al.* 1998). Furthermore, performance has been associated with duration of untreated psychosis, suggesting a process of pathological cognitive decline (Joyce *et al.* 2002).

Suggested cognitive markers of decline in psychosis are not limited to executive function. Wood *et al.* (2002) found significant impairment on the CANTAB visuospatial paired associative learning (PAL) task in established schizophrenia, with less impairment in first-episode psychosis. One explanation may be a progressive decline in associative learning ability throughout the disorder; this is notionally supported by neuroimaging evidence of structural change in the medial temporal lobe region during the transition from at-risk mental state to psychosis (Pantelis *et al.* 2003*a*).

If memory and executive deficits both occur during psychotic illnesses it is important to note whether the two arise independently. Two previous hypotheses have been suggested. Repeated structural imaging in early onset schizophrenia has shown grey matter loss spreading from parietal through temporal to prefrontal regions (Thompson *et al.* 2001), suggesting that in the early stages of psychosis, memory might be more impaired than 'frontal' functions such as attention-shifting. In contrast to this, Pantelis *et al.* (2003*b*) have proposed a neurodevelopmental model of psychosis that predicts greater impairment in those cognitive functions that develop later. They argue that an early-developing function such as memory has a greater chance to recover through brain plasticity, while those developing nearer the age of onset of psychosis (such as executive functions) are less likely to recover function.

To test these hypotheses, tasks that are dissociated in their memory and executive functioning loads are needed. There is strong evidence linking visuospatial associative learning with hippocampal function. Neuroimaging studies in healthy volunteers have demonstrated increased activation in right parahippocampal gyrus during tasks involving associating objects and locations (Owen *et al.* 1996; Maguire *et al.* 1998). This is supported by impaired associative learning in animals (Miyashita *et al.* 1998) and humans (Smith & Milner, 1981) with temporal lobe lesions, and from studies using PAL to predict Alzheimer's disease (Swainson *et al.* 2001; Blackwell *et al.* 2004), early pathological markers of which are relatively restricted to the hippocampus, transentorhinal and entorhinal cortices. A simplified view of the PAL task is therefore that it requires intact medial temporal lobe, and more specifically, hippocampi (Wood *et al.* 2002).

In contrast, the EDS stage of the IDED task reflects mainly frontostriatal processing, with PET imaging showing increased regional cerebral blood flow in right dorsolateral prefrontal cortex (Rogers *et al.* 2000). IDED performance is impaired in patients with frontal, but not temporal lobe or amygdala-hippocampus lesions (Owen *et al.* 1991). It is also highly sensitive to the frontostriatal impairment in Parkinson's

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disease (Owen *et al*. 1993*b*), and Huntington's disease (Lawrence *et al*. 1996, 1998).

Thus there is evidence for a broad dissociation between the cognitive systems required for the PAL and IDED tasks, with a greater burden on temporo-hippocampal processing in PAL, and a greater frontostriatal load in the EDS stage of the IDED task. While no neuropsychological tasks are entirely domain-specific (for example, both these tasks require limited working memory), these two are well suited to use as comparators of function in memory *versus* executive processing systems.

Groups of patients with early psychosis show considerable heterogeneity in their cognitive performance. Direct comparison of patients assessed in the CAMEO early psychosis clinic allowed us to test hypotheses regarding the nature and consequences of frontostriatal- and medial temporal lobe-based cognitive impairments, in groups of patients who are dissociated with respect to their performance on the IDED and PAL tasks.

We hypothesized that executive function and associative learning deficits would be dissociable such that some patients would show significant deficits on one but not both tests, and that this might reflect illness duration. Furthermore, we predicted that there would be clinical and functional differences between patients impaired on PAL compared with patients impaired on IDED attention-shifting. Since most neuropsychological tasks are polyfactorial in their processing demands, scoring patients on multiple tests of 'memory' or 'executive function' would probably result in little differentiation between the underpinning neural circuitries involved. Therefore we used just one, well validated, measure for each domain. In addition, using few tests allows us to assess cognitive function very early in the illness since the time and concentration requirement is low.

