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Timing dysfunctions in schizophrenia span from millisecond to several-second durations

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A B S T R A C T

Schizophrenia may be associated with a fundamental disturbance in the temporal coordination of information processing in the brain, leading to classic symptoms of schizophrenia such as thought disorder and disorganized and contextually inappropriate behavior. However, the majority of studies that have examined timing behavior in schizophrenia have employed temporal durations in the range of several seconds, which requires higher cognitive processes beyond initial sensory registration for temporal encoding. Accordingly, the present study assessed both millisecond and several-second duration estimates in schizophrenia using a well-established task of time perception. Twenty-eight individuals with schizophrenia and 31 non-psychiatric control participants completed two temporal bisection tasks, which required participants to make temporal judgments about auditory durations ranging from either 300 to 600 ms or 3000 to 6000 ms. Participants with schizophrenia displayed significantly greater timing variability under both millisecond and several-second timing conditions than the non-psychiatric group. These findings were consistent with parameter estimates obtained from a quantitative model of time estimation, and provide evidence for a fundamental timing deficit in schizophrenia that may be independent of the length of the to-be-timed duration.

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1. Introduction

Schizophrenia may be associated with a fundamental disturbance in the temporal coordination of information processing in the brain, leading to dysfunctions in the timing of perceptual, cognitive, and motor processes (Bressler, 2003; Paulus & Braff, 2003; Phillips & Silverstein, 2003; Tononi & Edelman, 2000). These impairments of neural timing have also been associated with "disturbances of consciousness," and may give rise to the expression of clinical symptoms associated with both positive (e.g., hallucinations, delusions) and negative (e.g., psychomotor poverty, poverty of speech) subtype classifications of the disorder (Andreasen, 1999; Hyde, Ziegler, & Weinberger, 1993; McGlashan & Hoffman, 2000). "Disconnection" models (e.g., Friston, 1998; McGlashan & Hoffman, 2000) of schizophrenia posit that deficits in neural coordination arise from reduced synaptic connectivity during development. Developmentally reduced synaptic connectiveness can result in spontaneous and autonomic localized brain activity as well as diminished cerebral cross-communication, which may be expressed phenomenologically as hallucinatory and negative symptoms, respectively (see McGlashan & Hoffman, 2000 for a review). Accordingly, other classic symptoms of schizophrenia such as thought disorder and disorganized and contextually inappropriate behavior may also be manifestations of a timing dysfunction (c.f., Andreasen, Paradiso, & O'Leary, 1998).

Support for these conceptualizations is emerging with evidence that brain structures and neurotransmitter systems – such as dopamine, glutamate, and serotonin – that are directly linked to neural timing processes are also impaired in schizophrenia (Andreasen, 1999; Andreasen et al., 1998; Buhusi & Meck, 2007; Cheng, Ali, & Meck, 2007; Rao, Mayer, & Harrington, 2001; Rao et al., 1997; Volz et al., 2001). Despite the growing interest and centrality of these time-dependent conceptualizations of the pathophysiology of schizophrenia, there remains a paucity of research directly examining overt timing performance in the disorder. In addition, the majority of studies that have examined timing behavior in schizophrenia have employed temporal durations in the range of several seconds (Densen, 1977; Johnson & Petzel, 1971; Tysk, 1983a, 1983b, 1990; Volz et al., 2001; Wahl & Sieg, 1980), requiring higher cognitive processes beyond initial sensory registration for temporal encoding (Fraisse, 1984; Michon, 1985; Rammsayer & Lima, 1991). Thus, the aim of the present study was to delineate deficits of temporal perception from more

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generalized cognitive impairments in schizophrenia by assessing duration estimates in both the millisecond and seconds range using a well-established task of time perception.

Given that schizophrenia is characterized by profound disturbances in perception, attention, and cognition, it is not surprising that schizophrenia has also been associated with systematic distortions of time across a variety of tasks (Densen, 1977; Johnson & Petzel, 1971; Tysk, 1983a, 1983b, 1990; Volz et al., 2001; Wahl & Sieg, 1980). Specifically, individuals diagnosed with schizophrenia have consistently been found to experience time as lengthened relative to objective time, which has been interpreted to reflect an increase in speed of a hypothetical "internal clock" (Densen, 1977; Johnson & Petzel, 1971; Lhamon & Goldstone, 1956; Tracy et al., 1998; Tysk, 1983a; Tysk, 1983b; Tysk, 1990; Wahl & Sieg, 1980).

Of further interest are the parallels between the neural circuitry proposed to underlie internal timing functions and those which have been implicated in the pathophysiology of schizophrenia (Andreasen, 1999; Andreasen et al., 1998; Rao et al., 1997; Rao et al., 2001; Volz et al., 2001). For instance, schizophrenia has been associated with impaired neural integration across the prefrontal, thalamic, and cerebellar regions (Andreasen, 1999), which are also involved in temporal estimation (Ivry & Keele, 1989; Jueptner et al., 1995; Nichelli, Always, & Grafman, 1996) and temporally-mediated motor tasks such as paced finger tapping (Ivry, 1993; Ivry & Keele, 1989; Ivry, Keele, & Diener, 1988) and eye-blink conditioning (Perret, Ruiz, & Mauk, 1993; Steinmetz, 2000; Steinmetz, Lavond, Ivkovich, Logan, & Thompson, 1992). Schizophrenia has been further associated with disturbed neural communication within cortical-striatal networks (Volz et al., 2001), which are integral to the encoding and explicit representation of temporal information (Hinton & Meck, 1997; Matell & Meck, 2000). Important to the integrity of the cortico-striatal timing network is the neurotransmitter dopamine (Buhusi & Meck, 2002; Maricq, Roberts, & Church, 1981; Meck 1983; Meck 1996; Santi, Weise, & Kuiper, 1995; Stanford & Santi, 1998; Tracy et al., 1998), which has also been linked to the manifestation of the schizophrenia (Carlsson et al., 2001).

