Schizophrenia

Computerised Assessment of Visuo-spatial Cognition in Schizophrenia – An Exploratory Meta-analysis of CANTAB Findings

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Abstract

The Cambridge Neuropsychological Test Automated Battery (CANTAB) allows a complete visuospatial profile of schizophrenic patients to be obtained with a wide validated neuropsychological battery. Cognitive tests include computerised tasks designed to assess visuo-spatial recognition memory, planning ability, working memory, strategy learning, sustained attention and attentional set shifting. This article reports a meta-analysis of 12 studies from 45 peer-reviewed published neuropsychological studies of neurocognitive assessment performed with CANTAB in schizophrenia. Unpublished or unclassifiable study data and studies with fewer than four participants, those missing a comparison group or those failing to present complete information were excluded from the analysis. These studies included 458 (working memory), 293 (shifting), 196 (recognition), 390 (planning and solving) exposed participants and 303 (working memory), 177 (shifting), 240 (planning), 131 (recognition) controls. Analysis indicated a consistent trend for patients to perform below par, with significant heterogeneity across studies. Sources of heterogeneity were analysed, and a need to ensure more appropriate composition of patient and control groups and to adopt a more refined and methodologically correct, hypothesis-driven approach was identified. There was homogeneity only in visuospatial planning ability deficits. The results displayed by this meta-analysis fit with those previously reported on schizophrenic deficits thanks to separate cognitive tests. Consequently, CANTAB appears to be useful and relevant for describing the visuo-spatial profiles of schizophrenic patients.

Key words

Schizophrenia, cognition, memory, neuropsychological assessment, meta-analysis

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Since Kraepelin and Bleuler’s early descriptions of schizophrenic symptoms, language disturbances have been considered to be at the heart of the disease. Consequently, numerous studies tried to experimentally describe the cognitive impairments underlying oral and written verbal deficits in patients. The overuse of verbal material in traditional testing may have contributed to biased conclusions on the exact nature of cognitive deficits in schizophrenia, and in fact visuo-spatial deficits of schizophrenic patients have been equally reported, such as memory span, attention and executive function compared with healthy controls.

Despite growing evidence for visuo-spatial deficits, the use of separate neurocognitive tasks did not allow us to define a clear profile of visuo-spatial impairments in schizophrenic patients. As a result, the Cambridge Neuropsychological Test Automated Battery (CANTAB), from the UK, includes a large number of visuo-spatial tasks (n=19) that are usually undervalued in neuropsychological batteries for traditional testing. The CANTAB is rigorously standardised and is computerised, providing precise recordings of qualitative or quantitative data and high homogeneity of testing conditions between clinicians. Although the CANTAB is now used more often in neuropsychiatry, a clear consensus on its usage and direction in research for the assessment of visuo-spatial cognitive functioning in schizophrenia is lacking.

One of the conclusions of the CANTAB literature is the presence of visuo-spatial cognitive deficits in schizophrenia.11,12 Qualitative reviews of the literature have indicated impairments in executive functions (measured by the Intra-Extra-dimensional (IED) Shift tests and the Stockings of Cambridge [SOC] test), attention (measured using Rapid Visual Information Processing test), working memory (Spatial Working Memory, Spatial Span tests) and declarative memory (Paired Associates Learning, Spatial Recognition Memory tests) in chronic patients with preserved intellectual quotient, as well as in first-episode patients.13 However, not all primary studies conducted to date have had sufficient power to detect statistically significant differences, and there have been few attempts to quantify the magnitude of these impairments.

In a recent systematic review,14 we considered quantifying the data obtained from a moderate set of studies using the CANTAB in schizophrenia, but we thought it was too premature in terms of available results. Individual studies have shown there to be significant deficits, and we detailed qualitative analysis in a previous article. This does not mean that performing the quantitative analysis was more of an exercise rather than finding out something new, but we were aware that a meta-analysis could help when looking for small differences that might be missed in underpowered studies. Moreover, sufficient data still seemed lacking for a number of domains. This...
Computerised Assessment of Visuo-spatial Cognition in Schizophrenia

This article aims to combine data from available studies to identify the profile of visuo-spatial deficits in schizophrenia patients and to quantify their magnitude using the CANTAB.

