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Is implicit sequence learning impaired in schizophrenia? A meta-analysis

Richard J. Siegert [a,*], Mark Weatherall [b], Elliot M. Bell [b]

[a] *King's College London, Department of Palliative Care, Policy and Rehabilitation, School of Medicine at Guy's, King's College and St. Thomas' Hospitals, Weston Education Centre, 3rd Floor, Cutcombe Road, Denmark Hill, London SE5 9RJ, UK*
[b] *University of Otago, Wellington, New Zealand*

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Abstract

Cognition in schizophrenia seems to be characterized by impaired performance on most tests of explicit or declarative learning contrasting with relatively intact performance on most tests of implicit or procedural learning. At the same time there have been conflicting results for studies that have used the Serial Reaction Time (SRT) task to examine implicit learning in people with schizophrenia. In the present research, we used meta-analysis to clarify whether or not people with schizophrenia show impaired performance on the SRT task. A systematic review found nine studies published in peer review journals that had each compared the performance of a group of people with schizophrenia with healthy controls on the standard SRT task or a variant of it. The resulting meta-analysis represented the responses of 205 participants with schizophrenia and 159 healthy controls on the SRT task. The analysis found that participants with schizophrenia perform less well than controls reflected by a pooled effect size of 0.51. A secondary analysis of all nine studies found that they all reported a point estimate of the change in reaction time between sequence and random trials that was greater for the controls. We conclude that there is a moderate impairment in implicit sequence learning among people with schizophrenia and speculate on the implications of this for understanding this disorder. Suggestions for improving the methodological quality and statistical reporting of studies of this topic are made.

Keywords: Schizophrenia; Implicit learning; Serial reaction time; SRT; Meta-analysis

1. Introduction

Contemporary accounts of human learning and memory draw a fundamental distinction between *explicit* and *implicit* learning (Baddelely, 2002; Squire, 1994, 2004). Explicit (or declarative) learning is learning that occurs with a high level of conscious awareness for the content of what has been learnt. For example, a student in a history lesson who can correctly recall the names of all the kings and queens of England demonstrates explicit learning. They remember all the regal names and are aware that they have this knowledge and can demonstrate it at will. Explicit learning is also displayed in most neuropsychological tests and in experimental tasks of recall and recognition. In contrast, implicit (or procedural) learning is used to refer to learning that is inferred from performance on a task where the individual typically cannot provide an accurate verbal account of their knowledge, skill or ability (Seger, 1994). Implicit learning is often used to describe perceptual-motor skills, such as juggling, surfing, or riding a bicycle—those kinds of skills where even a highly skilled performer has difficulty verbalising what they have learnt. Other forms of implicit learning include priming, classical conditioning and habituation (Squire, 1992, 2004). Seger (1994, p. 163) notes that "Implicit learning is nonepisodic learning of complex information in an incidental manner, without awareness of what has been learned." A number of laboratory tasks have been developed to study implicit learning including artificial grammar learning, assorted priming tasks and the serial reaction time task. It is the performance of people with schizophrenia on this latter task,

* Corresponding author. Fax: + 44 20 7848 5517.
E-mail address: richard.siegert@kcl.ac.uk (R.J. Siegert).

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the serial reaction time (SRT) task, (Nissen & Bullemer, 1987) that is the focus of the present article.

1.1. Implicit sequence learning and schizophrenia

Arguably what interests researchers the most about implicit learning is that it seems to be relatively intact or preserved even after quite serious brain damage where explicit processes are noticeably impaired (Reber, Walkenfeld, & Hernstadt, 1991). In the case of the SRT task, there is evidence of preserved implicit learning in a range of neuropathological conditions that include: Korsakoff's amnesia (Nissen & Bullemer, 1987), Alzheimer's disease (Knopman & Nissen, 1987) and traumatic brain injury (McDowall & Martin, 1996). The exceptions to this finding of relatively preserved implicit learning in the face of neural damage seem to be those conditions where the basal ganglia are damaged such as occurs in Parkinson's and Huntington's disease (Knopman & Nissen, 1991; Lieberman, 2000; Siegert, Taylor, Weatherall, & Abernethy, 2006).