Despite behavioral and neuropathological evidence for timing deficits in schizophrenia, the majority of studies of time estimation in schizophrenia have employed durations in the range of several seconds, requiring higher cognitive processes beyond initial sensory registration for temporal encoding (Fraisse, 1984; Michon, 1985; Rammsayer & Lima, 1991). For instance, studies of human timing have indicated that accurate processing of temporal intervals in the range of several seconds requires increased attentional and mnemonic demands (Fortin, 1999; Fortin, Rousseau, Bourque, & Kirouac, 1993; Zakay & Block, 1996), making it difficult to delineate deficits of temporal perception from generalized impairments of attention (Kimble et al., 2000; Nestor & O'Donnell, 1998) and memory (Chen & McKenna, 1996) commonly associated with schizophrenia. In the first study of temporal bisection in schizophrenia, Elvevåg and colleagues (2003) addressed this difficulty by employing brief stimuli in the range of milliseconds to better isolate timing mechanisms while minimizing the role of potentially confounding cognitive processes. They found patients with schizophrenia to be less accurate in their timing judgments than non-psychiatric controls, suggesting deficits specific to timing processes. Similar conclusions were reached in a study of both auditory and visual temporal bisection that was completed by our own research group (Carroll, Boggs, O'Donnell, Shekhar, & Hetrick, 2008). Specifically, individuals with schizophrenia exhibited less temporal precision in the estimation of extremely brief (i.e., 300–600 ms) auditory, but not visual, stimuli compared to control participants, providing further evidence for a fundamental deficit in temporal auditory precision in schizophrenia.

The present study aimed to replicate and expand on these previous findings in the following ways. First, a temporal bisection task was used to assess the timing of brief auditory durations (i.e., 300–600 ms) in individuals with schizophrenia and non-psychiatric control participants. The temporal bisection procedure required participants to first encode *short* and *long* anchor durations to which intermediate durations were subsequently compared and classified as most similar to either the short or the long anchor. The *bisection point* therefore refers to the duration at which short and long classifications are made with equal probability. In addition to brief durations in the millisecond range, participants in the present study were also required to estimate auditory durations in a second task employing intervals in the range of several seconds (i.e., 3–6 s). The inclusion of both millisecond (300–600 ms) and several-second (3–6 s) durations permitted further delineation of deficits in early sensory temporal perception from more generalized attentional and mnemonic cognitive impairments in schizophrenia, as temporal performance on the short and long bisection tasks could be directly compared within the same group of participants.

Finally, to complement the behavioral analysis of the bisection data, a quantitative assessment of the performance data was achieved using a formal model of Scalar Timing Theory (Gibbon, 1981). Scalar Timing Theory is a mathematical description of interval timing that attributes variability in temporally-mediated behavior to different stages of information processing (e.g., Gibbon, 1977; Gibbon, 1991; Gibbon & Church, 1984). As illustrated in Fig. 1, the conversion of real time into subjective time occurs during the clock stage, where a Poisson-variable pacemaker is assumed to emit pulses that get stored in the accumulator during a timed interval. A stimulus signaling the start of the interval causes an attention-modulated switch to close, which allows the pulses to flow into the accumulator where they are summed upon termination of the timed duration. The summation of pulses forms a subjective time estimate that is passed to working memory and compared with previously timed durations that are sampled from reference memory during the decisional stage. The Sample Known Exactly (SKE) model is an internal clock-based model specifically designed to account for performance variability in the bisection task (Gibbon, 1981). Although variability in duration estimates may be introduced during any of the three stages of the internal clock process, the bisection task was originally developed to assess temporal memory under the assumption that the comparison of intermediate durations to the short and long anchors would maximize reliance on memory for the anchor durations (Allan & Gibbon, 1991). Because the major source of imprecision in temporal bisection has been attributed to mnemonic variance, it is assumed that perceived time for any given sample duration is "known ex-

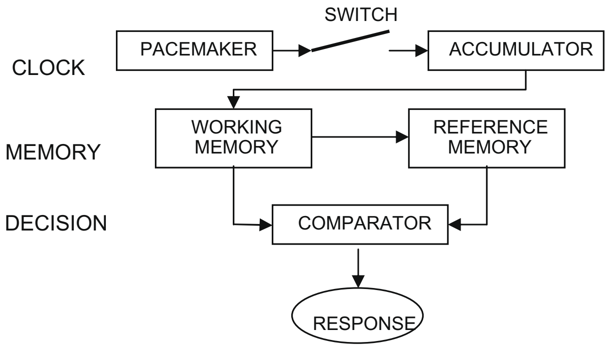

Fig. 1. Schematic representation of the three-stage internal clock model. Clock stage: pulses emitted from a pacemaker are passed via an attention-modulated switch into an accumulator during a to-be-timed interval. Memory stage: a subjective time estimate of the present duration is held in working memory. Decision stage: the subjective time estimate in working memory is compared with previously time durations sampled from reference memory.

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actly" (Gibbon, 1981). The degree of noise in the memory distributions is represented by the sensitivity parameter, gamma (γ). The SKE model also contains a parameter representing response bias (β), thus permitting a quantitative attribution of group differences to temporal memory and/or decisional influences on bisection performance.