METHOD

Design

CAMEO (www.cameo.nhs.uk) is a specialist NHS service for people in Cambridge and South Cambridgeshire who are experiencing first-episode psychosis (FEP) or who are thought to be in an 'at-risk mental state' (ARMS) for psychosis. On referral to CAMEO, patients receive a comprehensive clinical assessment including a one-hour neuropsychological battery. These assessments are the basis for this report.

Participants

Patients referred to the CAMEO service are categorized as FEP or ARMS according to the following criteria:

(1) First-episode psychosis (FEP): patients with psychotic symptoms or negative symptoms for the first time; patients with psychotic symptoms with previous untreated episodes, or who have been treated for less than 6 weeks with antipsychotic medication. Suspected drug-induced psychosis, affective psychoses and dual diagnoses are included.

(2) At-risk mental state (ARMS): attenuated psychotic symptoms (odd beliefs, magical thinking, ideas of reference, paranoid ideation, perceptual disturbances) occurring several times a week; transient psychotic symptoms; and 'trait plus state' cases who show a family history or vulnerability such as head injury, coupled with a recent significant change in mental state.

Since we believe that there is continuity between these categories, and since diagnoses are difficult in the early stages of psychotic disorders, we included both ARMS and FEP cases in this report. Seventy-five consecutive referrals were assessed by the CAMEO service. Most were assessed immediately upon referral to CAMEO; however, some ($n=18$) had been referred prior to the start of neuropsychological assessment and so were seen later than their initial referral. Most patients had been receiving antipsychotic (generally atypical) medication for a short period before assessment. A small minority of patients were not receiving antipsychotic medication; however, a substantial proportion were receiving mood-stabilizers or antidepressants. Local research ethics committee approval was gained to use the clinical data collected in CAMEO for research purposes.

Neuropsychological measures

The National Adult Reading Test (NART; Nelson, 1982) was used to estimate premorbid IQ. Neuropsychological tasks were taken from the CANTAB, a battery of neuropsychological paradigms presented on a touch-sensitive screen (see Sahakian & Owen, 1992 for details). The two tasks were presented as part of a longer

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battery, which took around 1 hour in total. IDED was presented first in each case.

IDED attention-shifting task (*executive measure*)

The IDED task (Roberts *et al.* 1988) is an attentional set-shifting paradigm. During the conceptually crucial extra-dimensional shift stage (EDS), divergent thinking is required in order to shift attention away from a previously correct stimulus dimension to a novel (previously irrelevant) one. The number of errors at the EDS stage was used as the measure of executive functioning.

Visuospatial paired associative learning task and memory task (*PAL*)

The CANTAB PAL task (Sahakian *et al.* 1988) requires subjects to associate visual patterns that cannot easily be verbalized with spatial locations on the computer screen. There are four levels of difficulty; the number of errors at each level is recorded. For participants who fail to complete all levels, an adjusted total is calculated that allows for errors predicted in the stages that were not attempted.

For both tests, an arbitrary 'failure' point was fixed as a z score below -2 according to manufacturer's normative data, which automatically adjusts for each subject's age and NART score. This arbitrary level was chosen to reflect a criterion of very poor performance relative to the norm, and to avoid the difficulties of cut-offs based on the distribution of errors found in the patient sample.

Clinical and functional measures

Clinical rating scales included the Beck Depression Inventory (BDI; Beck & Steer, 1987), Young Mania Scale (Young *et al.* 1978) and the Positive and Negative Syndrome Scale (PANSS; Kay *et al.* 1987). Several clinician-rated symptoms included in the PANSS scales have some obvious 'cognitive' aspect. These are of interest in their own right and may also inflate associations between cognition and symptom ratings. Therefore the following symptoms were considered separately as well as in the composite scores: N5 (abstract thinking), N6 (flow of conversation), N7 (stereotyped thinking), G11 (poor attention), G12 (insight). The Global Assessment of Function (GAF) (APA, 1994) was also used, and patients were accorded a clinical diagnosis using the Structured Clinical Interview for DSM-IV (First *et al.* 1997). All clinician ratings were completed blind to neuropsychological test performance.