It is of note that during the past decade the reliability of the CANTAB has been scrutinised. To date, its practice effect has been noted to be of modest quality. Hence, with this systematic quantitative review we aim first to clarify the degree of neuropsychological difference seen in this patient group compared with controls (healthy volunteers) via CANTAB, and second to facilitate standardisation by providing means by which to compare our findings with the comparable traditional neuropsychological tests available today.

**Methods**

**Search Strategy for Identification of Studies**
A structured search of the electronic literature via PubMed (all years), PsycINFO® (1987 to August 2006), Excerpta Medica Database (EMBASE, 1980–2006 week eight) and the CANTAB website’s bibliographic list was carried out. In addition, an exhaustive search of the reference lists of all trials were performed. Authors were then contacted to obtain extra information on missing data. There was no limitation on the language of studies. The keywords used were ‘schizophrenia’ and ‘CANTAB’ or ‘Cambridge Neuropsychological Test Automated Battery’.

**Methods of Review**
Following the Quality of Reports of Meta-analysis of Randomized Controlled Trials (QUOROM) guidelines, two of the authors (Amir Ali Sepehry and Emmanuel Stip) studied each of the publications that met the inclusion criteria and assessed them independently. We included all papers presenting original data of patients with schizophrenia compared with healthy volunteers. Cross-referencing of the studies was performed by Amir Ali Sepehry. We referred to test information provided by the authors and made reference to *The CANTAB Test Administration Guide* chapter 22 – ‘Description of Outcome Measures’. We categorised tests by the cognitive domains of memory, attention and executive function. Subsequently, to minimise diversity due to data manipulation, we analysed the data for test subscales, using D-stat to pool the continuous-type data (mean, standard deviation [SD], number [n]) for each subject group (schizophrenia versus control groups).

**Inclusion**
Studies consisted of schizophrenia-spectrum disorder patients compared with healthy volunteers (controls) tested for cognitive function with CANTAB.

**Exclusion**
Studies were excluded if they were letters, correspondence, reviews, case studies or animal studies, if the included the wrong study population or if they were explicitly reporting non-standardised results. It should be noted that CANTAB results are in either raw or standardised formats, and that standardised data are compared with healthy subjects.

**Homogeneity of Effect Size Estimates**
Combining effect size estimates is rational only when effect estimates are homogenous. Consequently, Q-statistics have been calculated for the effect size estimates. To reach homogeneity (non-significant distribution at p<0.1), studies introducing variability were excluded. A random effect model was used to resolve unexplainable heterogeneity, yet due to the small sample size efforts to evaluate diversity were minimal.

**Statistical Analysis**
Where available, mean, standard deviation and sample size (n) was used in each study to calculate effects. In the absence of these valuable data, we referred to other parametric data or contacted the author. Comprehensive meta-analysis (CMA) and D-stat was used alongside Microsoft Excel to calculate the effect size estimates for the continuous-scale data. All effect size estimates are calculated for 95% confidence intervals (CI). The primary analysis consisted of visuo-spatial cognitive tests on memory, attention and executive function. For each subtest, an effect estimate was calculated. Our secondary analysis consisted of verifying effect estimate modifiers in concordance with a posteriori potential effect modifiers (e.g. analysis by

**Figure 1: Synopsis of Original Data Retrieval**

Note: Four new studies emerged after August 2006. The new total is (n=45+4).
Table 1a: Demographic Representation of the Studies (n=12) Included in the Meta-analysis