The hypotheses for the present study were as follows: consistent with previous findings, individuals with schizophrenia were predicted to show greater timing variability (Carroll et al., 2008; Elvevåg et al., 2003) and a longer duration bisection point (Elvevåg et al., 2003; i.e., the duration at which short and long classifications are made with equal probability) during the millisecond bisection task compared to non-psychiatric participants. As mentioned previously, the temporal bisection procedure requires participants to first encode "short" and "long" anchor durations to which intermediate durations are subsequently compared and classified as closer to either the short or the long anchor. Hence, in contrast to simple estimation tasks, temporal bisection requires comparison between two *subjective* duration estimates: perception of the probe duration and a subjective estimate of the previously learned anchor. Therefore, if temporal processing abnormalities in schizophrenia are confined to perceptual processes (i.e., a faster "internal clock"), bisection point values would not be expected to differ between patients and non-psychiatric participants, as perceptions of both the probe and anchor durations would be rescaled in accordance with one's internal clock speed.

The increased bisection point values previously reported by Elvevåg and colleagues (2003) suggest that processes other than perception influenced timing of short durations (i.e., 200–800 ms) in schizophrenia, as purely perceptual timing would have allowed for temporal rescaling and the elimination of group differences in the location of the bisection point. Given that the encoding of extremely short durations has been shown to be primarily perceptual (Fraisse, 1984; Michon, 1985; Rammsayer & Lima, 1991), the nature of the observed timing deficits is unclear. Therefore, to better understand temporal bisection performance in schizophrenia, both millisecond (300–600 ms) and several-second (3–6 s) bisection tasks were employed in the present study. If the timing difficulties previously reported in schizophrenia are in part due to higher order cognitive impairments, the additional mnemonic and attentional demands required for the encoding of several-second durations should impair timing performance in the patient group to a greater degree than durations in the millisecond range. Specifically, patients with schizophrenia were predicted to show greater timing deficits on the second (3–6 s) compared to the millisecond (300–600 ms) version of the bisection procedure, as indexed by greater timing variability and larger group differences in the location of the bisection point for the long duration task.

As indicated above, the SKE model contains two parameters that correspond to memory variance (γ) and response bias (β). Given the increased temporal variability observed in schizophrenia on a variety of timing tasks (Brown et al., 2005; Carroll et al., 2008; Elvevåg et al., 2003; Goldstone, 1975; Lhamon & Goldstone, 1973; Tysk,1983a, 1983b), it is predicted that γ values will be higher (i.e., less temporal precision) in the patient relative to the non-psychiatric group in both millisecond and second duration conditions. However, the greater reliance on higher cognitive processes required for the timing of several-second durations suggests that γ values will be higher in the second compared to the millisecond bisection task, and that this increased variability will be greater in individuals with schizophrenia than in non-psychiatric participants. In addition, a slight bias toward "short" responses has been observed in the offspring of patients with schizophrenia (Penney, Meck, Roberts, Gibbon, & Erlenmeyer-Kimling, 2005). It is therefore predicted that patients will show a greater "short" response bias (i.e., smaller β values) compared to the non-psychiatric participants in both the millisecond and several-second bisection tasks.

2. Methods

2.1. Participants

Twenty-eight (21 male: mean age = 37.4, *SD* = 11.3; 7 female: mean age = 44.3, *SD* = 6.8) individuals meeting DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia and 31 (11 male: mean age = 32.1, *SD* = 9.2; 20 female: mean age = 43.6, *SD* = 11.2) non-psychiatric participants volunteered for the present study. A subgroup of participants (23 individuals with schizophrenia, 22 non-psychiatric participants) also volunteered for a second study of temporal bisection that was conducted approximately 2 weeks following the present study as part of a larger body of research on temporal processing in schizophrenia (Carroll et al., 2008). Each of the schizophrenia participants was evaluated using the Structured Clinical Interview for the DSM-IV (Diagnostic and Statistical Manual IV) for Axis I disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 2002a), supplemented by chart information. All control participants were interviewed using the SCID-NP (First, Spitzer, Gibbon, & Williams, 2002b) to exclude individuals with Axis I disorders, antisocial personality disorder, and schizophrenia spectrum personality disorders. The patient sample was recruited through outpatient and inpatient units at community and state hospitals and comparison participants were recruited via newspaper advertisement. Exclusion criteria for all participants included self-reported neurological disease, head injury resulting in loss of consciousness for more than 5 min, and personal or family history of schizophrenia in the non-psychiatric group. All participants had normal or corrected-to-normal vision and hearing acuity. Information regarding educational was available for 19 of the 28 individuals diagnosed with schizophrenia and 22 of the 31 non-psychiatric participants. Although educational attainment was significantly greater in the non-psychiatric participants (mean years = 14.3, *SD* = 2.5) compared to the patient sample (mean years = 11.3, *SD* = 1.6), $t(39) = 4.56$, and $p < .001$, Pearson correlations computed within each group revealed no significant relationships between years of education and any of the bisection measures. Indiana University's Human Subjects Institutional Review Board approved of this study and written informed consent was obtained from all participants.

Current symptom levels in the patient group were assessed by trained diagnosticians using the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). The PANSS contains 30 items, or symptoms, that are scored between 1 (absent) and 7 (extreme). Symptom ratings were categorized into a five-subscale structure (i.e., positive, negative, cognitive, hostility, and emotional discomfort) that has been suggested to provide a more sensitive subtype classification than the conventional Positive, Negative, and General subscale distribution (Bell, Lysaker, Beam-Goulet, Milstein, & Lindenmayer, 1994a; Bell, Lysaker, Milstein, & Beam-Goulet, 1994b; Kay & Sevy, 1990). The five-subscale composite scores were derived by summing the item scores that comprised the given subscale as follows: positive subscale: unusual thought content, delusions, grandiosity, lack of judgment/insight, hallucinations; negative subscale: emotional withdrawal, social withdrawal, lack of spontaneity, blunted affect, poor rapport, poor attention, active social avoidance, motor retardation, disturbance of volition, mannerisms and posturing; cognitive subscale: difficulty in abstract thinking, disorientation, conceptual disorganization, suspiciousness, stereotyped thinking; hostility subscale: excitement, poor impulse control, tension, hostility, uncooperativeness; emotional discomfort subscale: anxiety, guilt, depression, somatic concerns, preoccupation (Kay & Sevy, 1990).