Duration of untreated psychosis was assessed from patient and carer report and medical records where available. Two estimates were taken; the first reflected the time that current psychotic symptoms had been present without remittance before antipsychotic drug treatment was started, that is, duration of untreated psychosis for this episode only. The second was the time between the first psychotic symptom ever experienced and CAMEO cognitive assessment. Where reports from different sources conflicted, the longer duration was taken. These two measures were chosen to provide an estimate of both the long-term history of psychotic symptoms, and the short-term duration of full psychosis, both of which might affect cognitive performance.

Analyses

To estimate the extent to which performance on the PAL and IDED tests was dissociated a probabilistic approach was used. We estimated the probability of failing both tests given the probability of failing each test independently. This novel approach avoids the test sensitivity issue, since the overall rates of failure on each task are irrelevant.

To examine whether there were clinical and functional differences between patients based on their cognitive status, several approaches were employed. First, Spearman's correlations were calculated between total error scores for PAL and the IDED EDS stage, and the clinical and functional measures. Second, the patients were divided into groups based on their status as failing both tests, failing neither test, only failing PAL or only failing IDED. Due to inequality in group sizes, these groups were then compared using non-parametric Kruskal–Wallis tests for multiple-group comparisons, and Mann–Whitney U tests for comparisons between two groups. These comparisons lacked statistical power due to the small sample sizes in some groups. Consequently, comparisons were then made on the basis of PAL or IDED failure

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regardless of status on the other test. Although not theoretically ideal, this approach allowed reasonable sample sizes in each group and greatly increased the statistical power.

Comparisons between PAL-passers *versus* PAL-failers were made with *t* tests (negative symptoms were first normalized using an inverse square root transform); comparisons between PANSS 'cognitive symptoms' and all comparisons between IDED pass/fail groups were made using non-parametric Mann–Whitney tests.

RESULTS

Patient diagnoses and demographic effects

The group comprised 11 ARMS cases and 64 FEP, of whom 8 ARMS and 11 FEP cases were women. The mean age for the group was 26·8 years (S.D. = 9·54) and mean NART-predicted IQ was 109.7 (S.D. = 8·36). Four FEP patients did not complete both IDED and PAL tasks at cognitive assessment due to time constraints or the patient being too unwell, leaving 71 patients included in subsequent analyses.

CAMEO patients often have too short a history of psychosis to be fully diagnosed at first assessment. Nonetheless, SCID diagnoses broke down as follows: schizophrenia ($n = 13$), schizoaffective disorder (2) delusional disorder (3), bipolar disorders (11), major depressive episode (12), psychosis not otherwise specified or brief psychotic disorder (23), psychotic symptoms present but not diagnostically significant (6). One patient was too unwell to complete the SCID.

Median duration of untreated psychosis for this episode was 7·5 months, with a range from 0 to 288 months. Mean length of time between first-ever psychotic symptom and cognitive testing was 2·0 years, with a range from 0 to 27 years.

There were no differences between males and females on the number of EDS errors ($z = -0{\cdot}398$, $p > 0{\cdot}05$) or PAL errors ($z = -1{\cdot}183$, $p > 0{\cdot}05$) made. No differences were found between the number of EDS errors ($\chi^2 = 4{\cdot}663$, df = 5, $p > 0{\cdot}05$) or PAL errors ($\chi^2 = 3{\cdot}154$, df = 5, $p > 0{\cdot}05$) by SCID diagnosis. Spearman's correlations between age and NART-predicted IQ and PAL and EDS errors found no significant associations.

Performance on IDED and PAL tasks

On the IDED task, all patients successfully completed all stages prior to the EDS. Thirteen patients failed to complete the EDS while eight patients completed the EDS but did not then complete the final stage. Errors at both EDS and pre-EDS stages were not normally distributed; the median of EDS errors was six (mode = 3, range 0–32 errors), while median errors prior to the EDS stage was seven (mode = 4, range 3–21). EDS and pre-EDS errors were not associated (Spearman's rho = −0·08). Fifty-one patients completed the PAL task, with 14 completing the six- but not eight-box stage, and a small minority ($n = 6$) dropping out before completing the six-box task. Total error scores were adjusted for patients who failed to complete all the stages; the median of adjusted errors was 15 (mode = 18, range 0–155).