<table>
<thead>
<tr>
<th>Studies</th>
<th>N</th>
<th>Sz</th>
<th>Age (mean)</th>
<th>IQ (NART) (mean)</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Badcock et al., 2005a</td>
<td>24</td>
<td>33</td>
<td>32.83 (8.22)</td>
<td>101.42 (9.2)</td>
<td>M-atypical</td>
</tr>
<tr>
<td>Elliott et al., 1998b</td>
<td>12</td>
<td>12</td>
<td>43.4 (3.3)</td>
<td>110.4 (2.9)</td>
<td>M-atypical</td>
</tr>
<tr>
<td>Elliott et al., 1995a</td>
<td>32</td>
<td>24</td>
<td>39.8 (2.2)</td>
<td>109.5 (1.6)</td>
<td>M-atypical</td>
</tr>
<tr>
<td>Hutton et al., 2004d</td>
<td>59</td>
<td>59</td>
<td>25.3 (7.3)</td>
<td>100.8 (10.4)</td>
<td>M-typical</td>
</tr>
<tr>
<td>Hutton et al., 1998c</td>
<td>30</td>
<td>30</td>
<td>27.77 (NR)</td>
<td>109.33 (NR)</td>
<td>Medicated</td>
</tr>
<tr>
<td>Joyce et al., 2005c</td>
<td>93</td>
<td>50</td>
<td>25.56 (7.54)</td>
<td>99.64 (8.99)</td>
<td>Less than 12 months</td>
</tr>
<tr>
<td>Joyce et al., 1995b</td>
<td>81</td>
<td>25</td>
<td>27.99 (5.19)</td>
<td>99.67 (10.37)</td>
<td>Less than 12 months</td>
</tr>
<tr>
<td>Mathes et al., 2005f</td>
<td>56</td>
<td>24</td>
<td>29.8 (9.4)</td>
<td>93.9 (12.8)</td>
<td>M-atypical</td>
</tr>
<tr>
<td>McIntosh et al., 2005h</td>
<td>50</td>
<td>50</td>
<td>37.6 (14)</td>
<td>NR (NR)</td>
<td>M-atypical</td>
</tr>
<tr>
<td>Pantelis et al., 1997c</td>
<td>31</td>
<td>48.31 (1.7)</td>
<td>NR</td>
<td>101.27 (1.36)</td>
<td>Medicated</td>
</tr>
<tr>
<td>Turner et al., 2004a</td>
<td>20</td>
<td>43</td>
<td>9</td>
<td>NR</td>
<td>M-atypical</td>
</tr>
<tr>
<td>Tyson et al., 2004f</td>
<td>28</td>
<td>17</td>
<td>33.85 (10)</td>
<td>NR</td>
<td>M-atypical</td>
</tr>
</tbody>
</table>

NR = not reported; M = majority; NART = National Adult Reading Test; IQ = intelligence quotient; SD = standard deviation; Sz = schizophrenia; CS = control subjects.

Table 1b: Studies Retrieved After the Cut-off Date (Not Included in the Overall Analysis)

<table>
<thead>
<tr>
<th>Studies</th>
<th>Subjects</th>
<th>Age, Mean (SD)</th>
<th>Treatment</th>
<th>CANTAB Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jazbec et al., 2007c</td>
<td>36</td>
<td>26</td>
<td>34.6 (8.8)</td>
<td>M-atypical antipsychotics</td>
</tr>
<tr>
<td>Shamay-Tsoory et al., 2007a</td>
<td>26</td>
<td>31</td>
<td>29.65 (NR)</td>
<td>Medicated</td>
</tr>
<tr>
<td>Fornito et al., 2006c</td>
<td>37</td>
<td>43</td>
<td>29.89 (8.66)</td>
<td>M-atypical antipsychotics</td>
</tr>
<tr>
<td>Catapan-Ludwing et al., 2005e</td>
<td>18</td>
<td>18</td>
<td>46.5 (9.1)</td>
<td>M-atypical antipsychotics</td>
</tr>
</tbody>
</table>

NR = not reported; RVP = rapid visual processing; M = majority; MOT = motor screening; EDS = extra-dimensional shift; ID-ED = intra-extra dimensional shift. Intelligence quotient was only reported by colleagues via WRAT-R results.

Results

Primary Analysis

Our primary analysis consisted of the cognitive subdomains of memory, attention and executive function. Each domain contained several subtests. Later analysis to investigate heterogeneity has been carried out, first utilising random effect models to explain unexplainable homogeneity, and second using meta-analytic techniques, such as meta-regression, to provide an explanation of the heterogeneous effect estimates. Finally, we used an a priori set of viable influential factors. The definition and description of the tasks and the domains tested are listed in Tables 1a and 1b.

A Priori Moderating Variables

We have investigated the large heterogeneity factor for the CANTAB subscales using random effect models by first controlling for medication type and patient type (first episode versus long-term) and then by meta-regression analysis. Although Cochrane do not encourage meta-regression for fewer than 10 studies in a meta-analysis, we have attempted to explain our large heterogeneity in the subscales of CANTAB with more than three included studies.
Hence, with the a priori set of variables we have run the meta-regression based on a fixed effect model.

