Schizophrenia Research: Cognition 7 (2017) 8–12

Contents lists available at ScienceDirect

Schizophrenia Research: Cognition

journal homepage: http://www.schizrescognition.com/

Is performance on probed serial recall tasks in schizophrenia related to duration of Attentional Blink?

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ARTICLE INFO

Article history:
Received 18 August 2016
Received in revised form 2 December 2016
Accepted 26 December 2016
Available online 17 January 2017

Keywords:
Schizophrenia
Visual working memory
Attentional Blink
Memory consolidation
Probed serial recall

ABSTRACT

Schizophrenia is associated with a deficit in working memory, with the degree of working memory impairment related to the level of social and occupational functioning. This study tests the hypothesis that the working memory deficits in individuals with schizophrenia can be explained by slow processing of visual stimuli, as measured by the attentional blink (AB) task. Individuals with schizophrenia (SC) and controls (HC) were recruited from an early intervention service for psychosis and the local community. Data from 16 SC (11M/5F, mean = 26.4 yo) and 20 age-matched HC (11M/9F, mean = 25.8 yo) were analyzed. Each subject performed an AB task to determine their AB duration, defined as the lag to reach their plateau performance (ltpp). As expected, mean AB duration in the SC group (575 ms) was significantly slower than HC (460 ms; $p = 0.007$). Recall accuracy of the SC group on a working memory task, a 6-item probed serial recall task (PSR), was reduced compared to the HC group at a standard interstimulus interval (ISI) ($p = 0.002$). When the individual's AB duration was then used to adjust the ISI on the PSR task to three relative ISI rates (Slow ($2 \times$ ltpp), Medium (ltpp) and Fast ($1/2 \times$ ltpp)), performance on the PSR task was affected by group, position and ISI and qualified by an ISI * position ($p = 0.001$) and a trend to a triple interaction ($p = 0.054$). There was main effect of group at all ISIs, but group * position interaction only at Slow ISI ($p = 0.01$). Our interpretation of the results is that absolute ISI, rather than ISI relative to AB duration, affected performance.

1. Introduction

Working memory, an important cognitive function that underlies diverse aspects of thought and action (Baddeley, 1992), is impaired in individuals with schizophrenia (Lee and Park, 2005) and is contributory to the degree of social and occupational impairment that may result (Heinrichs and Zakzanis, 1998; Cervellione et al., 2007). Thus a further understanding of this impairment is important, allowing for directed and novel treatment approaches to optimize potential outcomes.

Working memory provides a substrate for the processing of serial events; as Stephane and Pellizzer, 2007, state "memory for serial order is crucial for the organization of purposeful actions, including motor control (Rosenbaum, 1990) and language (Levelt, 1989; Dell et al., 1997)." Processing of serial events can be investigated using a serial recall paradigm in which individuals are presented with a sequential list of items and then memory for these items is probed using a recognition test. Observed since the earliest days of experimental psychology (Bigham, 1894) is that the first and last items are remembered better than the items in the middle of the list, the primacy and recency effect, respectively.

Individuals with schizophrenia are reported to have impaired performance on probed serial recall (PSR); in general findings suggest that recency is preserved while primacy and middle items are impaired (Elvevag et al., 2002; Frame and Oltmanns, 1982; Stephane and Pellizzer, 2007). This impaired serial order processing may underlie some of the language deficits seen in individuals with schizophrenia since appropriate processing of serial order is important for language function, in which words are presented serially and memory of the words must be maintained in order to make sense of the sentence, or to produce the sentence. Support for this hypothesis includes reports of working memory capacity for language and language comprehension being correlated in both healthy controls and people with schizophrenia (Condray et al., 1996) and serial order abilities linked to anticipatory and perseverative errors in language production (Dell et al., 1997).

Impairments in PSR can result from slowed working memory processes, of which encoding has been the phase found most impaired in

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http://dx.doi.org/10.1016/j.scog.2016.12.001

schizophrenia (Hartman et al., 2003; Lee and Park, 2005). The time course of early stages of serial visual processing and encoding can be related to the Attentional Blink (AB).

The AB is shown by a Rapid Serial Visual Presentation (RSVP) in which a series of stimuli are presented rapidly (<100 ms per stimulus). The viewer tries to detect 2 designated targets (T1 and T2) within the stream, such as detecting 2 letters in a stream of numbers. The AB is measured by quantifying the accuracy of identifying T2 given accurate identification of T1. In young adults, a T2 that appears within the period of 200–500 ms after T1 may be missed (Raymond et al., 1992). There are many different models of AB and a review can be found in Dux and Marois (2009). Regardless of the model of AB used, there must be an encoding step that is time-dependent – a step that is also in PSR tasks and has already been identified as impaired in schizophrenia.