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Intellectual and cognitive functioning was assessed using the two-subtest form of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) and the Digit Span (forward and backward), Digit Symbol, Picture Completion, and Similarities subtests from the Wechsler Adult Intelligence Scale – III (WAIS-III; Wechsler, 1997). The WASI two-subtest format gives an estimate of general intellectual ability, and includes the Vocabulary subtest, which is used to assess crystallized intelligence, and the Matrix Reasoning subtest as a measure of nonverbal fluid abilities. Intelligence estimates from the WASI were available for 20 individuals diagnosed with schizophrenia and 26 control participants, with a significant difference in estimated intellectual ability observed between the schizophrenia and non-psychiatric groups, $t(44) = 5.64$, and $p < .001$ (see Table 1). Scores from the WAIS subtests were available for 28 individuals diagnosed with schizophrenia and 27 control participants. The Digit Span (forward and backward) subtest provides a measure of working memory ability, the Digit Symbol subtest is a timed measure that assesses learning speed, Picture Completion is used to assess visual alertness and visual memory, and the Similarities subtest provides a measure of abstract thinking. Independent-sample *t*-tests revealed significantly lower scores for individuals diagnosed with schizophrenia than non-psychiatric participants on all four measures ($p < .001$; see Table 1). Bonferroni-corrected Pearson correlations computed within each group revealed no significant correlations between intellectual and cognitive measures and any of the bisection measures.

At the time of testing, 18 individuals with schizophrenia were taking antipsychotic medications (12 atypical, 6 typical), one individual was not medicated, and the medication status of nine patients could not be determined due to unavailable information. Chlorpromazine equivalents were computed for patients receiving antipsychotic medication, and the resulting dosages were correlated with all behavioral measures to assess for medication effects on timing performance. No significant relationships were noted.

2.2. Temporal stimuli

The duration bisection tasks were administered to each participant in counterbalanced order using sub-second and several-second tone durations. In the millisecond condition, 300 and 600 ms anchors were presented, with five arithmetically spaced intermediate durations of 350, 400, 450, 500, and 550 ms. The several-second condition employed anchor durations of 3.0 and 6.0 s and intermediate durations of 3.5, 4.0, 4.5, 5.0, and 5.5 s. Aside from the different stimulus durations, the task procedure was identical for the millisecond and second conditions.

2.3. Task procedure

Filled durations were presented in the auditory (880 Hz tones) modality, and classified according to their perceived similarity to the short (i.e., 300 ms/3.0 s) or long (i.e., 600 ms/6.0 s) anchor values. To address potential difficulties related to task comprehension, a concrete procedural context related to bird classification was adapted from Elvevåg and colleagues (2003).

The task procedure was divided into training, practice, and test phases. The experiment began with a training phase in which the short and long anchors were paired with a small (1.84 × 1.92 in.) and a large (3.60 × 3.78 in.) bird silhouette, respectively. To ensure that participants had learned the anchor durations, six presentations of each anchor were randomly administered within a 12-trial practice block in the absence of the associated bird silhouette. Following each presentation, participants received on-screen instructions to press the “Short” key if the sound was made by the small bird and to press the “Long” key if the sound belonged to the big bird. Visual feedback (i.e., “correct” or “incorrect”) was provided after each response, and correct responses were associated with a monetary bonus of 10 cents. A 1 s inter-trial interval separated feedback offset and stimulus presentation. The practice phase was repeated in 12-trial blocks until an accuracy level of 75% or greater was reached: the session was aborted if 75% accuracy had not been achieved after three practice blocks.

The test phase of the experiment was presented in three blocks of 35 trials each (five presentations of each auditory duration). Participants were asked to classify each auditory stimulus as either “Short” or “Long” based on their perceived similarity to the sounds made by the small or large bird. Because the bisection task is an assessment of subjective time perception, response accuracy could only be determined for the anchor durations during the test phase. Each correct classification of the short and long anchors earned participants a reward of 10 cents, for a possible bonus of $3.00. To help ensure that the participants understood the task, a practice block consisting of one presentation of each stimulus was administered immediately prior to the test phase to allow participants to ask questions and become familiar with the procedure.

Each test block was preceded by a short (<5 min) rest period. To minimize memory demands for the anchor values, the short and long anchors were presented and paired with the small and big bird silhouettes, respectively, prior to the commencement of each of the three test blocks.

2.4. Behavioral data and analysis

The proportion of *long* responses, $p(long)$, made to the anchors and intermediate signals were quantified separately for each participant and duration condition. The proportional data can be plotted as a function of signal duration to yield a psychometric response curve that is typically sigmoidal in form, indicating a near absence of long responses to signals that fall close to the short anchor value, to a predominance of long responses as signals come to approach the duration of the long anchor. Sigmoidal functions were fit to the proportional response data from each participant using the regression feature of SigmaPlot (2001, Version 7.0), which employs a least squares method to estimate equation parameters and identify the durations that correspond to $p(long)$ values of 0.25, 0.50, and 0.75 from the fitted sigmoidal curve.

The duration at which the proportion of *long* responses was equivalent to 0.50 for each duration condition was identified as the bisection point, or the duration at which *short* and *long* responses occurred with equal probability. In addition to the bisection point, the values derived from the fitted sigmoidal functions were used to calculate the difference limen (DL) and Weber fraction (WF), which represent the slope of the psychometric response curves and can be interpreted as an index of timing variability. The DL is calculated as one-half the difference between the durations corresponding to $p(long) = 0.75$ and $p(long) = 0.25$ $((0.75 - 0.25)/2)$, where smaller values indicate steeper slopes and greater temporal precision. The WF is computed by dividing the DL by the bisection point, which normalizes the DL values with respect to

Table 1
Intelligence and cognitive scores for individuals diagnosed with schizophrenia and control participants.