The performance of people with schizophrenia on the SRT task is of considerable theoretical importance because current thinking has it that schizophrenia is characterised by impairments on most explicit tests of cognition but relatively normal performance on implicit tasks. For example Heinrichs (2005) recently noted that: "The general consensus in schizophrenia research is that multiple aspects of cognition are impaired, including attention, working memory, encoding acquisition, and executive ability…" (p. 236). Heinrichs' own work has demonstrated using meta-analysis that effect sizes of close to one standard deviation are commonly reported in studies that have compared healthy controls with people with schizophrenia on a wide range of standard neuropsychological tests.

Compare this with the following statement from McKenna, Ornstein, and Baddeley (2002) in a review chapter on memory in schizophrenia where they noted that "Almost all studies of implicit memory in schizophrenia have found it to be intact" (p. 423). Although McKenna et al. did not draw a clear distinction between implicit learning and implicit memory in their review chapter, their summary of this topic included studies of rotor-pursuit and SRT performance. Both of these perceptual-motor tasks are considered to be implicit learning tasks. However, they only cited one study that had used the SRT task (*Green, Kern, Williams, McGurk, & Kee, 1997). In contrast they cited five studies that employed the rotor-pursuit task and six that used stem completion.

Since that first study by Green et al. there has been a number of subsequent articles examining the performance of people with schizophrenia on the SRT task—but with mixed results. Some authors have reported that people with schizophrenia demonstrate intact IL on the SRT task (Dominey & Georgieff, 1997; Reiss et al., 2006), some report reduced sequence learning (Green et al., 1997; *Marvel, Schwartz, Howard, & Howard, 2005) and others have reported impaired IL (*Exner, Weniger, Schmidt-Samoa, & Irle, 2006; Kumari et al., 2002; *Schwartz, Howard, Howard, Hovaguimian, & Deutsch, 2003). To complicate this picture even further, other authors have claimed that IL on the SRT task is impaired in people with schizophrenia on conventional antipsychotics but not atypical antipsychotics (Stevens et al., 2002), and during the acute phase of the illness but not in remission (*Exner, Boucsein, Degner, & Irle, 2006). Schwartz and colleagues noted that while recent studies have reported intact implicit learning on tasks such as the artificial grammar task and a probabilistic classification task, several recent studies have found, as they did, impaired SRT performance. They conjectured that "pathology in motor sequencing systems and poor working memory may lead to deficits in learning sequence structure in schizophrenia" (p. 517).

1.2. Implicit learning on the SRT task

The SRT task was originally developed by Nissen and Bullemer who used it to examine the attentional requirements of learning (Nissen & Bullemer, 1987). In that study, they showed that participants with amnesia due to Korsakoff's syndrome demonstrated improved performance on the task without any conscious awareness of their learning. The SRT task itself involves participants viewing a computer monitor on which an asterisk appears according to a specified sequence at any one of four locations on the screen. The participants are required to press one of four keys on a keyboard, with each key corresponding to one of the four locations, as quickly as they can. After the participant makes a correct response the asterisk disappears and a new stimulus appears at one of the four locations after a 500 ms interval. In the classic Nissen and Bullemer procedure, the sequence used was D-B-C-A-C-B-D-C-B-A and this was used over eight blocks of ten trials (Nissen & Bullemer, 1987). Because of the length of the sequence and the speed of presentation it is rare for participants to ever learn the sequence to the extent that they can verbally describe it upon request. Learning is inferred from the fact that, in spite of their inability to report the sequence correctly, most participants get faster on the sequence. Nonetheless, over successive blocks of trials, participants become faster at responding, regardless of their lack of awareness of a pattern in the stimuli presentation. If, however, the sequence is interrupted and the stimuli are then presented in random order, reaction times increase significantly (Ferraro & Okerlund, 1995). It is the reduced mean reaction time over successive blocks of trials that is taken as evidence of learning having occurred (Seger, 1998). However, an increase in mean reaction time, when a random sequence is introduced, is necessary to demonstrate that participants are actually learning the sequence, rather than just showing a decrease in simple reaction time to the presentation of the stimulus (Curran, 1998).

The aim of the present article is to examine the evidence in support of the notion that implicit sequence learning as measured by the SRT task is intact in people with schizo-

phrenia. As the published evidence is conflicting and typically involves relatively small samples of participants with varying clinical characteristics we used meta-analysis. By pooling the results of several studies that each involves a relatively small sample meta-analysis can overcome the problem of insufficient statistical power. It also reduces the possibility that any results are a consequence of the specific characteristics of one sample of participants such as medication or duration of illness.