In schizophrenia, the AB has been shown to be protracted (longer time interval between T1 and T2 needed to return to peak accuracy) as well as exaggerated (decreased accuracy at identifying the second target) (Cheung et al., 2002; Li et al., 2002; Wynn et al., 2006; Mathis et al., 2011; Mathis et al., 2012; Jahshan et al., 2014). The deficits in AB may help to explain the pattern of deficits in PSR tests in schizophrenia, i.e. a potential relationship between temporal processing deficits shown by AB and performance in PSR. The performance on the final item in the list would not be affected as the final item is not overwritten by a following prompt (Giesbrecht and Di Lollo, 1998), resulting in a preserved memory for the last item in the list, and matching the pattern of preserved recency but impaired general performance in people with schizophrenia. It is not suggested that PSR items are being "blinked", only that there may be a relationship between the individual's time course of attention as shown by a protraction of their AB duration and their encoding efficiency in PSR since both depend on temporal processing of an encoding step. AB does not affect the first item (unless the subject reverses the order of the items), so this hypothesis does not explain reduced performance on the first item in people with schizophrenia.

This study aims to investigate whether the PSR deficit in schizophrenia is connected to impairment in AB. The objectives of this study were to:

1. Use the AB paradigm to investigate temporal serial processing in individuals with schizophrenia, compared to age and gender-matched controls, on an individual basis. It was hypothesized that the AB will be protracted and exaggerated in the individuals with schizophrenia compared to the controls.
2. Apply the above information on an individual's AB to set the interstimulus interval (ISI) in a PSR paradigm. The purpose of this second paradigm was to examine if providing the appropriate ISI can improve performance in individuals with schizophrenia. It was hypothesized that adjusting ISI consistent with an individual's AB duration will improve that individual's performance on the PSR paradigm, while primacy and recency would remain unchanged.

2. Method

The study was approved by the Capital Health Research Ethics Board in Halifax, Nova Scotia. Healthy controls and individuals with schizophrenia were recruited to the study using word of mouth with clinicians, posters in mental health clinics, universities and colleges, and the website Kijiji. Participants who responded were initially screened by telephone or email for exclusion and inclusion criteria, and subsequently invited to participate.

After signed consent was obtained, the Structured Clinical Interview for DSM-IV (SCID-IV) was conducted by a trained examiner to confirm diagnosis. Other criteria for the schizophrenia group included being on atypical antipsychotics for at least 3 years with no recent changes in medications, were between 18 and 50 years of age, and absence of any medical or neurological illness that could affect cognition. Healthy controls were excluded if they had a current or past DSM-IV Axis 1 disorder, first-degree relatives with a psychotic disorder, head injury causing unconsciousness, or neurological condition that could affect cognition. After the screening, 28 healthy controls (HC group) and 29 individuals with schizophrenia (SC group) participated in the study.

2.1. Experiment 1: Attentional Blink paradigm

A standard RSVP was used to evaluate the AB in each participant based on the method used by Cheung et al. (2002) and Wynn et al. (2006), pioneered by Chun and Potter (1995) to avoid a task switch, and modified to include longer lags to allow full recovery to normal accuracy in people with schizophrenia and with enough repetitions at each lag to be able to detect changes between lags statistically on an individual level. The application presentation (Neurobehavioural Systems Inc., CA) was programmed to present the target letters (T1 and T2) in a stream of numbers (2–9) on each trial. Each item was displayed for 50 ms (3 refreshes on 60 Hz monitor) with a gap of 50 ms between items. The lag between T1 and T2 varied from 200 to 1000 ms in intervals of 200 ms. At least 2 numbers were always displayed before any target letters, and at least 2 numbers were displayed after any target. At the longest lag, there were at least 15 items in a stream, so every stream was presented with 16 items. Target letters were from the set [ACEJKRTY]. There were 24 trials for each of 5 lags; thus, 120 trials were required. As the AB calculation is based on accuracy of identifying T2 given correct identification of T1, T1 identification was enhanced by presenting it in red, amongst black distractors and black T2 (color change discussed by Chun (1997) and Chun and Potter (2001)). The participants gave their responses orally to the examiner who entered the responses on a keyboard, allowing the participants to keep their attention on the screen. An unlimited amount of time was allowed for response. The participants initiated each trial with a key press.

