Effect of interval duration on temporal processing in schizophrenia

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Abstract

Introduction: Temporal processing has received scant attention in the literature pertaining to cognitive deficits in patients with schizophrenia. Previous research suggests that patients with schizophrenia exhibit temporal perception deficits on both auditory and visual stimuli. The current study investigated the effects of interval manipulation to (1) replicate the original findings with a larger sample and an increased number of trials (2) assess the degree to which both patients and controls can differentiate temporal changes in a range of experimental interstimulus intervals, and (3) explore whether different interstimulus interval durations pose different levels of difficulty for the patients with schizophrenia. Methods: Participants were asked to decide whether temporal intervals were shorter or longer than standard interval on a computer-based auditory temporal perception task. The standard interval remained the same duration throughout the various tasks. The interstimulus interval separating the standard and experimental intervals varied in the range of 500, 1000, or 3000 ms. Data are presented for a sample of 16 patients with schizophrenia and 15 controls. Results: Data suggest that patients with schizophrenia exhibit deficits in differentiating interval durations across all paradigms compared to their control-group peers on a range of auditory tasks (p < .001). Conclusions: These results are consistent with a general temporal deficit in schizophrenia. However, the roles of medication and localization are also addressed.

Keywords: Schizophrenia; Time perception; Timing; Interval discrimination

1. Introduction

Over the years, there has been increasing interest in the ability to process temporal information, including the relationship to clinical symptomatology and neural dysfunction. Researchers have argued that temporal processing deficits appear to be associated with specific disorders, such as Parkinson’s disease and amnesia or with specific types of brain damage, specifically cerebellum, basal ganglia, or frontal lobe insult (Artieda, Pastor, Lacruz, & Oses, 1992; Casini & Ivy, 1999; Harrington & Haland, 1998; Heatherington, Dennis, & Spiegl, 2000; Ivy & Keele, 1989; Nichelli, Clark, Hollnagel, & Grafman, 1995; Rammsayer, 1993). One argument that has arisen is that subtle differences in time interval tasks may result in varied performances in clinical populations. Researchers studying both animals and patients with localized lesions have argued that the cerebellum may be associated with short-duration processing while the perception of longer durations may be linked to the prefrontal cortex (Clarke, Ivy, Grinband, & Roberts, 1996; Heatherington et al., 2000; Mangels, Ivy, & Shimizu, 1998). Other studies have supported the notion that the cerebellum is associated with relatively automatic short-duration processing, but add that it may be either the basal ganglia or cortex that take over for longer durations (Hazeltine, Helmuth, & Ivy, 1997; Ivy, 1996; Ivy & Keele, 1989). Another hypothesis is that there may be an “internal clock” that allows representation of real-time information that is used to process all temporal information (Mangels et al., 1998). Temporal processing deficits would then be attributed to a general deficit in the area of the brain responsible for the “internal clock.” However, there is little consensus regarding the localization associated with the internal clock. Multiple researchers have argued that the prefrontal cortex is not only involved in the general capacity to process time, but it may be responsible for our “internal clocks” (Nichelli, Alway, &
Grafman, 1996; Pastor, Artieda, Jahanshahi, & Obesa, 1992). Others have argued that general temporal processing deficits are associated with the cerebellum (Bononno & Mauk, 1994; Ivry & Keele, 1989; Juettner et al., 1995). Others believe that the basal ganglia is likely responsible for the processing of the internal clock and is involved in both short duration, largely automatic processing of time and in longer intervals (Meck, 1996; Rammayer, 1993; Rammayer & Lima, 1991). The argument that both the cerebellum and basal ganglia are involved in a coordinated timing system with a convergence of central cortical control has also been asserted (Gibbon, Malapani, Dale, & Gallistel, 1997).