2. Method

2.1. Systematic review

The following electronic databases were searched: Medline, PsycINFO, Embase, CINAHL and All Evidence Based Reviews (which includes the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, ACP Journal Club, and DARE). The search was restricted to research printed since 1987 as that was the year Nissen and Bullemer reported their original description of the SRT task. All studies were published before the 17th of November 2006. We subsequently included one additional study that was not available in print on that date but which had been available online as *in press* (*Zedkova, Woodward, Harding, Tibbo, & Purdon, 2006). In our search, we combined both the subject heading *Schizophrenia* and all variants of the keyword schizophrenia (i.e. *schiz**) with each of the following keywords: *SRT*, *serial reaction*, *serial learn**, *sequence*, *implicit*, *learn**, and *procedural learn**. This search strategy resulted in 217 published articles for screening.

2.2. Criteria for inclusion in systematic review

To meet inclusion criteria for the systematic review, articles had to be: (1) published in English in a peer review journal; (2) involve human participants; (3) report original research; (4) include participants with schizophrenia; (5) have a healthy control group; and (6) compare participants with schizophrenia and controls on a serial reaction time task. The SRT task was limited to Nissen and Bullemer's (1987) version or variants of this that appeared conceptually and methodologically similar enough to warrant inclusion. The abstracts of all 217 publications were assessed against these criteria independently by two examiners (E. B. and R. S.). Ten were excluded because they were not published in English. On the basis of reading the titles and abstracts of the remaining 207 articles, the examiners agreed that 165 publications did not meet inclusion criteria. Copies of the remaining 42 articles were obtained.

After reading the full text of the 42 obtained articles another 31 were excluded because they did not meet the inclusion criteria. Of these excluded papers four did not report original research and six either failed to include participants with schizophrenia or did not use healthy controls. An additional 20 of the excluded articles either did not assess implicit learning or used tasks other than the SRT task. One article (Marvel, 2003) was excluded because it was published as a conference abstract only and did not contain sufficient information to be used in the review or analysis. The eleven remaining articles all compared groups with schizophrenia and healthy controls on Nissen and Bullemer's (1987) SRT task or a variation of this task. Because of the small number of studies we included one study (Marvel et al., 2005) in which the clinical group comprised 13 people with schizophrenia and 11 with schizoaffective disorder.

The reference lists of these articles were checked for additional studies, with abstracts and (if necessary) full texts of relevant looking citations examined. No additional studies meeting the inclusion criteria for the review were identified through this process. Of the previously mentioned eleven studies, two (Inadomi, Tanaka, Kikuchi, Ohta, & Ozawa, 2005; Perry, Light, Davis, & Braff, 2000) were excluded because their tasks did not include a random sequence block following the patterned sequence trials. One further study was excluded because the participants with schizophrenia had been "explicitly informed about the existence of the abstract structure" of the sequence (Dominey & Georgieff, 1997, p.2879). Studies that embedded random trials within blocks of sequence trials, known as the Alternating Serial Response Time (ASRT; [Howard & Howard, 1997; Song, Howard, & Howard, 2007]), were included as long as mean scores for both sequence and random trials could be obtained. This left eight articles and we subsequently included a ninth article that was not available in hard copy journal format on the 17th November 2006 but which had been available online as 'in press'. This paper was drawn to our attention at the reviewing phase. The final nine articles that were included in the meta-analysis and secondary analysis are marked with an asterisk in the reference list.

2.3. Meta-analysis

The meta-analysis used the inverse variance weighted method applied to the standardized mean difference between groups. The standardized mean difference was used because when reviewing the articles, it became apparent that there were several adaptations of the originally described SRT methodology used. Therefore, it was uncertain if the actual reaction times could be directly compared on the original scale of measurement. The standardized difference in means was calculated as the difference in sample means divided by their pooled standard deviation according to the following formula:

$$\frac{\bar{X}_1 - \bar{X}_2}{S_p}$$

This statistic (also known as Cohen's d) can be biased in small samples and so a correction for bias was used as recommended by Whitehead (2002). Heterogeneity was exam-

ined and I^2 calculated. Both fixed and random effects models were used. We assessed publication bias using both a funnel plot and by a formal statistical test (Higgins & Thompson, 2002; Whitehead, 2002). A secondary analysis was to categorize each study by whether the point estimate for the difference in reaction time change was larger in one group or another and to compare the proportion to 0.5 by means of the Fisher's exact test for a proportion. SAS 9.1 was used for all analyses.