Number of correct T1 items and percentage of correct T2 items given accurate report of T1 at each lag were recorded. The AB duration was defined as the first lag at which significant improvement in accuracy is not subsequently seen (i.e., performance has reached a plateau), as shown in Fig. 1. The AB duration was individually defined for each participant by calculating the chi-square statistic for consecutive lags. The start of the AB plateau was defined as the lag where the last chi-square critical threshold was exceeded in comparison to the previous lag at $p < 0.1$ for 2 degrees of freedom. In cases where individual chi-squares did not exceed the critical threshold, but the chi-square of the first to last lag exceeded the threshold, the lag with the highest chi-square was used as the AB duration, as long as at least 80% performance was achieved by the final lag.

In addition, two control tasks were given to ensure that all participants could detect the letters presented at the same ISIs and with the same lags as on the AB, but with no distracter numbers. Performance on T1 only and T2 given correct T1 was measured in this way. No participants scored <80% in one of these control tasks.

Participants were given a short practice with a single target and distracters to allow them to get accustomed to the presentation. Once participants had attained 9 of 10 right on the single target task, they were progressed to practice the dual-target task, and were allowed to practice until they felt comfortable with the task and procedures (typically 10 trials).

Analysis consisted of a 2-sample *t*-test with 95% confidence intervals to compare the mean AB durations of the two groups.

2.2. Experiment 2: probed serial recall (PSR) paradigm

Participants did not move to Experiment 2 if unable to find a measurable AB duration in Experiment 1, as individualized AB durations are needed for application to the PSR task.

Presentation (Neurobehavioural Systems Inc., CA) was used to program the PSR task. Letters were serially presented one at a time at an ISI based on their AB duration. Three ISIs for each participant were determined from their AB duration: i) Medium; ISI equivalent to the AB

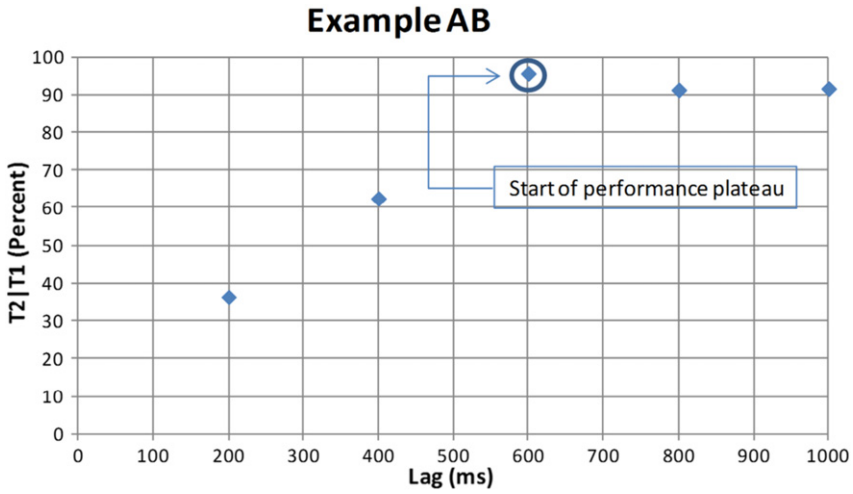

Fig. 1. Example of individual Attentional Blink (AB) result. Circle shows the lag that would be used to define the Attentional Blink duration for this participant (600 ms). This value would then be chosen to set the Interstimulus Intervals (ISIs) for Experiment 2.

duration; ii) Slow; twice the AB duration; and iii) Fast; 50% of AB duration; generally resulting in ISIs in the range of 200 ms to 1200 ms. Varied ISIs are required to evaluate changes in performance on PSR, as the duration of AB does not necessarily correspond directly to the appropriate presentation rate in PSR tasks, and to control other factors such as retention time. Participants were also given a standard ISI of 750 ms to compare to Elvevag et al. (2002). Recall was tested by presenting a number probe 500 ms after the last item to indicate the serial position of the item to be recalled and response was untimed. There were 12 trials at each of the 6 serial positions, with 72 total trials at each ISI. In order to move performance of controls from ceiling, phonologically similar letters [BCDGPTV] with 6 letters in a list were used, resulting in 73% overall accuracy for controls (in Elvevag et al., 2002). Patients were given the same number and type of items in the list.