Finally, others have argued that differences in temporal processing performances during varying interval durations may result from the employment of different cognitive processes. Michon (1990) points out that depending on the particular task, temporal processing measures may vary in the degree of abstraction and complexity. Mangels et al. (1998) argue that longer durations (e.g., 3 or 4 s) in interval comparison tasks may have to be kept on-line via working memory and may be particularly sensitive to frontal lobe deficits in working memory versus reflecting temporal processing deficits. Nichelli et al. (1996) suggest that the cerebellum may be involved in short interval duration estimation, however, timing beyond 2 or 3 s may exceed intervals requiring “motor routines” and may reflect deficits in sustained attention and/or strategy use. In both animal and human studies, the prefrontal cortex has been implicated in working memory processes (Chein & Fiez, 2001; Goldman-Rakic, 1999; Mull & Seyal, 2001; Wall & Messier, 2001). Given that prefrontal dysfunction has historically been associated with schizophrenia, it is possible that particular impairments would be expected on longer duration temporal tasks that may require working memory (Goldman-Rakic, 1999; Goldman-Rakic & Selemon, 1997; Perlstein, Carter, Noll, & Cohen, 2001).

One way to explore the possibility of widespread temporal deficits due to “internal clock” difficulties versus localized damage or the degree to which other cognitive processes mediate performance would be to explore temporal processing across a variety of conditions.

Schizophrenia is one clinical syndrome that has received limited attention regarding temporal processing. Previous neuropsychological research has often focused on deficits pertaining to “executive functioning” (e.g., attention, working memory, and planning) (Stern & Prohaska, 1996; Szeszko et al., 2000). These deficits are thought to be related to frontal lobe dysfunction and have historically been associated with the daily living difficulties patients with schizophrenia face (Green, Kern, Braff, & Mintz, 2000). Relatively few researchers have addressed the possibility that deficits in everyday living may instead be affected by difficulties with temporal processing.

Some have argued that the ability to process time may have far reaching effects in a person’s daily living and quality of life. Tracy et al. (1998) have discussed the role of time estimation in understanding “warning signals” that predict later events. Others have presented temporal dysfunction as a deficit that may affect a wide range of behaviors, such as sequencing motor behavior and planning time-based events (Volz et al., 2001). More obvious problems associated with temporal processing deficits include difficulty estimating how long tasks will take or trouble scheduling sequential events appropriately. In schizophrenia, difficulties with these endeavors along with other daily living difficulties may be partially explained by deficits in processing time rather than traditional cognitive deficits associated with schizophrenia such as executive functioning deficits and problems with working memory (Perry et al., 2001).

In the past, research focusing on schizophrenia and temporal processing deficits has been limited due to very small sample sizes and the lack of consensus in tasks described as “temporal processing” measures. Some temporal processing experiments utilize what would be considered estimation tasks and perception tasks together as a measure of temporal processing, rather than breaking up the tasks to better clarify the processes. A further limitation is the degree of nontemporal information that has been included in the temporal processing tasks utilized. Earlier research suggested that temporal perception tasks often required the subject to attend to nontemporal information, which likely affected the temporal processing (Poynter & Homa, 1983). Many of the studies around the 1970s required subjects to estimate duration of words and nonwords (Avante, Lyman, & Antes, 1975; Thomas & Weaver, 1975; Warm & McCray, 1969). Duration judgments were affected by the familiarity of the word, suggesting that subjects attend to other nontemporal qualities of information in their time estimations.

The present study attempted to limit the nontemporal qualities of the task and subjects were exposed to only one stimulus that was 50 ms in duration and 1000 Hz throughout the entire study. Subjects had to respond to the stimuli, which introduces the possibility of mediating cognitive factors. However, it has been noted that responding versus producing time may be a better measurement of perceptual processing versus perception/attentional processing (Fortin & Rousseau, 1987). In addition, it has been hypothesized that when interstimulus intervals (ISIs) are expanded beyond about 2 s, there is a loss of coherence between successive events, rather each stimulus becomes processes as an independent event (Vos & Ellerman, 1989). Mates, Müller, Radil, and Pöppel (1994), also found a breakdown in the ability to time and synchronize behavior when ISIs reached about 2400 ms. The authors suggest that the short-term memory trace in temporal processing of the
preceding stimuli may begin to fade out after about 2–3 s. The paradigm utilized in the current study addresses the possibility that longer intervals may affect temporal processing performance by including longer intervals in the selected ISI durations.