3. Results

Nine studies, all of which were published between 1997 and 2006, met the statistical criteria for inclusion in the meta-analysis. For inclusion in the meta-analysis the studies had to have reported point estimates (i.e. mean reaction time) of the SRT scores for both groups on both sequence and random blocks (or random trials nested within sequence blocks). In some cases, these data were not tabulated but could be derived from figures. They also had to have reported a measure of the variance of these scores or sufficient information for an estimate of the variance to be calculated. The remaining four studies did not report point estimates (or gave no estimate of the variance) but these data were kindly and promptly supplied upon request by their authors. The quantitative data derived from all nine papers and details as to how these were derived are shown in Table 1.

3.1. Meta-analysis

A total of 205 participants with schizophrenia and 159 healthy controls were included in the nine studies. The effect sizes for all nine studies with their 95% confidence intervals are reported in Table 2. The forest plot of the nine studies included in the meta-analysis is reported in Fig. 1. The fixed effects difference was 0.51 (95% CI 0.30–0.73). There was no evidence of heterogeneity, χ^2 statistic 7.6, 8 DF, $P = .48$. The I^2 statistic was 0.0 (95% CI 0.0–62.8).

Table 2
Effect sizes with upper and lower 95% confidence intervals (CIs) for the nine studies included in meta-analysis

Study	Estimate of control minus schizophrenia	LCL	UCL
Exner, Boucsein, et al. (2006)	0.84	0.18	1.50
Exner, Weniger, et al. (2006)	1.07	0.29	1.85
Green et al. (1997)	0.35	−0.15	0.85
Kumari et al. (2002)	1.17	−0.05	2.40
Marvel et al. (2005)	0.22	−0.35	0.79
Reiss et al. (2006)	0.33	−0.56	1.21
Schwartz et al. (2003)	0.81	0.22	1.40
Stevens et al. (2002)	0.30	−0.19	0.78
Zedkova et al. (2006)	0.35	−0.49	1.18

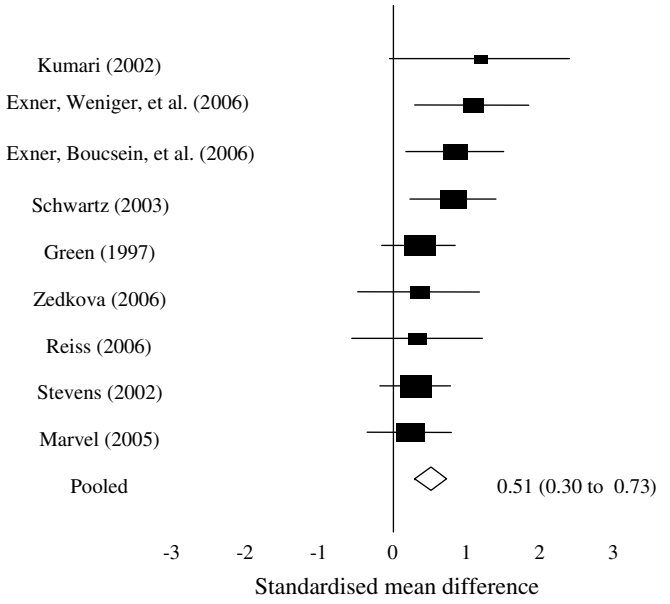

Fig. 1. Forest plot of the nine studies included in the meta-analysis. The standardized mean difference and its 95% confidence interval (CI) are shown for each study. The area of the box is inversely proportional to the variance for an individual study estimate, and the lines and diamond correspond to the 95% CI for the individual study estimates and pooled estimate, respectively.