Accuracy on the probed serial recall (PSR) task was evaluated using repeated measures analysis of variance (RMANOVA) with serial position and ISI as the within-subjects factors and group as the between-subjects factor. We expected to see normalization of performance in the schizophrenia group at Slow ISI; greater time was not expected to help healthy controls. A triple interaction would indicate that there is an interaction of AB duration and ISI with PSR performance that depends on the group.

Participants were given a practice (12 trials) before testing started, and they could repeat the practice if desired. Breaks between runs were offered. Total interview and testing time was 2–3 h, and testing was scheduled in one or two sessions as needed.

3. Results

6 healthy controls and 2 participants with schizophrenia had high performance across all lags (non-blinkers). 1 healthy control and 7 participants with schizophrenia did not reach acceptable performance (80%) at any lag. The PSR tasks for 1 healthy control and 3 participants with schizophrenia were run with a different ISI than was determined by later review of their AB results, and 1 participant with schizophrenia who had a measurable AB did not perform above chance on the first 2 PSR tests and did not continue.

3.1. Experiment 1

After removing the participants described above, a data set of 20 HC and 16 SC remained. Subject information and comparison of the AB durations is found in Table 1. Groups were not different in age ($t(34) = 0.49$, $p = 0.63$), or gender composition ($\chi^2(1) = 0.70$, $p > 0.1$). The groups showed a statistically significant difference in AB Duration ($t(34) = 2.89$, $p = 0.007$). Fig. 2 illustrates the T1 and T2|T1 measures by group and lag.

3.2. Experiment 2

Results of experiment 2 were evaluated using the same 20 HCs and 16 SCs included in Table 1. Mauchly's test of sphericity was violated for serial position, so Greenhouse-Geisser correction was used for position analysis.

Standard ISI (750 ms): we compared results at the standard ISI used in the Elvevag et al. (2002) study. Overall performance was similar between studies: SC: 55% correct in our study vs. 54% in Elvevag et al.; HC: 74% vs. 73%. RMANOVA of the standard-only results confirmed that individuals with schizophrenia performed worse than healthy controls (HC mean 8.89, standard error 0.44; SC mean 6.59, standard error 0.50; $F(1,28) = 12.0$, $p = 0.002$). Position was also significant ($p < 0.001$) but there was no interaction of position * group ($p = 0.17$). These results give confidence that our method was a successful replication of PSR in this cohort.

The 3-way RMANOVA showed a main effect of group ($F(1,34) = 9.4$, $p = 0.004$), main effect of ISI ($F(2,68) = 47$, $p < 0.001$), and main effect of position ($F(3.4,113.8) = 57.6$, $p < 0.001$). These main effects were qualified by a significant interaction of ISI * position ($F(6.8,231.6) = 3.7$, $p = 0.001$) (Table 2). Fig. 3 illustrates the group comparisons at each ISI. There was a trend to significance for the triple interaction ($F(6.8,231.6) = 9.6$, $p = 0.054$), which allowed for the continuation of the analysis with RMANOVA at each position separately to investigate the source of the interaction.

The RMANOVAs at each position were uniform. At all positions, there was a main effect of group and main effect of ISI. The main effect of group was always better performance in HCs. The main effect of ISI was always poorer performance at Fast ISI, although this was outside significance at position 6 (Wilks' Lambda = 0.84, $p < 0.056$). There was interaction of group and ISI only at position 4 ($F(5.145)=$, $p < 0.008$).

Table 1
Participant demographics and attentional blink (AB) performance.

	Healthy Controls (HC)	Schizophrenia (SC)
N (males/females)	11/9	11/5
Age[a] (yrs)	25.8 (4.1)	26.4 (4.4)
Age range	19–32	20–34
AB duration[a] (ms)	460 (94)	575 (144)*

[a] Mean (SD).
* Significantly different from HC, $p = 0.007$.