	Schizophrenia		Control	
	M	*SD*	*M*	*SD*
WASI-IQ**	83.15	14.92	106.96	13.61
Digit Span**	13.54	3.91	19.59	4.08
Digit Symbol**	46.93	13.27	80.59	17.11
Picture Completion**	14.07	3.88	19.33	4.52
Similarities**	16.29	6.01	22.81	5.28

** $p < .001$.

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the timed durations. Thus, the WF provides an index of Weber's Law (i.e., a constant coefficient of variation of subjective time across various temporal durations) by allowing for a direct comparison of timing variability across various anchor pairs.

The different duration ranges between millisecond and several-second conditions restrained bisection point and DL analyses to within-condition one-way ANOVAs with a between-subjects factor of Group (schizophrenia/non-psychiatric control). The Weber fraction was submitted to a repeated-measures ANOVA, with Condition (millisecond/second) as a within-subjects factor and Group (schizophrenia/non-psychiatric control) as a between-subjects factor. Although the anchor values were explicitly presented between each of the three test blocks, potential confounding effects of memory on timing performance were evaluated by examining average response accuracy to the anchor trials and change in response accuracy between Blocks 1 and 3. Accuracy analyses were conducted within each duration condition using repeated-measures ANOVAs with Anchor (short/long) as a within-subjects variable and Group (schizophrenia/non-psychiatric control) as a between-subjects variable.

2.5. Theoretical model

The two-parameter Sample Known Exactly (SKE) model is a clock-based model specifically designed to account for performance variability in the bisection task (Gibbon, 1981). As indicated previously, the bisection task was originally developed to assess temporal memory under the assumption that probe trials would maximize reliance on memory for the anchor durations (Allan & Gibbon, 1991). Therefore, the major source of variability in temporal bisection has been attributed to the reference memories of the anchor durations, which are conceptualized as normal distributions of remembered time with means μ_S and μ_L for the short (S) and long (L) anchors, respectively (Gibbon, 1981). Because the major source of imprecision in temporal bisection has been attributed to mnemonic variance, it is assumed that perceived time (χ_t) for any given sample duration is "known exactly" (i.e., $\chi_t = \mu_t$), and that the referent memories for the anchor durations are samples drawn from the short (χ_S) and long (χ_L) memory distributions.

The degree of noise in the memory distributions is represented by the sensitivity parameter, gamma (γ). The sensitivity parameter is the coefficient of variation of remembered time, and affects the slope of the psychometric bisection function with smaller values (higher sensitivity) indicating steeper slopes. Although not identical to the empirically based Weber ratio, γ can be viewed as a comparable measure of proportionality in time estimations (Gibbon, 1981; Penney, Allen, Meck, & Gibbon, 1998). In addition to the sensitivity parameter, the SKE model contains a bias parameter, β, which serves as the threshold value between "short" (R_S) and "long" (R_L) response alternatives and represents a bias towards R_L (i.e., $\beta > 1$). Specifically, the decision to respond R_S is based upon a similarity ratio rule

$$\frac{\chi_S/T}{T/\chi_L} > \beta, \tag{1}$$

which states that a trial duration (T) will be judged "short" when the similarity of χ_S to T, compared to the similarity of T to χ_L, is less than a threshold value that is possibly biased in favor of R_L (Gibbon, 1981).

The SKE model was fit to individual mean response data from the millisecond and several-second bisection tasks using Matlab's (version 6.5, 2002) fminsearch function, which uses a simplex search algorithm to minimize the parameter space. Gamma (γ) and beta (β) parameters were allowed to vary, and parameter values from the best fit were recorded and submitted for analysis. The parameter values were each analyzed using repeated-measures ANOVAs, with Condition (millisecond/second) as a within-subjects factor and Group (schizophrenia/non-psychiatric control) as a between-subjects factor.

2.6. Planned correlations

Theoretical considerations. Pearson product-moment correlations were performed between behavioral and parameter estimates of temporal precision to assess the correspondence between theoretical "clock" accounts of temporal processing and actual timing behavior. Specifically, DL and WF measures from the millisecond and several seconds bisection tasks were correlated with their respective γ values derived from the SKE model, with a Bonferroni correction applied for multiple comparisons.

Symptom correlates. Pearson product-moment correlation coefficients were computed between PANSS symptom ratings and temporal variability (i.e., DL, WF) using a Bonferroni correction for multiple comparisons.

2.7. Outlier considerations

A within-group boxplot method of outlier identification was performed separately for each analysis to classify extreme cases, defined as data values more than six quartiles from the upper or lower ends of the interquartile range. A single extreme case was identified for the Weber fraction, resulting in the removal of one individual with schizophrenia from the analysis. In addition, two individuals with schizophrenia were removed from analysis of the bias parameter, β.

Results of the major dependent variables are reported with their corresponding partial eta^2 [η_p^2] effect sizes, where small effect sizes are less than .06, moderate effect sizes range from .06 to .14, and large effect sizes are greater than .14 (Cohen, 1973).