An initial study attempted to provide a preliminary examination of a cross modal measure of temporal perception in schizophrenia (Davalos, Kisley, & Ross, 2002). Subjects were presented with two time intervals that differed by only tens of milliseconds. Using a forced choice paradigm, differences were noted between groups on tasks of both auditory and visual temporal perception.

The current study investigates the effects of interval manipulation on performance between individuals with schizophrenia and controls. Both patients and controls are exposed to a range of experimental interstimulus intervals. Nontemporal variables are limited by utilizing the same stimuli across conditions. This study explored whether different interstimulus interval durations pose different levels of difficulty for the patients with schizophrenia.

2. Method

2.1. Participants

Subjects consisted of 15 subjects (nine males, six females; age range = 20–50 years) who met DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia, confirmed via a structured interview (Endicott & Spitzer, 1978). Given that the use of typical neuroleptics may be associated with adverse effects on timing tasks (Gibbon et al., 1997; Meck, 1983), only subjects treated with atypical neuroleptics were selected. Fourteen subjects were treated with either olanzapine or risperidone, one subject was unmedicated.

Sixteen controls (four males, 12 females; age range 23–58 years) were recruited through advertisements. Respondents were screened for psychiatric histories. Individuals were excluded for a current diagnosis of major depression, substance abuse, neurological disorders, head trauma, or for any personal or first-degree family member history of psychosis. All subjects gave written consent for participation, as approved by an appropriate Institutional Review Board, and were paid $30 for participation.

Mean years of age ± SD at the time of testing were 41.24 ± 8.45 for patients with schizophrenia and 38.50 ± 12.08 for control subjects; \( t = .74, p = .47 \).

2.2. Procedure

Auditory time perception was measured using a method introduced by Ivry and Keele (1989). In short, subjects compare successive intervals of two pairs of tones. The first pair of tones is used as a “standard” interval. Each tone is 50 ms in duration, 1000 Hz, and the initial time between the standard pair is consistently 400 ms. Either 500, 1000, or 3000 ms after the initial pair, the subject hears a second experimental pair of tones. This second interval is called the “experimental” interval. On half the trials, the experimental interval is shorter than the 400 ms first interval, either 310, 340, 355, or 370 ms in duration. On the other half of trials, the experimental interval is longer than the 400 ms first interval, either 430, 445, 460, or 490 ms in duration. The subjects are presented with 20 trials per experimental interval (e.g., 310 ms) per interstimulus interval (ISI) duration (e.g., 1000 ms). The presentation order for the experimental interval duration was randomized over 160 trials per ISI. The presentation order of stimuli was 80 trials of 1000, 500, and 3000 ms, a short break, and then the same order repeated. The subject was asked to manually respond by pressing the “S” key if the experimental interval was “shorter” than the standard interval and the “L” key if the experimental interval was longer than the standard interval. The presentation of each new trial was contingent on a response to the previous trial. Therefore, all participants responded to all trials. Each subject performed an initial control task to assess the participant’s hearing and appropriate volume for the task.

Four individuals with schizophrenia and three controls had their scores averaged from only one of the two trials (80 comparison intervals rather than 160) due to their inability to respond using the correct keys consistently. Two of those individuals with schizophrenia had to have their 3000 ms trials completely dropped since they had not completed either of the two trials correct. Therefore, the data presented for the 3000 ms ISI is based on 16 controls and 13 patients.

2.3. Data analysis

For each subject, the number of errors was recorded for each of the experimental intervals at each of the ISI’s. Groups were compared on the mean percentage of errors at each experimental interval duration (e.g., 310 ms) within each ISI (e.g., 3000 ms). Repeated measures ANOVAs were computed for mean percentage of errors, with ISI and experimental interval as within-group factors, and diagnosis as between group factor. Two-tailed \( t \) test post hoc comparisons were conducted.