**Memory**

**Spatial Working Memory Error**

An analysis of the subscales for the spatial working memory (SWM) test has been performed. Four of the eight studies that provided SWM error scores and matched our inclusion criteria needed extra data transformation. For the study by Badcock et al.,28 we pooled the between and within error scores to yield a raw Cohen’s d score (4.1888) from the schizophrenia group (x=24.210 [3.57], n=24) and the control group (x=11.924 [2.365], n=33). For Elliot et al.29 we pooled SWM scores to yield the following: schizophrenia group x=13.567 (3.167), n=12; control group x=7.3 (2.837), n=12. For the patient’s pre-morbid functioning IQ and age (n=8), as the variable of interest increased, the slope of the point estimate decreased (-0.174; p=0.003). The second run was based on seven studies with completed data for age and the IQ of the control group (healthy volunteers) (see Table 2).

For the patient’s pre-morbid functioning IQ and age (n=8), as the variable of interest increased, the slope of the point estimate decreased (-0.045, p=0.13 ns; and -0.109, p=0.0001, respectively). For the control IQ and age (n=7), as the variable increased, the slope of the point estimate decreased (-0.174; p=0.001 significant; and -0.137, p=0.0001 significant, respectively). Medication type did not influence the heterogeneity factor; on the contrary, the patient type influenced heterogeneity. First-episode patients (n=3) were homogeneous (ES=-0.646, p=0.0001; Q=0.476, p=0.8) and long-term patients (n=5) were homogeneous (ES=-2.241, p=0.0001; Q=67.32, p=0.0001).

**Spatial Working Memory Strategy**

People with schizophrenia demonstrated the worst approach (strategy) to solving questions in a test of SWM compared with healthy subjects. For the patients’ pre-morbid functioning IQ and age (n=8), as the variable of interest increased, the slope of the point estimate decreased (-0.032, p=0.04 ns; and -0.104, p=0.0001, respectively). For the control IQ and age groups (n=7), as the variable increased, the slope of the point estimate decreased (-0.103, p=0.008, -0.144, p=0.0001, respectively). Medication type did not influence the heterogeneity factor; on the contrary, the patient type influenced heterogeneity. First-episode patients (n=3) were homogeneous (ES=-0.885, p=0.0001; Q=3.982, p=0.137) while long-term patients (n=5) were heterogeneous (ES=-2.256, p=0.0001; Q=97.89, p=0.0001).

**Spatial Span – Span Length**

For clarification on span length description, a reference to the CANTAB manual has been made. Eight studies reported a head-to-head comparison of schizophrenia patients (n=458) with healthy volunteers (n=303). The total number of studies reporting span error (n=1) was not enough to carry further analysis.

Our analysis is divided into two categories. First, we have run our meta-regression on eight studies with complete data for age and pre-morbid functioning IQ, tested with the NART scores of schizophrenia patients. As the age increased, the effect slope point estimate decreased (-0.148; p=0.0001), and as the pre-morbid IQ increased, the slope of the point estimate decreased (-0.119; p=0.003). The second run was based on seven studies with completed data for age and the IQ of the control.
As the age increased, the slope of the point estimate decreased (-0.147; p=0.0001), and as the IQ increased, the slope of the point estimate decreased (-0.189; p=0.0001). Moreover, when we controlled for the type of medication, the heterogeneity remained unchanged. However, a later run controlling for types of patient revealed that the effect estimate for the first-episode patients group (n=3) was no longer heterogeneous (ES=-0.647, p=0.0001; Q=1.59, p=0.45), but the long-term patient group (n=5) was still heterogeneous (ES=-2.359, p=0.0001; Q=125.95, p=0.000).

**Delayed Matching-to-sample Correct Responses**
Three studies reported delayed matching-to-sample (DMS) assessment: one reported on the per cent age of correct responses and two reported latency. Pursuit of a meta-analytic examination has, at this point, stopped.

**Pattern Recognition Memory – Per Cent Correct and Incorrect**
The pattern recognition memory (PRM) test is an assessment of visual short-term recognition memory, and has two forms: immediate and delayed. We could pursue a meta-analytic analysis of the immediate form only, as the total number of delayed examples was close to null (n=1). In this context, we had four (n=196 schizophrenia, n=131 control subjects) studies that reported on the per cent correct and incorrect, and two on the latency quotient.