Table 1
Means and standard deviations for the average increase in median reaction time (RT) from a sequenced block to a random block on the serial reaction time task for schizophrenia and control participants

Study	Control			Schizophrenia			Control > Schizophrenia
	N	Mean	*SD*	*N*	Mean	*SD*	
Exner, Boucsein, et al. (2006)[a]	19	70	39.0	19	3.3	102.7	Yes
Exner, Weniger, et al. (2006)[a]	15	68.2	28.3	14	22.7	51.8	Yes
Green et al. (1997)[b]	23	90	55	48	53	122	Yes
Kumari et al. (2002)[c]	6	53.3	61.7	6	−4.4	18.1	Yes
Marvel et al. (2005)[d]	24	23.8	16.0	24	19.4	22.8	Yes
Reiss et al. (2006)[d]	10	22.1	18.7	10	16.8	11.6	Yes
Schwartz et al. (2003)[d]	24	20.4	9.5	24	11.3	12.5	Yes
Stevens et al. (2002)[b]	25	48	16	50	43	17	Yes
Zedkova et al. (2006)[d]	13	33.6	38.0	10	20.5	34.2	Yes

[a] Means read from plot, SD from inverting *t*-statistic.
[b] From text of paper.
[c] Means and SD from plot.
[d] Data from authors.

There was no evidence of publication bias on formal testing, $P = .21$, although a funnel plot (not shown) suggested small studies with a point estimate for the standardized mean difference of between 0.0 and 0.2 might not have been published. If such studies were not published, there would be upward bias in the point estimate from this analysis. The random effects estimate was the same as the fixed effects estimate.

For the secondary analysis, all nine studies had a value for the change in reaction time between the sequences and the random block that was greater for the controls, proportion 1.0 (95% CI 0.66–1.0) with an exact *P*-value for a difference from 0.5 of 0.004.

4. Discussion

In the present article, we used meta-analysis to examine the evidence from published research for the idea that implicit learning is preserved in people with schizophrenia. Our meta-analysis of nine studies that compared people with schizophrenia and healthy controls on the SRT task suggested otherwise. Each of the nine studies with full quantitative data had a point estimate suggesting that participants with schizophrenia showed less learning on the SRT task than controls. Moreover, the pooled standardised mean difference (for the change in reaction time from the sequence to the random condition) indicated that this decrement is around half of a standard deviation.

A secondary analysis reached a similar conclusion with all the nine studies finding people with schizophrenia demonstrating less sequence learning than controls—although this analysis gives equal weight to all studies regardless of the size or the precision of the estimate, if available. Admittedly, the secondary analysis only considers whether or not the number of studies that found less implicit learning in the schizophrenia group is greater than chance—it does not consider whether an absolute difference between the two groups in a study is statistically significant. However, it is interesting to note that one of these studies concluded that there was no impairment in IL for the schizophrenia group based upon a non-significant difference between the groups, despite the fact that with only 10 participants in each group the study was under-powered to begin with (Reiss et al., 2006).

In summary, then it appears that people with schizophrenia typically show a moderate degree of impairment in implicit learning as indexed by the SRT task. This finding suggests that it may be premature to conclude that cognition in schizophrenia is characterised by entirely normal performance on all tests of implicit or procedural learning. The SRT task seems to be an exception to this rule. In this discussion, we will attempt to make sense of this finding in terms of current understanding of motor skill acquisition and brain circuitry. We will also speculate as to what this finding could mean for understanding the disorder of schizophrenia. However, this finding must be interpreted carefully in view of the limitations of our present study and of those studies that contributed data to the meta-analysis. Consequently, we will consider both of these issues before looking at the broader issues.

4.1. Limitations of the present study

There are several criticisms that could be levelled at the present research. The principal one, given that we undertook a meta-analysis, is that we did not systematically search for all existing studies. In this regard, there were two major limitations or potential sources of bias in our search strategy. One is that for pragmatic reasons we only included articles that were published in the English language. However, this criterion only excluded ten articles out of 217 that our electronic search identified. A second potential source of bias is that we restricted our literature search to articles published in peer review journals and did not systematically search the so-called "grey literature", such as conference proceedings and PhD theses. However, while we acknowledge these potential sources of bias, we would argue that in confining our search to peer review articles we have summarised the best quality research widely available in English on this topic. Also, the inclusion of unpublished research studies can introduce bias as well as reduce it. For example, Egger, Dickersin, and Davey Smith (1995) have noted that the inclusion of unpublished research relies heavily upon the willingness of researchers to provide their data and their willingness to do this can sometimes be influenced by their results. At the same time, while there was no evidence of publication bias on formal testing, a funnel plot suggested that small studies with a point estimate for the standardized mean difference of between 0.0 and −0.2 might not have been published. This would result in a small upward bias of the point estimate of the difference between participants with schizophrenia and healthy controls. Thus we cannot be completely sure that there are no unpublished studies sitting in a desk drawer somewhere and we acknowledge that this is a limitation.