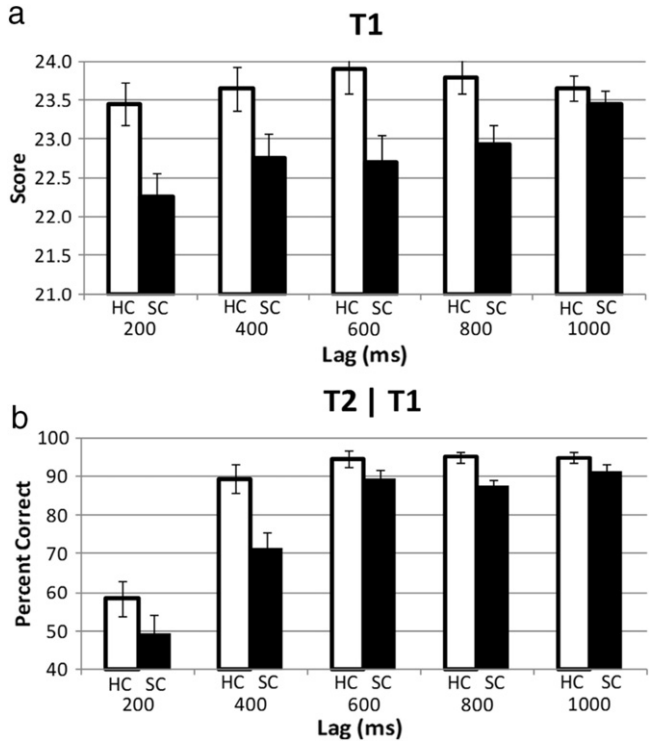

Fig. 2. Attentional Blink results showing mean of a) correct identification of target 1 (T1), b) correct identification of target 2 given correct identification of target 1 (T2|T1) compared across lags by group (HC – healthy controls, SC – subjects with schizophrenia). Error bars show standard error of the mean.

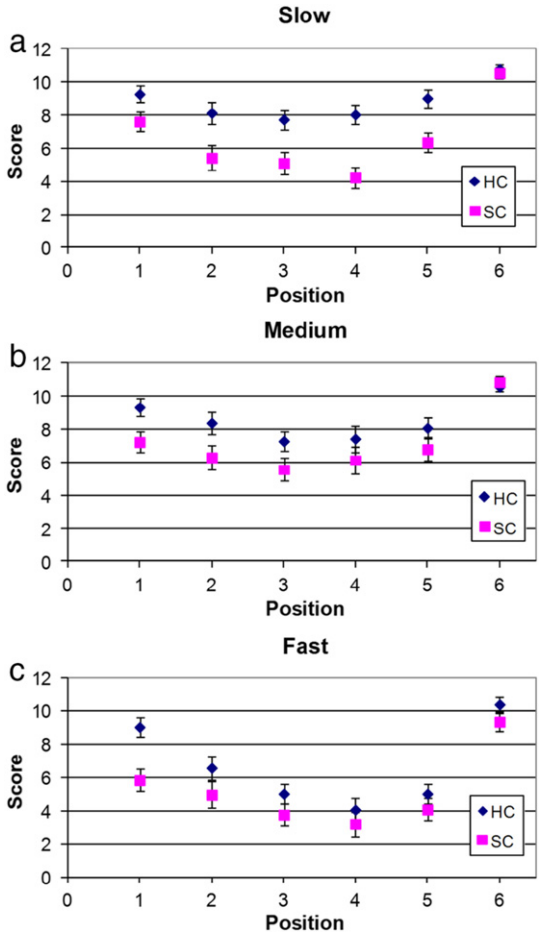

Fig. 3. Probed serial recall test results showing performance of the 2 groups (HC – healthy controls, SC – subjects with schizophrenia) at each Inter Stimulus Interval (ISI) A. Slow, B. Medium, C. Fast. Error bars show standard error of the mean, and scores are number correct out of 12.

4. Discussion

We report that individuals with schizophrenia have a protracted AB, replicating previous work in this area. There was also the expected poorer performance of the patients than controls when performing the PSR with the same presentation rate (standard ISI). A unique further examination found that adjusting the ISI for AB did not normalize the performance of individuals with schizophrenia, as there were still group differences at each ISI.

In further examination of our finding of a trend to a triple interaction, we report a group difference at each position, and ISI difference at each position, but a ISI * group interaction only at position 4. The finding of an ISI effect is consistent with literature in recognition memory (Intraub (1980); Wright et al. (1990)); however these findings do not suggest normalization of performance.

There are some potential issues with the methodology of the study. The individualized analysis of our AB task highlighted some performance issues. There were participants, both healthy controls and individuals with schizophrenia, who did not perform as expected on the AB. Those who showed high performance but no significant dip at smaller lag were noted. Other studies have also noted these "non-blinkers" (Martens et al., 2006; Martens and Valchev, 2009; Willems et al., 2013). The evidence is that AB is not robust at the individual level, though this depends on details of how the AB is elicited. Since in our protocol, T1 was made easier to detect (via color change) and there is evidence that the difficulty of identifying T1 affects the magnitude of the AB effect (Chun and Potter, 1995; Giesbrecht et al., 2009; Martens et al., 2006; Seiffert and Di Lollo, 1997; Visser, 2007), this may have made it possible for performance in more subjects in the healthy control group to avoid a 'blink'. We also saw poor performance at all lags (mostly in the schizophrenia group). We have not seen reports of this before, but also have not seen other papers define a limiting performance measure as well as there are no other studies of individualized AB in people with schizophrenia where most of the performance problems were found.