3. Results

A repeated measures ANOVA with ISI as independent factor indicated a significant difference between groups on total errors committed, across all
experimental intervals, during the auditory perception task \((F = 20.50, p < .001)\). Overall, ISI duration significantly affected performance \((F = 7.67, p = .001)\). In particular, more total errors were committed at the 500 ms ISI than either the 1000 msec ISI \((t = 4.79, p < .001)\) or 3000 ms ISI tasks \((t = 2.26, p = .032)\). No significant difference in errors was noted at the 1000 ms ISI compared to the 3000 ms ISI \((t = 1.24, p = .22)\). No significant group-by-ISI interaction existed \((F = 1.16, p = .32)\), suggesting that patients exhibited a general impairment in performance across all ISIs.

Regarding the effects of experimental interval duration, the ANOVA revealed a significant effect of experimental interval duration (e.g., 310 ms) on performance overall across all ISIs \((p < .001)\). In general, performance declined when the experimental interval was most similar to the standard interval. However, there were no significant group-by-interval duration interactions for any ISI, suggesting that patient group is uniformly impaired across all interval durations. The differences in performance between groups across all experimental intervals during all three ISI duration conditions are displayed in Figs. 1–3. Mean percentages of errors for the two groups are displayed in Table 1.

4. Discussion

Previous research suggested that patients with schizophrenia might have temporal processing deficits, at least with regards to specific temporal intervals (Davalos et al., 2002). In the current study, one goal was to replicate the original pilot study with a larger sample and an increased number of trials. Similar to the first study, patients with schizophrenia exhibited temporal processing deficits across the array of experimental interval durations. Schizophrenic’s performance appears to follow the same curve of performance that the controls exhibit, however the patients are consistently impaired across the different conditions and experimental interval durations.

One question that arose from the previous study related to the possibility of a general temporal deficit versus a temporal deficit specific to the single interval duration that was assessed (1000 ms). Previous researchers have found that specific localized brain damage may contribute to distinct temporal deficits rather than general temporal processing dysfunction. Specifically, group differences in cerebellar or basal ganglia functioning were hypothesized to result in poorer performance on short-duration perception, whereas frontal lobe abnormalities would likely result in specific impairment on tasks requiring discrimination of longer interval durations in the seconds range (Heatherington et al., 2000; Mangels et al., 1998). In the initial study, only the 1000 ms ISI was assessed. The current study assessed a range of intervals in an attempt to rule out the possibility that the differences between groups that were initially cited resulted from a specific localized dysfunction associated with the 1000 ms ISI duration.

A further hypothesis was that the different ISI durations might pose different types of problems for the schizophrenia group. As can be seen in Fig. 4, all of the ISI durations appear to be more difficult for the schizophrenia group compared to the controls. While it
was noted that the 500 ms interval duration was more difficult overall, the increased difficulty does not appear to be specific to schizophrenia. It is possible that the more distinct deficit noted at the 500 ms interval may be due to mediating cognitive factors that are associated with processing short interval durations. One cognitive process that may play a role in the ISI deficit seen at 500 ms is backward masking. The idea of backward masking in temporal perception tasks has been analyzed (Cantor & Thomas, 1976; Idson & Massaro, 1977; Massaro & Idson, 1976, 1978). Massaro (1975) theorized that an auditory stimulus is stored in preperceptual memory and if a second auditory stimulus is presented before the processing is complete, the representation of the first auditory stimulus is lost and processing is terminated. While the typical duration that has been associated with the “preperceptual” memory or short auditory store is 200–300 ms (Cowan, 1984; March et al., 1999), it is possible that the difficulties noted on the 500 ms ISI may be explained, in part, due to backward masking effects. This argument would be in accord with research finding that backward masking causes impaired performance on cognitive tasks. Regarding the role of backward masking specifically in schizophrenia, research findings have been mixed with some finding deficits in schizophrenia and other stating that no significant differences exist (Kallstrand, Montnemery, Nielzen, & Olsson, 2002; March et al., 1999). It appears that forward masking may be more difficult for this population while deficits on simultaneous and backward masking appear to be more task-specific than generally impaired (McKay, Headlam, & Copolov, 2000). Similarly, differences have been noted regarding the regions associated with the different types of masking. Backward masking has been linked to central nervous network systems in the frontal cortical areas (Kallstrand et al., 2002). This lack of significant differences between groups on the 500 ms ISI and on the 3000 ms ISI would suggest that temporal processing deficits in schizophrenia do not appear to be further exacerbated by frontal cortical deficits as we once hypothesized. It would seem that if frontal cortex areas were largely involved in temporal processing, you would expect to see increased difficulty relative to the 1000 ms task on the two tasks that may be affected by backward masking and working memory difficulties. It was hypothesized that the longer duration ISI (3000 ms) and the shorter duration ISI (500 ms) might require additional cognitive processes that could selectively impair the patients’ performances. While the shorter duration appeared to be more difficult for everyone, neither ISI duration associated with frontal cortex processing posed specific problems for the individuals with schizophrenia.