Dissociation between PAL and IDED tests

Of the 71 patients who completed both tasks, 23 (32%) failed PAL yet passed IDED, while 9 (13%) showed the opposite pattern. Four patients (6%) failed both tasks while the remaining 35 (49%) passed both tests.

The degree of dissociation between PAL and IDED test failure was estimated probabilistically as described above. If performance on the tasks were dissociated, the probability of failing both tests would be 6·95%, given the prevalence of failure on each test. The number of patients in the sample who did fail both tests was, in fact, 5·63%, implying no association between tests; that is, a patient who failed one test was not more likely to fail the other. In addition, Spearman's correlations between PAL and EDS errors showed no significant association ($r = 0{\cdot}143$, $p > 0{\cdot}05$).

Clinical and functional associations

Associations between the cognitive test scores and clinical and functional measures can be seen in Table 1 and are summarized in Fig. 1. PAL errors correlated with a number of clinical and functional measures including PANSS Negative symptom scores and GAF disability. EDS errors did not correlate strongly with any clinical measures; however, there was a modest correlation with abstract thinking.

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Table 1. *Spearman's correlations between PAL and IDED error scores, and clinical and functional measures*

Measure	*n*	Association with EDS errors (rho)	Association with PAL errors (rho)
Demographics			
NART	64	−0·15	−0·12
Age	71	0·12	0·03
DUP this episode	48	−0·03	0·16
DUP lifetime history	59	0·00	0·07
PANSS scale scores			
Positive	64	−0·05	0·22
Negative	64	0·06	0·34**
General	64	−0·05	0·25
Symptom scales			
Young mania	45	−0·13	0·32*
BDI	42	0·16	−0·39*
Global Assessment of Function			
Symptoms	63	0·06	−0·22
Disability	64	−0·10	−0·41**
Total	64	−0·14	−0·28*
PANSS 'cognitive' symptoms			
Abstract thinking	62	0·26*	0·29*
Flow of conversation	62	−0·04	0·14
Stereotyped thinking	62	0·00	0·39**
Poor attention	62	0·08	0·32*
Insight	62	−0·16	0·39**

PAL, Paired associative learning; IDED, intradimensional-extradimensional; EDS, extradimensional shift; NART, National Adult Reading Test; DUP, duration of untreated psychosis; PANSS, Positive and Negative Syndrome Scale; BDI, Beck Depression Inventory.
* $p<0·05$, ** $p<0·01$.

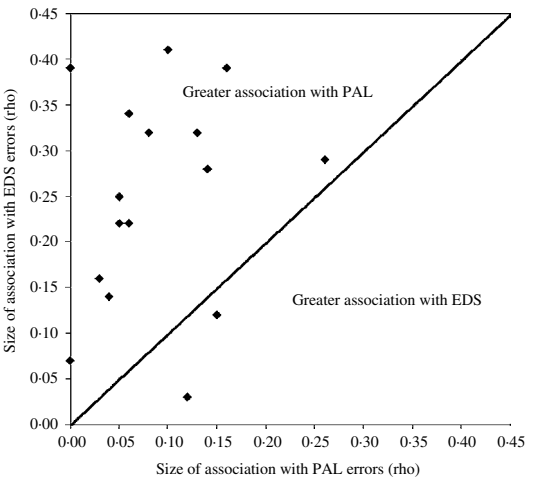


FIG. 1. Magnitude of associations between PAL (paired associative learning) and EDS (extradimensional shift) errors, and clinical, functional and demographic measures shown in Table 1.

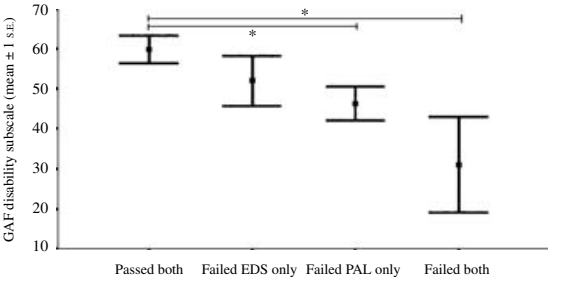


FIG. 2. Global Assessment of Function (GAF) disability subscale scores of cognitively dissociated patient groups (mean ± 1 S.E.M.). * Group differences significant at $p<0·05$.