An analysis considering patient and medication types as possible influential factors on the heterogeneous effect estimate for PRM per cent correct did not help in finding the cause of our large heterogeneity. Meta-regression considering the IQ of the patients (n=4) revealed a non-significant slope of point estimate (p=0.412). As IQ increased, the effect increased. On the contrary, a meta-regression with age as a variable led to a non-significant slope of point estimate (p=0.004). As age increased, the effect decreased. Meta-regression on the age and IQ of controls (n=3) revealed that, as the age increased, the effect estimate increased (slope of the point estimate 4.399; p=0.000), and as IQ increased, the effect estimate decreased (slope of the point estimate -0.358; p=0.034).

**Spatial Recognition Memory – Per Cent Correct**
Three studies reported the on the per cent of SRM that was correct. One study reported the total number of correct responses and one reported the mean correct latency.

**Attention**

**Intra/Extra-dimensional Shift – Attention Set Shifting Errors**
The total number of studies providing data for this analysis were four (n=293 schizophrenia patients, n=177 control participants), comparing schizophrenia patients with healthy volunteers. For the study by Joyce et al.,29 the F-values were transformed to t-values by taking their square root, and were subsequently crunched into the CMA along with other studies for meta-analysis. Only one study reported the per cent of the completed quotient. For subscale analysis of the IED, there were two studies with this stage completed, and two intra-dimensional shifts (IDS), one error at extra-dimensional shift (EDS) and one error up to EDS.

For the pre-morbid functioning IQ and age of schizophrenia patients (n=4), as the variable increased, the slope of the point estimate decreased (-0.103; p=0.001; and -0.072, p=0.0001, respectively). As for the IQ and age of controls, although limited to three studies, the slope of the point estimates were significant (-0.509, p=0.026; and -0.395, p=0.0001, respectively). Controlling for both medication and patient type was not possible, as in doing so each category was limited to two or fewer number of studies, so interpretation was unreasonable.

**Executive Dysfunction**

**Stockings of Cambridge – Problem Solved in Minimum Number of Moves**
Five studies were included in this analysis (n=390 schizophrenia patients, and n=240 control subjects). Initial thinking time (ITT) in milliseconds was the variable of interest, consisting of zero moves, two moves, three moves, four moves and five moves. The effect estimate yielded for ITT with three moves was the only non-heterogeneous effect size. For the study by Joyce et al., F-values were transformed to raw-d using D-stat, and later crunched with other studies into the CMA. For the subscale of subsequent thinking, the number of moves was the discriminating factor in studies. Studies reporting the ‘one-touch’ Tower of London spatial planning task (NTOL) (n=2) and the Tower of London (TOL) task (n=3) were omitted from the analysis as the tests are not comparable to SOC, and the subscale data provided by the authors were not consistent for a meta-analytic approach.

For the patients’ pre-morbid functioning IQ and age (n=5), as the variable of interest increased, the slope of the point estimate decreased (-0.494, p=0.0001, and -0.288, p=0.0001, respectively). For the control IQ and age (n=4), as the variable increased, the slope of the point estimate decreased (-0.229, p=0.0001; and -0.249, p=0.0001, respectively). An analysis based on medication type was not appropriate, as dividing the studies by medication type would render the conclusion difficult based on two or fewer studies in each category. On the contrary, the patient type influenced the heterogeneity: first-episode patients (n=3) were homogeneous (ES=-0.685, p=0.0001; Q=3.069, p=0.216) and long-term patients (n=2) were heterogeneous.

**Discussion**
CANTAB assesses mainly visuo-spatial abilities. The battery does not include verbal memory assessment (it is supposed to include a verbal recognition memory task, but none of the reviewed studies actually included this test). This might be considered as a strength (non-linguistic) with regard to the population tested, despite evidence that verbal abilities are impaired in schizophrenia and the deficit showing the strongest relationship with social outcome is verbal memory. This systematic quantitative review of the CANTAB literature described a profile of visuo-spatial deficits in schizophrenic patients, reflecting results previously reported with isolated neuropsychological tasks.