3. Results

3.1. Practice accuracy

All participants were able to correctly differentiate between the anchor durations at or above 75% accuracy following the practice phase of the millisecond and several-second bisection tasks. Individuals with schizophrenia did however achieve significantly lower accuracy levels than non-psychiatric control participants for both millisecond (schizophrenia: $M = 82.8$, $SD = 12.6$; non-psychiatric: $M = 94.5$, $SD = 10.0$) and second (schizophrenia: $M = 90.5$, $SD = 10.8$; non-psychiatric: $M = 95.3$, $SD = 6.3$) duration conditions, $F(1,57) = 15.69$, $\eta_p^2 = 0.22$, and $p < .001$. In addition, a significant Group × Condition interaction indicated reduced accuracy for individuals with schizophrenia in the correct differentiation of the anchor durations from the millisecond bisection condition, $F(1,57) = 4.51$, $\eta_p^2 = 0.07$, and $p = .038$.

3.2. Bisection point

Averaged psychophysical functions for the millisecond and second conditions are presented in Fig. 2, representing the proportion of *long* responses made to the anchors and intermediate durations. As illustrated in Fig. 2, the duration at which the proportion of *long* responses is equivalent to 0.5 in both conditions is similar between the schizophrenia and non-psychiatric groups. This observation was confirmed statistically, with no significant differences in the location of the bisection point between the schizophrenia and non-psychiatric groups in either the millisecond or second condition (see Table 2).

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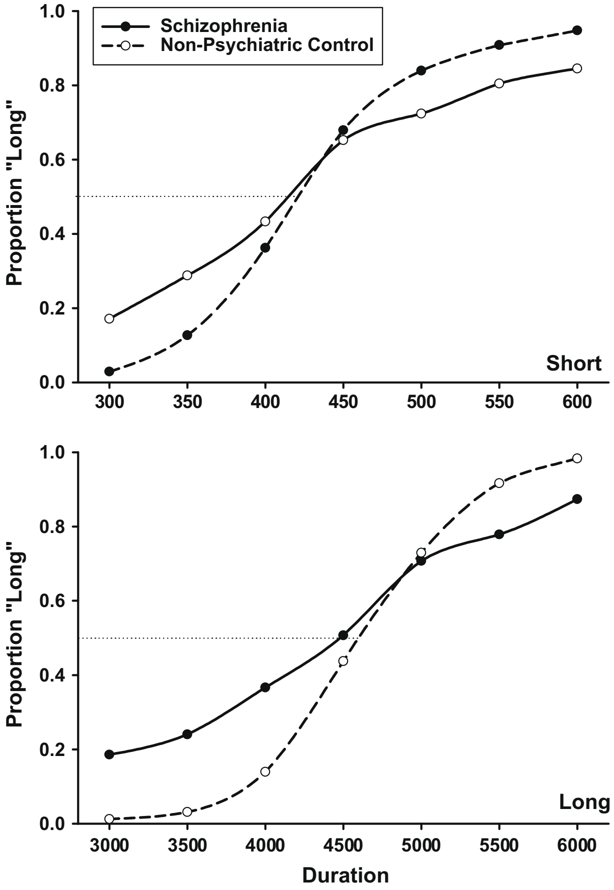

Fig. 2. The proportion of long responses as a function of signal duration for the millisecond (top) and several-second (bottom) conditions. Bisection point values are indicated by the dotted horizontal lines at 0.5 along the *y*-axis.

Table 2
Bisection point, difference limen, and Weber fraction values from short and long duration conditions for non-psychiatric control participants and individuals with schizophrenia (SZ).

Condition	Control		SZ	
	M	*SD*	*M*	*SD*
Bisection point				
Short	424.77	37.74	413.76	41.62
Long	4627.13	307.29	4531.29	471.84
Difference limen				
Short*	38.83	15.3	51.33	29.92
Long**	371.87	137.75	576.93	284.56
Weber fraction				
Short**	0.094	0.036	0.119	0.048
Long**	0.080	0.033	0.118	0.075

* $p < .05$.
** $p < .01$.

3.3. Response variability

As shown in Table 2, individuals with schizophrenia displayed greater response variability than non-psychiatric participants, as indexed by DL and WF measures. Increased response variability in the schizophrenia group is also evident in Fig. 2, where individuals with schizophrenia displayed flatter response curves and less response precision around the anchor durations. Analysis of the difference limen indicated significant group differences for both millisecond, $F(1,62) = 4.52$, $\eta_p^2 = 0.07$, and $p = .038$, and several second, $F(1,61) = 13.39$, $\eta_p^2 = 0.18$, $p = .001$, and durations. A similar group effect associated with a large effect size was found for the Weber fraction, $F(1,57) = 15.69$, $\eta_p^2 = 0.22$, and $p < .001$, which allows for comparison of response variability across different duration ranges. However, no significant effect of condition or Group × Condition interaction was found.

3.4. Anchor accuracy

The proportion of correct responses to the short and long anchor durations was analyzed to assess retention of the anchor values during the testing phase of the task. In the millisecond condition, non-psychiatric participants (300 ms: $M = 0.97$, $SD = 0.06$; 600 ms: $M = 0.95$, $SD = 0.16$) responded with significantly greater accuracy to the 300 ms and 600 ms anchor durations than individuals with schizophrenia (300 ms: $M = 0.84$, $SD = 0.18$; 600 ms: $M = 0.85$, $SD = 0.16$), $F(1,62) = 19.19$, $\eta_p^2 = 0.24$, and $p < .001$. The main effect of anchor and the Group × Anchor interaction did not reach significance. Similar results were obtained for the seconds condition, with non-psychiatric participants (3 s: $M = 0.99$, $SD = 0.04$; 6 s: $M = 0.98$, $SD = 0.03$) showing a significantly higher response accuracy to the 3 s and 6 s anchors than the schizophrenia group (3 s: $M = 0.81$, $SD = 0.19$; 6 s $= M = 0.86$, $SD = 0.15$), $F(1,61) = 37.30$, $\eta_p^2 = 0.38$, and $p < .001$. No other effects reached significance.