Dissociating the effect of PAL failure *versus* IDED failure

Comparison of clinical and functional measures between groups defined by their performance on both tests ('pass both', 'fail both', 'fail PAL only', 'fail IDED only') tests was problematic owing to the inequalities of group size (see above). Despite this, significant differences were found in GAF disability ($\chi^2=10·50$, df = 3, $p<0·05$), stereotyped thinking ($\chi^2=15·03$, df = 3, $p<0·01$) and insight ($\chi^2=9·57$, df = 3, $p<0·05$). *Post-hoc* Mann–Whitney *U* tests revealed that the significant differences were between 'fail PAL only' and 'pass both' groups, between 'fail EDS only' and 'fail both', and between 'fail both' and 'pass both' groups (see Figs 2 and 3). In all cases the group that failed PAL performed non-significantly better than the group that failed both tests, but worse than the group that failed the EDS only; the latter could not be differentiated from the group that passed both tests.

Direct comparison of patients who were doubly dissociated in terms of their PAL and IDED performance was statistically underpowered due to unequal group sizes. Kruskal–Wallis tests revealed no differences between these two groups in terms of their clinical or function scores.

Effect of PAL failure alone

Comparisons between PAL-passers and PAL-failers were made using *t* tests (see Table 2). Significant differences were found in some symptom rating scores, with PAL-failers showing higher PANSS negative and general psychopathology scores, and trends towards

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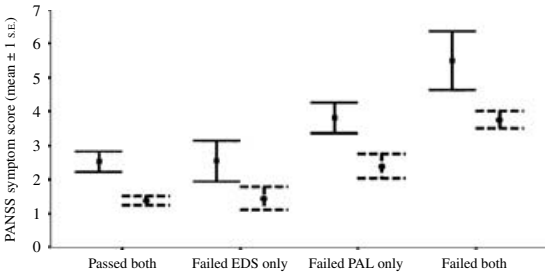


FIG. 3. PANSS insight scores (solid lines) and stereotyped thinking scores (broken lines) of cognitively dissociated patient groups (mean ±1 S.E.M.). Significant differences ($p<0{\cdot}05$) in both cases between 'passed both' and 'failed PAL only', 'passed both' and 'failed both', and 'failed EDS only' and 'failed both'. In neither case can those who failed both be distinguished from those who failed PAL only, nor those who passed both from those who failed EDS only. (PANSS, positive and negative syndrome scale; PAL, paired associative learning; EDS, extradimensional shift.)

higher positive symptom and mania scores. Some of the differences in PANSS scores may reflect differences in 'cognitive' symptom levels, as PAL-passers had lower symptom scores on the insight, stereotyped thinking and attention ratings. PAL-passers showed better functioning on the GAF total and disability ratings.

Effect of IDED failure alone

Again, unequal group sizes between those who passed/failed the IDED EDS meant that comparisons were lacking in statistical power. No significant clinical or functional differences were found between those who passed *versus* failed this test.

Duration of illness

There were no differences between groups defined by PAL and EDS performance in either the duration of untreated psychosis for this episode ($\chi^2=3{\cdot}152$, df$=3$, $p>0{\cdot}05$) or in the length of time between first psychotic symptoms appearing and cognitive testing ($\chi^2=1{\cdot}705$, df$=3$, $p>0{\cdot}05$). This was not simply due to low power: Spearman's correlations between PAL and EDS errors and the two measures of illness duration were all less than 0·2.

DISCUSSION

In this group of early psychosis patients, failure on the memory and executive tasks was dissociated, in that patients were no more likely to fail both tasks than would be expected by the overall failure rates on the individual tests. This finding is not affected by differences in failure rates on the two tasks; however, more patients failed the associative learning task than the attention-switching task. This may reflect differences in task sensitivity; alternately it may reflect a greater impairment in memory than executive functions.