The results of this study suggest that patients with schizophrenia exhibit general deficits in auditory temporal perception. It was shown that whereas controls could differentiate minute differences in duration (e.g., 45 ms), patients with schizophrenia continued to make errors up to 150 ms. These findings are consistent with our previous study and suggest that rather than a localized temporal deficit, patients with schizophrenia possess a general timing dysfunction. However, there are limitations that may be addressed in future studies. The
effect of psychopharmacological intervention on temporal processing tasks is not well understood. Traditional neuroleptics have been found to increase variability on temporal tasks and effect “clock speed” in both animal and human studies (Gibbon et al., 1997; Meck, 1996). However, little is known about the effects of atypical medications, particularly olanzapine on temporal tasks. It should be noted that recent studies have found that olanzapine effects other types of cognitive tasks and results in structural changes in the basal ganglia and cerebral activation changes in the cerebellum and prefrontal regions, all areas that have both been hypothesized to be involved in temporal processing (Andersson, Hamer, Lawler, Mailman, & Lieberman, 2002; Stephan et al., 2001). In particular, olanzapine was found to “normalize” cerebellar functional connectivity in only the right, but not left cerebellum, during a finger tapping task. Studies assessing the effects of olanzapine on these structures and on similar cognitive tasks have been rare and have resulted in inconsistent findings. However, given that olanzapine has been shown to effect the majority of areas associated with temporal processing, it should be noted that the between group differences described in the current study can not be ruled out as being related to olanzapine use. Future studies should address this limitation by including neuroleptic naive patients to rule out the effects of both typical and atypical medications.

In addition, there is little consensus regarding the localization of the internal clock. In the current study, we asserted that more significant impairment on the longer ISI (e.g., 3000 ms) versus the shorter interval tasks might shed light on the use of mediating cognitive variables associated with decision making in responses and the role of the prefrontal cortex. Whereas, significant differences across all variables may reflect a general timing deficit. The current findings suggest that patients with schizophrenia exhibit timing deficits across all interval durations. The deficits noted do not support the idea that the frontal cortex-related ISIs are particularly problematic for individuals with schizophrenia. Furthermore, while being cognizant of the possible confounding effects of medication, it appears that the idea of a general timing deficit may best describe the temporal processing dysfunction noted in this population.

Future studies addressing different decision making strategies or response biases between the groups may be useful in understanding the cognitive processes involved in behavioral measures of temporal processing. Additionally, research utilizing complementary methods such as electrophysiology and functional neuroimaging are planned to help clarify the facets of temporal processing and the physiological etiology of temporal dysfunction. While we posit that there may be a general timing dysfunction in this population, the physiology of this dysfunction is poorly understood. As additional studies suggest structural and functional abnormalities in schizophrenia in areas including the cerebellum and basal ganglia, it appears that a number of brain structures could be contributing to the temporal dysfunction noted in this population. Future studies addressing these localization questions and the types of cognition involved in temporal processing may lead to greater understanding of the physiology and neuropsychology of temporal deficits associated with schizophrenia.

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References