**Executive Functions and Attention**
Executive functions and attention were impaired in schizophrenic patients compared with healthy subjects as assessed by the IED task, a computerised version of the Wisconsin Card Sorting Task (WCST). More specifically, the shifting errors score of patients was higher than that of controls. Visuo-spatial executive deficits were previously described in numerous tasks, such as the original version of the WCST,9,10,35 the self-ordered pointing task,2 the Penn Conditional Exclusion Test36 and the IED task.9,29,24,32,37 These executive deficits gave support to an impairment of prefrontal abilities in set shifting in schizophrenia. However, several studies demonstrated different profiles.
of executive functioning in schizophrenic patients, with unimpaired performances in the WCST, variations of performances according to the syndromes or clinical state or correlation between age at onset, the Positive and Negative Syndrome Scale (PANSS) score for negative symptoms and the number of perseverative errors on the WCST. Our data fitted with these studies according to the significant heterogeneity among studies that we reported with IED scores.

On the other hand, the effect estimate yielded for ITT with three moves for the SOC test, another measure of executive function, was the only non-heterogeneous effect size. ITT was always longer in patients compared with controls. SOC is a visuo-spatial planning task, which requires the subject to move coloured balls to copy different patterns of balls. The results of our quantitative review agreed with those obtained with the TOL (or Hanoi) test, a task requiring participants to move coloured balls within a limited number of moves in order to achieve a given goal configuration. Schizophrenic patients were likely to spend more time on successfully achieving appropriate configurations. Interestingly, Bustini and colleagues compared the performances of schizophrenic patients in the WCST and the Tower of Hanoi test with those of healthy controls and suggested that a common underlying factor could be responsible for the planning used in these tasks. We can also hypothesise that altered performances in the IED and SOC tasks of the CANTAB could reveal a general planning deficit in schizophrenics.

**Short-term and Working Memory**

We reported altered performances of the SSP of patients compared with healthy controls, in concordance with previous studies. This result demonstrated that schizophrenic patients differed in the maintenance and retrieval of simple spatial information. A recent quantitative review of the literature confirms that schizophrenic patients display working memory deficits independent of the specific modality of the task (spatial or verbal). Verbal and SWM deficits could then be working memory in patients suffering from schizophrenia, and the CANTAB could become a useful tool in order to diagnose schizophrenia, notably in the prodromal phase.

**Episodic Memory**

According to the literature, the results of this meta-analysis confirmed that the recognition of visual stimuli is impaired in schizophrenic patients compared with healthy controls. This deficit in non-verbal stimuli could be of particular interest, since recognition of verbal material was equally reported as impaired in schizophrenia, but recognition of verbal material appeared to be less impaired than recognition of non-verbal memory. Consequently, episodic memory for non-verbal material has to be assessed as many times as possible to describe a complete profile of the neurocognitive deficits of schizophrenic patients. In these conditions, the CANTAB battery could complete the traditional neuropsychological evaluation of schizophrenic cognition that frequently addresses only verbal memory.

**Limits**

Among the studies, the psychopathological assessment had some discrepancies. First, the clinical assessment was heterogeneous (e.g., PANSS or Scale for the Assessment of Negative Symptoms [SANS] or Scale for the Assessment of Positive Symptoms [SAPS]). Second, not all studies reported symptom severity assessment. This weakness renders interpretation of the neurocognitive results difficult because symptom fluctuation may alter neurocognitive performances, rendering the study samples heterogeneous. All but one subscale (SOC, initial thinking time in three moves) effect estimate were heterogeneous at first. After further analysis using the type of medication and patient type as moderating variables, the ‘first-episode’ patient category was singled out as the homogeneous group in the majority of memory subdomains (SSP span length, SWM error and strategy) and executive function (SOC problem solved).

However, patient type did not alter heterogeneity for PRM per cent correct. This analysis was not carried out on a subscale, with fewer than four reported studies. This variability in the effect estimate of the memory subdomain may suggest that patients with schizophrenia have heterogeneous memory deficits specific to visuo-spatial ability, and that patients are perhaps heterogeneous with no categorical definition of schizophrenia. The latter possibility cannot be justified at this point, as the complete symptomology of these patients has not been reported clearly. However, with regards to overall primary analysis, we have reached a homogenous effect estimate on SOC (three moves); this may lead to the interpretation that, first, the total number of studies included were not enough to draw a robust conclusion, and second, it can be an anomaly in the overall data.

With this systematic quantitative review we aim first to clarify the degree of neuropsychological difference seen in this patient group compared with controls.