Evidence from previous studies supports the dissociation between PAL and IDED task performance. A factor analytic study including the PAL and IDED tasks in a large group of normal volunteers found that the two tasks loaded on separate factors (Robbins *et al.* 1998). In addition there is a broad dissociation in groups of patients in the early stages of other neuropsychiatric disorders, with mild Alzheimer's patients tending to fail the PAL task but pass the IDED (Sahakian *et al.* 1988, 1990), and mild Parkinson's patients showing impairments on IDED shifting (Owen *et al.* 1993*b*) but with the

Table 2. *Between-group comparisons (t test/ Mann–Whitney U test) of demographic, clinical and functional measures between patients who pass (n=34) versus fail (n=27) the PAL test*

Measure	Mean (S.D.) for PAL passers	Mean (S.D.) for PAL failers	*t*
Demographics			
NART	110·4 (7·68)	109·3 (9·54)	0·467
Age	28·3 (10·82)	24·6 (7·14)	1·562
PANSS scales			
PANSS General	28·9 (6·06)	34·8 (10·97)	−2·764*
PANSS Positive	15·2 (5·85)	17·8 (5·64)	−1·783
PANSS Negative	11·9 (5·12)	14·7 (6·03)	−2·468*
Symptom scales			
Young mania	8·6 (7·28)	12·9 (7·99)	−1·825
BDI	20·7 (12·34)	19·2 (17·20)	0·328
Global Assessment of Function (GAF)			
GAF symptoms	45·8 (20·96)	36·6 (16·78)	1·810
GAF disability	58·5 (18·64)	45·3 (19·57)	2·697**
GAF total	49·8 (18·54)	39·5 (15·63)	2·266*
PANSS 'cognitive' symptoms			*z*
Abstract thinking	1·97 (1·16)	2·36 (1·18)	−1·630
Flow of conversation	1·51 (0·91)	1·78 (1·09)	−1·613
Stereotyped thinking	1·41 (0·85)	2·48 (1·44)	−3·233**
Poor attention	1·38 (0·85)	1·87 (1·10)	−2·039*
Insight	2·54 (1·76)	4·00 (2·02)	−2·609**

PAL, Paired associative learning; NART, National Adult Reading Test; PANSS, Positive and Negative Syndrome Scale; BDI, Beck Depression Inventory.
* $p<0{\cdot}05$, ** $p<0{\cdot}01$.

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majority passing the PAL task (Sahakian *et al.* 1988; Owen *et al.* 1993*a*).

CAMEO patients who failed the PAL task were clinically worse-off than those who passed, while this distinction is not found using the IDED task. Failure on the PAL test was associated with higher PANSS general and negative symptoms and lower GAF score. In addition, there were trends towards increased mania and positive symptoms. This suggests that PAL failure detects patients with a globally more severe clinical presentation. Poor associative learning and memory may be a cognitive marker of illness severity, while EDS failure, which is not associated with clinical presentation, may reflect a more long-term, trait-like cognitive dysfunction.

Although associations between cognition and functioning have been consistently shown in schizophrenia, associations in earlier stages of psychosis are less established. In neither case has associative learning been singled out as a particular indicator. However, until recently few non-verbal associative learning tests have been available. The CANTAB PAL may be particularly sensitive because context-dependent spatial memory is known to involve the hippocampus. Since grey matter volume changes in this region have been demonstrated in the very early stages of psychosis (Pantelis *et al.* 2003*a*), tests sensitive to changes in temporo-hippocampal regions may be good candidates for predictors of functional and clinical outcome in early psychosis. Since these two tests together take under 30 minutes to complete, they may prove useful in busy clinical settings for broadly characterizing cognitive states in early psychosis.

The significant differences in PANSS 'cognitive' symptoms of insight and stereotyped thinking are of interest; the effects here were strong enough to be detected even in the small samples where test performances were doubly dissociated. Those who only failed the PAL showed less severe symptoms than those who failed both tests but were worse than those who failed only the IDED task. It is interesting that these symptoms were related to PAL failure and not to IDED failure, since poor insight and stereotyped thinking are typically thought of as symptoms of frontal dysfunction, and would therefore be expected to show associations with executive tasks. Again, this may simply reflect increased sensitivity to symptomatic states in PAL compared with IDED. Alternately it may reflect a genuine neuropathological association between the brain systems subserving learning and memory and the cognitive symptoms of psychosis.