The present study might also be criticized for including the Marvel et al. (2005) data in which the clinical group comprised 13 people with schizophrenia and 11 with schizoaffective disorder. We made this decision because of the relatively small number of studies. This is an important point though and it is interesting to note that the Marvel study had the smallest effect size of the nine studies included in the meta-analysis (see Fig. 1). Presumably then excluding the Marvel study would have meant an increase in the pooled estimate and even stronger support for our conclusion that people with schizophrenia show deficits on the SRT task. It should also be mentioned here that the Exner, Boucsein, et al. (2006) study reported that their participants with schizophrenia were impaired on the SRT task while in the acute phase but showed normal performance 20 months later in remission. In the present study, we include their data from the acute phase as evidence that performance is impaired in people with schizophrenia.

4.2. Limitations of SRT studies and implications for future meta-analytic research

This meta-analysis only included nine studies because we only located nine studies that were both (a) sufficiently methodologically rigorous, and (b) reported their data in a form that could be used in a meta-analysis or made their data available on request. For minimal methodological rigour, we required that the design included both sequence learning and random trials. These two design features are generally accepted as the minimal requirements to substantiate a claim that IL has occurred. It is also preferable that a test for explicit learning is included to establish that the sequence has not been explicitly acquired. However, requiring this would have reduced the number of studies included even further.

The important point at issue here is that a more definitive meta-analysis will only be possible if subsequent studies of SRT learning in people with schizophrenia include the following: (a) demonstration of sequence learning (b) a random block or randomised trials within blocks, and (c) report the mean and standard deviation for the difference between random and sequence conditions. A test of explicit sequence knowledge is also highly desirable if not essential. Other methodological improvements could include the increasing use of Howard and Howard's probabilistic sequence (alternating SRT or ASRT) which makes explicit learning less likely to occur and the advent of fully probabilistic sequences that allow investigation of third and fourth-order dependencies in a sequence (Remillard, 2007).

The importance of meta-analysis for this area is evidenced by the fact that all the studies we found were under-powered to detect a type two error. In fairness, this may be less of an issue for neuroimaging studies, where the focus is on observing differences in neural activation between groups performing the same task, rather than on measuring behavioural differences in performance. Based on the pooled standardised mean difference we observed of 0.51 a power calculation indicates that a study of this nature will require a minimum of 64 participants in both experimental groups (i.e. $n = 128$) to have an 80% chance of detecting such a difference.

Another significant limitation of the present study results from the different clinical characteristics of the participants with schizophrenia in the nine studies included in the meta-analysis. For example Exner, Weniger, et al. (2006) reported data from 15 patients with first-episode schizophrenia, whereas the patients recruited by Green et al. (1997) all had "a chronic form of the illness requiring lengthy hospitalisation" (p. 126). As noted earlier in one study (Marvel et al., 2005), the clinical group comprised 13 people with schizophrenia and 11 with schizoaffective disorder. Studies also varied according to whether they used inpatients, outpatients or a mixture. Of course it could be argued that this clinical heterogeneity actually supports the robustness of the finding that performance is impaired on the SRT task among people with schizophrenia. In other words, it is not restricted to the acute phase or only evident in chronic patients after years of medication. It is relevant to note in this regard that a recent article by Woodward, Tibbo, and Purdon (2007) reported evidence that SRT performance is normal in unaffected siblings of people with schizophrenia although their performance was characterised by reduced activation of frontal, parietal and basal ganglia regions.

Moreover, the medications that participants were on varied across and within studies. Studies typically combined patients on conventional and atypical antipsychotic drugs and it was not always reported how many were on each form of antipsychotic. One study that separated patients on the two types of antipsychotic medication actually reported that implicit learning was intact in the group on atypicals and impaired in the group on conventional antipsychotics (Stevens et al., 2002) (although because they shared the same control group they had to be treated as one group for the present meta-analysis). Another issue is that some reported a significant number of participants were on other psychoactive medications. For example in the Green et al. (1997) study 27 out of 48 patients were also on anti-Parkinsonian medication and in another paper almost half the schizophrenia group were also on benzodiazepines (Exner, Weniger, et al., 2006).