However, when controlling for types of patients, our analysis revealed that the effect estimate for the first-episode patient groups were homogeneous with SSP, SWM and SOC, while long-term patient groups remained heterogeneous. Consequently, the profile of visuo-spatial deficits appeared to be more homogeneous in first-episode patients than in long-term patients. It could then be hypothesised that visuo-spatial deficits are quite homogeneous at the beginning of the illness and evolve heterogeneously along the course of the disease. This hypothesis tallies with the heterogeneity of cognitive profiles according to the symptomatic subtypes of schizophrenia previously described.

Earlier in this article, we stated that our analysis was restricted to visuo-spatial tasks in the CANTAB. CANTAB does test semantic/verbal memory (Graded Naming Test [GNT] and Verbal Recognition Memory [VRM]), as noted by our previous work, as the number of studies related to schizophrenia is minimal. We also state that the CANTAB includes 19 tests to date focusing on visuo-spatial abilities. With new developments within the CANTAB, three additional tests have been added to the list: the Information Sampling Test (IST), the Stop Sampling Test (SST) and the One Touch Stocking of Cambridge (OTS).

However, head-to-head comparison of schizophrenia-spectrum disorder patients with healthy controls using these tests is at ground zero. Performing funnel plot or eggers tests to ascertain publication bias was, at this time, omitted.

Since August 2006, several studies, such as the Donohue and colleagues study, have emerged. In particular, four matched our criteria: Fornito and

12. Ruiz JC, Soler MJ, Fuentes I, Tomas P,
13. Rund BR, colleagues,
14. Spindler KA, Sullivan EV, Menon V, et al.,
15. Lowe C, Rabbitt P,
16. Michel C, Cavezian C, d’Amato T, et al.,
18. Borenstein M, Rothstein H, Shamay-Tsoory et al., respectively, prohibit us from including data from these two studies in the meta-analysis because of shortage of data for aggregation. Nonetheless, SWM error outcome reported by Forino et al. supports our results.

59. Cattapan-Ludwig and colleagues,9 In contrast to our included studies, the CANTAB allows a complete visuo-spatial profile of schizophrenic patients to be made with a widely validated neuropsychological battery. Thanks to its computerised design, the CANTAB ensures standardised conditions of testing, and consequently limits the experimenter effect. Given its standardised testing procedure, the CANTAB battery can be considered as an objective method by which to target the cognitive remediation of schizophrenic deficits. The playful, attractive interface and game-like quality often ensure optimal motivation among participants. The CANTAB can be checked as many times as necessary to ensure that task demands are correctly understood, and levels of difficulty can be continuously adjusted. From the computer’s portal, specific tasks can be selected according to the clinical interests. It then allows a continuous adaptation of tasks to the deficits and progress of patients throughout the remediation. However, Kurtz et al.31 demonstrated that improvement in working memory was greater when patients could interact with a clinician compared with training in computer literacy alone. Consequently, in spite of a relative autonomy in the testing procedure provided by the computerised design, the CANTAB battery should not be used as a remediation technique without an experienced clinician with neuropsychological skills to optimise the advances made by patients.

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One of the conclusions of the CANTAB literature is the presence of visuo-spatial cognitive deficits in schizophrenia.

The Future of the Cambridge Neuropsychological Test Automated Battery
Of particular interest, the CANTAB allows a complete visuo-spatial profile of schizophrenic patients to be made with a widely validated neuropsychological battery. Thanks to its computerised design, the CANTAB ensures standardised conditions of testing, and consequently limits the experimenter effect. Given its standardised testing procedure, the CANTAB battery can be considered as an objective method by which to target the cognitive remediation of schizophrenic deficits. The playful, attractive interface and game-like quality often ensure optimal motivation among participants. The CANTAB can be checked as many times as necessary to ensure that task demands are correctly understood, and levels of difficulty can be continuously adjusted. From the computer’s portal, specific tasks can be selected according to the clinical interests. It then allows a continuous adaptation of tasks to the deficits and progress of patients throughout the remediation. However, Kurtz et al.31 demonstrated that improvement in working memory was greater when patients could interact with a clinician compared with training in computer literacy alone. Consequently, in spite of a relative autonomy in the testing procedure provided by the computerised design, the CANTAB battery should not be used as a remediation technique without an experienced clinician with neuropsychological skills to optimise the advances made by patients.