Since relatively few patients failed the IDED task alone, it is possible that the task is not sufficiently sensitive to detect small deficits in executive function and thus only patients who have a very strong executive impairment fail the IDED and not PAL task. However, performance on the IDED task is clearly impaired in chronic schizophrenia (Elliott *et al.* 1995), and in frontal patients (Owen *et al.* 1991), and not affected in temporal lobe or amygdalo-hippocampal patients (Owen *et al.* 1991). Moreover, the EDS is conceptually identical to the Wisconsin Card Sort Test, the archetypal neuropsychological test for executive function, which has been repeatedly used to demonstrate executive deficits in patients with schizophrenia and their healthy relatives (Goldberg *et al.* 1988; Franke *et al.* 1992; Egan *et al.* 2001).

It is interesting therefore that we find clinical associations with failure on the PAL and not the IDED task. From this we might speculate that, in early psychosis, the association between cognitive impairment and symptoms/functioning is stronger for memory tests and, by inference, temporo-hippocampal dysfunction than it is for frontostriatal and executive function. However, since EDS and PAL failure were dissociated in this group, we find no evidence to support hypotheses of a fixed order of onset of cognitive impairments in psychosis. While the comparison of performance on two tasks does not allow us to determine which domain was ultimately the more impaired, nearly half of our patients showed double dissociations on these tests. In addition, no association was found between performance on these two tests and duration of untreated psychosis (DUP) for this episode, or time since onset of psychotic symptoms. This result is in contrast to previous findings in first-episode psychosis (Joyce *et al.* 2002) but may reflect differences in cohort, for example a 10-point difference in NART-predicted IQ between our group and the study by Joyce and colleagues. The lack of association with DUP and the dissociation between task failures strongly suggest that there is no fixed order of cognitive decline in early psychosis.

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Instead, we suggest that there is more than one route to cognitive impairment in psychosis and that the heterogeneity of cognitive function found in psychotic disorders results from this. Memory and executive impairments may result ultimately from differential genetic or environmental aetiological factors, which are in turn responsible for the underlying structural or neurochemical dysfunctions. Moreover, the healthy population presumably shows strengths and weaknesses in different cognitive domains. These domains may be independently affected by the onset of psychosis, pushing some test performances down the continuum of functioning to below the cut-off of 'normal' function, which is then detected as a specific neuropsychological deficit.

The majority of patients in this study were being treated with antipsychotic drugs. While we cannot rule out the possibility that some cognitive impairment would result from this, studies in unmedicated first-episode patients (for example, Saykin *et al*. 1994) have also found substantial impairment, and studies of the newer 'atypical' antipsychotics (Keefe *et al*. 1999; Bilder *et al*. 2002) in fact find some amelioration of cognitive deficits, at least when compared with older drugs.

Until we have follow-up data on these subjects, we do not know whether the group defined by PAL failure will differ in their prognosis and outcome. At this stage we can only speculate that this group, who potentially have a more 'structural' basis for psychosis, and a more severe clinical profile at the time of testing, may follow a different and perhaps more severe course than those who are cognitively intact at this stage.

In conclusion, this study demonstrates that deficits in visuospatial associative learning are dissociated from deficits in attention-shifting in patients early in their first episode of psychosis, regardless of the relative sensitivity of the two tests. Associative learning, but not attention-shifting performance, is associated with clinical and functional presentation. This may suggest that temporo-hippocampal dysfunction is more detrimental to well-being than frontostriatal dysfunction in the early stages of psychosis, or alternately that executive function reflects more trait-like impairments and is less sensitive to symptom severity. We suggest that the dissociation found here suggests no common pattern of cognitive impairment in psychosis, but rather that multiple factors including the patients premorbid strengths and weaknesses may be reflected in the impairments that show at onset of psychosis.

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DECLARATION OF INTEREST

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