4.3. Neural mechanisms

Probably the major question arising from the results of the present study is what they suggest with regard to brain function in people with schizophrenia? We will first consider some evidence that comes from three recent studies that used functional imaging to examine brain activity in people with schizophrenia performing the SRT task. In possibly the first functional imaging study comparing SRT performance by people with schizophrenia and healthy controls Kumari et al. compared six healthy participants and six patients on conventional antipsychotics. They reported that controls showed implicit learning but people with schizophrenia did not. The functional magnetic imaging (fMRI) of SRT performance for the controls showed increased brain activation in the "striatum, thalamus, cerebellum, precuneus, medial frontal lobe, and cingulate gyrus" (p. 97). In contrast, the participants with schizophrenia did not demonstrate usual procedural learning and the only brain region notably activated was the anterior inferior gyrus. Reiss et al. (2006) compared 10 participants with schizophrenia on atypical antipsychotics with matched controls on the SRT task using fMRI. They reported that participants with schizophrenia did show learning on the SRT task and the most notable finding from imaging was "a relative lack of striatal activation in the patients" (p. 127). In the most recent imaging study, Zedkova et al. (2006) compared 10 patients (some on atypical and some on mixed conventional/atypical medications) with healthy controls. In this case, they reported that pro-

cedural learning occurred in both groups. However, they noted different patterns of brain activation between the two groups. While the controls demonstrated typical activation of "dorsal striatum, anterior cingulate, parietal cortex and frontal cortex" the patient group showed a "paucity of activation in bilateral frontal cortex, left parietal cortex and bilateral caudate nucleus" and greater activation of "right superior temporal gyrus, the right anterior cingulate cortex and the left globus pallidus" (p. 198). These authors concluded that this picture was consistent with disruption of normal frontal subcortical circuits in people with schizophrenia and resultant compensatory activity.

It is perhaps fair to say then that the results of functional imaging studies of SRT learning in schizophrenia to date, vary both in the characteristics of the participants (i.e. medications, learning intact versus impaired), and also the brain regions that they highlight. However, this type of research is also in its infancy and it may require several more studies before a clear picture emerges. It is worth noting though that this area of research is also characterised by small samples and the comments made earlier with respect to the design and reporting of SRT studies are equally pertinent for imaging studies employing the task. However, one brain region that is implicated to some degree, by all three of these imaging studies, is the striatum, and this is consistent with previous research. It also fits with a recent study by Reiss et al. (2006) which found that among 15 healthy participants those who showed learning on the SRT task also demonstrated striatal activation, whereas non-learners did not.

There is also a substantial body of evidence that performance on the SRT task is reduced or impaired in those disorders characterised by damage to the basal ganglia such as Parkinson's and Huntington's (Knopman & Nissen, 1991; Lieberman, 2000; Siegert et al., 2006; Wilkinson & Jahanshahi, 2007) and also that the striatum is activated in healthy participants by the SRT task (Peigneux et al., 2000; Poldrack et al., 2005; Rauch et al., 1997; Reiss et al., 2006; Seger, 2006). Converging with these lines of research is a growing body of evidence for striatal abnormalities occurring in schizophrenia (e.g. Gur et al., 1998; Vink, Ramsey, Raemaekers, & Kahn, 2006).

4.4. Speculation on the implications of impaired SRT performance

To summarise thus far, implicit sequence learning is impaired to a moderate extent in people with schizophrenia, and this probably reflects some dysfunction of frontal–striatal circuits. Neither of which seems particularly surprising or controversial. The challenge here is how to relate these two conclusions to our existing knowledge and understanding of the disorder itself. It is of course of some theoretical interest to know that people with schizophrenia typically demonstrate less implicit SRT sequence learning than healthy controls by about half of a standard deviation. But what possible relevance does this have for understanding and managing a major mental disorder that can cause substantial and prolonged social impairment (Walker, Kestler, Bollini, & Hochman, 2004)? We can only speculate about the answer to this question but a review paper by Lieberman offers some potentially relevant ideas (Lieberman, 2000).