Another methodological issue is that the variation in AB duration was not large, being largely restricted to 400 and 600 ms with only 2 people with schizophrenia at 800 ms. Although the coarseness of this measure may hide the actual distribution of AB performance, the results are unlikely to be different with a better measure of AB duration as the performance at Slow and Medium ISIs cover the likely range of the actual distribution and performance was not significantly different between these ISIs.

A further issue may be in the PSR experiment with varying the retention time required systematically between groups. A variable waiting interval before the probe could have been introduced, but this

Table 2
Performance on probed serial recall at each position, according to ISI.

Position	Slow	Medium	Fast
1	8.46 (0.38)[a]	8.30 (0.42)	7.41 (0.44)
2	6.79 (0.50)	7.36 (0.51)	5.74 (0.52)
3	6.44 (0.44)	6.43 (0.47)	4.38 (0.43)
4	6.15 (0.44)	6.79 (0.59)	3.62 (0.50)*
5	7.71 (0.41)***	7.46 (0.48)	4.53 (0.44)**
6	10.68 (0.21)	10.74 (0.23)	9.83 (0.35)

[a] Mean (SE) number correct out of 12.
* Significantly different, $p < 0.05$, by False Discovery Rate for correction for multiple comparisons for Fast 4 to Medium 4.
** Significantly different, $p < 0.05$, by False Discovery Rate for correction for multiple comparisons for Fast 5 to Slow 5.
*** Significantly different, $p < 0.05$, by False Discovery Rate for correction for multiple comparisons for Fast 5 to Medium 5.

would affect the performance on the last item (recency is affected by the delay before the final probe (Baddeley (1986)), and it is unlikely that varying retention time is confounding the results because performance at Slow and Medium ISIs were so similar.

Often, memory tasks are accompanied by a vocal task that is meant to interfere with the phonological loop (i.e. rehearsal for maintenance, dual task). It may be useful to include a dual task in this experiment to make the results more directly comparable to standard psychological tests. In our case, we chose not to do this in order to compare to a published result in schizophrenia (Elvevag et al., 2002). As well, a recent paper challenged the phonological loop interpretation for serial order memory (Stephane, 2012), as the role of rehearsal in primacy effect was earlier challenged (Wright et al., 1990).

If the AB deficit is not responsible for decreased performance on PSR for individuals with schizophrenia, then what is? Schizophrenia is recognized to have an effect on cognition across a multitude of domains (summarized by Buchanan et al., 2005) and this generalized cognitive deficit may also play a role in the PSR and AB deficits, although the generalized cognitive deficits presumably don't affect all measures (such as recency).

This study used a younger SC sample than previous reports (mean age 26 years vs. for example 33 years for Elvevag et al. (2002), 47 years for Wynn et al. (2006), 46 years for Jahshan et al. (2014)) and had fewer years of illness and drug usage. However, the sample still showed similar AB results to these previous studies. The protraction of AB in our schizophrenia patients was not large and older patients may benefit more from making adjustments to the PSR ISIs.

Further to the finding that the protraction of AB in schizophrenia is not large, a recent paper (Su et al., 2015) has provided an explanation that the reported differences in AB in people with schizophrenia are due to differences in the baseline, shown by reanalyzing published data and conducting an experiment that normalized performance at baseline (T1) by adjusting the presentation rate in the AB and found no group difference in T2|T1.

Although there is no convincing evidence for normalization in our results, there is evidence that ISI is an important factor in performance on the PSR task. Post-hoc analysis of the main effect of ISI showed that the Fast ISI had significantly lower scores, while Medium and Slow do not differ. The results reported here could be used as a guide to choice of ISI of PSR tasks.

Although our hypothesis was not supported, this study remains important in that it is a first study of individualized AB in people with schizophrenia, and the first to examine the impact of varying ISIs on performance of a PSR task.

Conflict of interest

None.

Funding sources

Funding for this study was provided by the Dalhousie University Department of Psychiatry. The funding body played no role in design of the study, data gathering, interpretation of data, writing of the manuscript or decision to publish.

Acknowledgements

The study was funded by the Dalhousie University Department of Psychiatry Research Fund to DM, PT and GE. The authors thank Emily Keefe for recruitment, data collection and entry.

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