In addition to overall accuracy, retention of the anchor values was evaluated to assess whether patients showed poorer memory for the anchors across the duration of the experiment. For the millisecond duration condition, the difference in response accuracy between Block 1 and Block 3 of the test phase yielded a marginally significant group effect in which individuals with schizophrenia slightly increased (300 ms: $M = -0.05$, $SD = 0.26$; 600 ms: $M = -0.01$, $SD = 0.21$) and non-psychiatric participants slightly decreased (300 ms: $M = 0.04$, $SD = 0.10$; 600 ms: $M = 0.03$, $SD = 0.08$) in response accuracy to both short and long anchors, $F(1,61) = 4.09$, $\eta_p^2 = 0.06$, and $p = 0.047$. The main effect of anchor and the Group × Anchor interaction did not reach significance. No significant differences between the schizophrenia (3 s: $M = -0.04$; $SD = 0.29$; 6 s: $M = 0.11$, $SD = 0.29$) and non-psychiatric (3 s: $M = 0.01$, $SD = 0.06$; 6 s: $M = 0.03$, $SD = 0.09$) groups were found for the several seconds condition, and the main effect of anchor and the Group × Anchor interaction also failed to reach significance. Thus, although individuals with schizophrenia showed lower anchor accuracy overall, their change in accuracy was equivalent to – if not better than – the non-psychiatric group, indicating that individuals with schizophrenia did not demonstrate poorer retention of the anchors across the duration of the task.

Finally, because individuals with schizophrenia were shown to have greater response variability, it was important to determine whether a relationship existed between anchor accuracy and DL and WF indices of performance variance. Pearson correlations indicated no significant associations, suggesting that increased performance variability was not related to poorer retention of the anchor durations in the patient sample.

3.5. Theoretical model

The obtained and model-predicted response curves for each group-by-duration condition are illustrated in Fig. 3 and Table 3 displays the parameter values obtained from the millisecond and several-second conditions. A significant main effect of group associated with a large effect size was found for the sensitivity parameter (γ), $F(1,57) = 31.89$, $\eta_p^2 = 0.36$, and $p < .001$, suggesting that individuals with schizophrenia had greater distributional overlap in reference memory than the non-psychiatric group. No effect of duration or Group × Duration interaction was found. Although no

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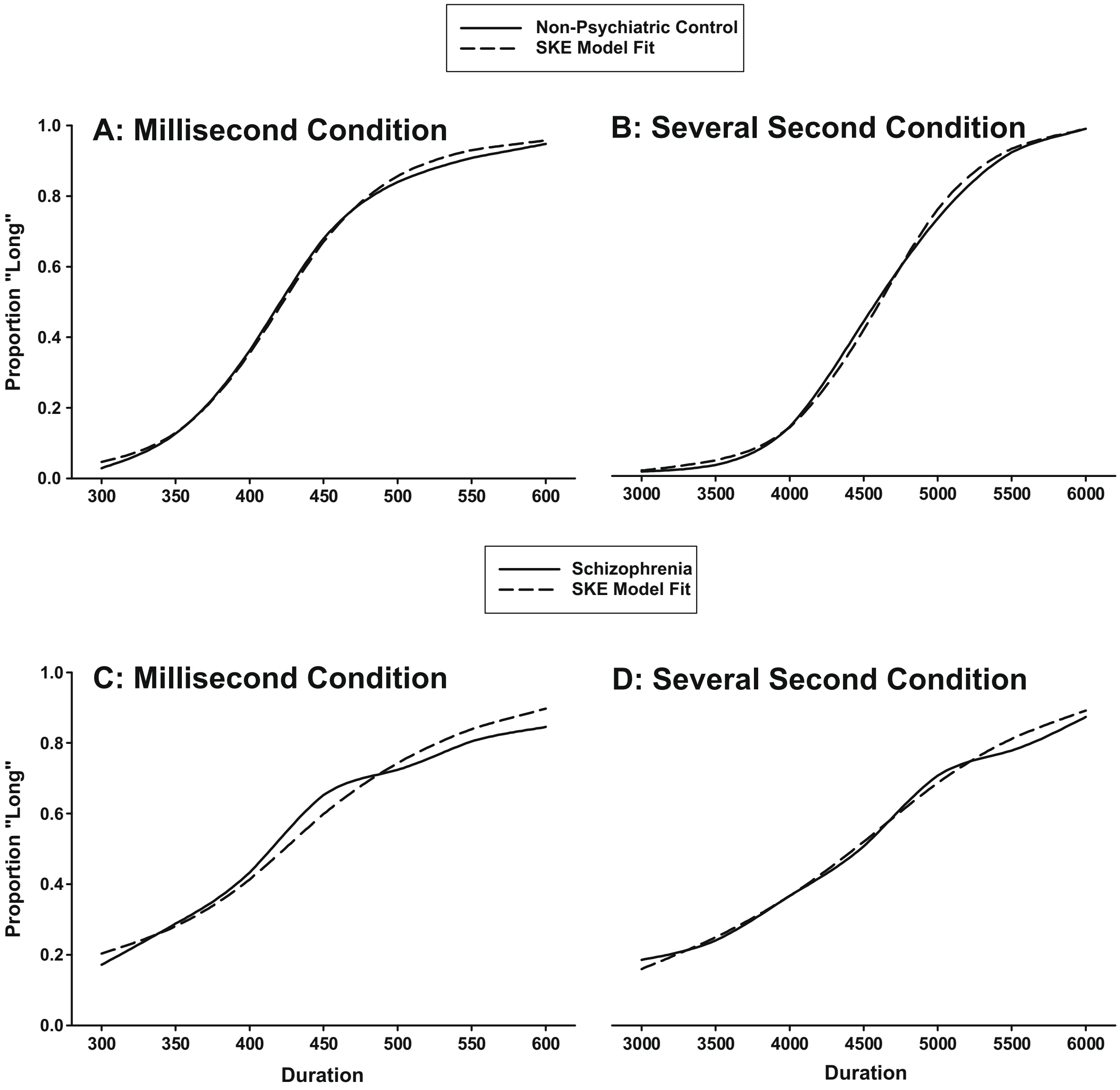

Fig. 3. Actual and SKE model-predicted responses for the millisecond (A and C) and several-second (B and D) conditions for the non-psychiatric (top) and schizophrenia (bottom) groups. Greater overlap indicates a better fit between the model-predicted response and the behavioral data.