In that article, Lieberman reviewed a substantial body of research on intuition and on implicit learning and argued that the two are closely related. In particular, he argues that the anatomical substrate that these phenomena have in common are the basal ganglia. In essence, Lieberman is arguing that much of our social behaviour is based upon procedural learning and that this relies upon the basal ganglia. Interestingly, Lieberman bases much of his case upon an extensive body of research involving participants with Parkinson's disease or Huntington's disease, both prototypical basal ganglia disorders, but the article does not really consider schizophrenia. However, if Lieberman's hypothesis is correct it may well have relevance for our understanding of the social and emotional dimensions of schizophrenia. Lieberman reviews extensive neuropsychological evidence that supports the notion that the basal ganglia may play an important role in nonverbal communication, emotional cognition and language. In essence, he is arguing that so-called "intuition" is really implicit social cognition and that the basal ganglia are important in processing such information. If this hypothesis is correct it could help to explain, to take just one example, why people with schizophrenia show less facial emotion and expressiveness than controls and perform less well at reading the facial emotions expressed by others (Walker et al., 2004). Such skills as 'reading' another person's facial expressions are typically acquired implicitly. That is we learn them in the course of normal development through repeated exposure and practice and while most people master such skills by an early age they might struggle to explain in words how they can instantly distinguish between say, a 'puzzled' look and a 'weary' look, on their friend's face. Putting to one side the specific example of interpreting other people's facial expressions, the point at issue here is that a deficit in procedural learning capacity could have a significant impact upon the development of social cognition and behaviour.

4.5. Some possible directions for future research

We have already made some suggestions above for improving data reporting to facilitate further meta-analyses in this area and also noted that imaging research of SRT performance in people with schizophrenia is still in its infancy. Now we wish to suggest some other possible lines of enquiry for researchers interested in implicit learning among people with schizophrenia. One issue that requires further investigation is the relationship between performance on the SRT task and other implicit learning tasks in people with schizophrenia. As noted in the intro-

duction to this article researchers have typically reported normal performance on other IL tasks among people with schizophrenia (e.g. rotor-pursuit learning, word stem completion; McKenna et al., 2002). However, some of these studies only administered a single test of implicit learning and it is likely that the same issues pertaining to sample size and statistical power could be of concern. Hence a properly powered study examining the performance of people with schizophrenia on a range of qualitatively different implicit learning tasks could be informative. For example, Lieberman listed the following types of implicit or procedural learning tasks that have been used for this kind of research in patients with Huntington's and Parkinson's: Mirror reading, pursuit rotor, Tower of London, SRT, artificial grammar and probabilistic classification tasks. A key question here would be whether implicit sequence learning is a special case of implicit learning that is impaired in schizophrenia while these other forms of IL remain intact? Also, given Lieberman's (2000) hypothesis that some social behaviour, such as simple social scripts, is learnt implicitly it could be of interest to see whether or not individual differences in IL among people with schizophrenia showed any relationship with deficits in social skills and competencies?

One other important line of research for further investigation in this field concerns the potential role of antipsychotic medications in performance on implicit sequence learning tasks. This area is important to explore further because it is conceivable that any observed deficits in implicit learning could actually be an effect of these medications rather than simply being due to abnormal striatal functioning as we have argued earlier. It is interesting to note in this regard that Stevens et al. (2002) did separate their patients who were on conventional and atypical antipsychotics and concluded that "Olanzapine seems to interfere less with unattended learning and motor speed that classical neuroleptics" (p. 299). Indeed, they went as far as suggesting that implicit learning is not impaired in schizophrenia *per se*, but rather is impaired by conventional antipsychotic or neuroleptic medications. This makes some sense given that atypical antipsychotics are often preferred because of their lack of extra-pyramidal side effects which is thought to be due to their preferential binding with D_2receptors in extrastriatal limbic and "...intrastriatal associative regions in preference to motor regions of the striatum... (Stone, Morrison, & Pilowsky, 2007).

At the same time a recent paper by Pedersen et al. (2008) reported impaired performance on the SRT task in a sample of 37 people with schizophrenia who were all treated with atypical antipsychotics. Also, as noted above the study by Woodward et al. (2007) found impaired SRT performance in first-order relatives who were not on any antipsychotics. Indeed the relationship (between symptom severity, medication exposure and implicit learning capacity) may be a complex one given the evidence that neuroleptic exposure is itself related to striatal hypertophy (Gur et al., 1998).

4.6. Conclusion

A meta-analysis of nine studies comparing people with schizophrenia and healthy controls on the SRT task found that the implicit sequence learning of people with schizophrenia was less than that of controls. An effect size of 0.51 was observed. Thus while implicit memory and learning are generally preserved in people with schizophrenia the exception seems to be sequence learning. This probably reflects some dysfunction of frontal–striatal networks. We speculate on how impaired procedural learning could have broader implications for psychosocial development and our current understanding of schizophrenia.

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