Table 3
Parameter values from the SKE model obtained for non-psychiatric control participants and individuals with schizophrenia (SZ).

Condition	Control		SZ	
	M	*SD*	*M*	*SD*
Gamma (γ)				
Short**	0.18	0.08	0.46	0.28
Long**	0.16	0.07	0.4	0.27
Beta (β)				
Short	1.05	0.37	0.82	0.54
Long	0.86	0.23	0.82	0.57

** $p < .001$.

significant differences in response bias (β) were found between the schizophrenia and non-psychiatric groups, a significant Group × Duration interaction, $F(1,56) = 4.74$, $\eta_p^2 = 0.08$, and $p = .034$, suggested a larger group disparity in the millisecond condition, with non-psychiatric participants showing a larger *long* response bias. A significant effect of duration further indicated a greater propensity toward *long* responses in the millisecond ($M = 0.95$, $SD = 0.47$) compared to the several seconds ($M = 0.84$, $SD = 0.41$) duration condition, $F(1,56) = 4.63$, $\eta_p^2 = 0.08$, and $p = .036$.

3.6. Planned correlations

Theoretical considerations. To assess the relationship between behavioral and parameter estimates of temporal precision, difference limen and Weber fraction indices of response variability from the millisecond and several-second conditions were correlated with their respective gamma (γ) estimates of timing variability derived from the SKE model. For non-psychiatric participants, both DL ($r(31) = 0.88$ and $p < .001$) and WF ($r(31) = 0.92$ and $p < .001$) values from the millisecond condition were significantly related to corresponding γ values estimated from the millisecond bisection data. Similarly, DL ($r(31) = 0.77$ and $p < .001$) and WF ($r(31) = 0.68$ and $p < .001$) indices of temporal precision significantly correlated with corresponding γ estimates from the several seconds bisection data. In contrast, a similar pattern of results was not obtained for individuals with schizophrenia, who showed no significant correla-

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tions between millisecond and second bisection and theoretical predictions of timing variability.

Symptom correlates. Positive ($M = 15.8$, $SD = 6.4$), negative ($M = 16.5$, $SD = 5.8$), cognitive ($M = 15.4$, $SD = 5.5$), hostility ($M = 6.5$, $SD = 3.4$), and emotional discomfort ($M = 7.6$, $SD = 3.3$) symptom ratings from the PANSS were not significantly related to measures of timing from the temporal bisection (i.e., DL, WF) task (see Table 4).

4. Discussion

The primary aim of the present study was to delineate deficits in early sensory temporal perception from more generalized cognitive impairments in schizophrenia using both behavioral and quantitative modeling methodologies. As indexed by both DL (difference limen) and WF (Weber fraction) measures of response variance, participants with schizophrenia displayed significantly greater temporal variability under both millisecond and several-second timing conditions than the non-psychiatric group. In contrast, bisection point values did not differ significantly between participants with schizophrenia and non-psychiatric participants in either duration condition, suggesting minimal influence of higher-level cognitive disturbances in the timing of several-second durations for participants with schizophrenia. The absence of duration effects indicates that the decreased temporal precision found for the schizophrenia group can be attributed to a common source of variance between the millisecond and several-second conditions that is not specific to the timing of longer durations. Results from the SKE model were consistent with behavioral observations, showing greater temporal variability in the schizophrenia compared to the non-psychiatric group. However, β values did not indicate a general bias towards short responses in schizophrenia, which is contrary to that observed in the offspring of patients with schizophrenia (Penney et al., 2005). These above results are discussed in detail below.

Temporal bisection is unique to other tasks of time estimation with respect to its predictions and the inferences that can be drawn from temporal performance. In a simple timing task involving the estimation of a presented duration, differences in clock rate are reflected in performance differences. Specifically, a faster "internal clock" would result in the accumulation of a larger number of clock "pulses" during the timed interval, such that the summation of pulses would correspond to a longer duration than actually presented. A similar outcome would be observed for a slowed clock, with underestimations resulting from the accumulation of fewer pulses than would be needed to represent the presented duration.

In contrast, differences in clock speed should not be evident from bisection performance alone, as the comparison of two subjective durations will result in the rescaling of temporal judgments. As opposed to a task that requires a perceptual judgment of an objective duration, bisection judgments rely on a comparison between durations that have both been encoded in accordance with one's internal clock speed. Hence, timing differences due to perceptual, or "clock speed," differences alone should not be evident in the location of the bisection point. If processes other than perception are influencing temporal performance, however, shifts in the location of the bisection point would be expected. For instance, memory disturbances may alter the stored durations of the short and long anchors. Such distortions would result in probe-anchor comparisons that are not "subjectively" equivalent, as the anchor memories will have also been affected by non-perceptual factors. Similarly, attentional disturbances that differentially affect encoding on a trial-by-trial basis would also introduce differences in pulse accumulation independent of clock speed.

Both millisecond (300–600 ms) and several-second (3–6 s) durations were employed in the present study to better assess the influence of such non-perceptual factors on temporal performance. Because the majority of timing studies in schizophrenia have employed durations in the range of several seconds, it is unclear whether reported timing deficits are due to "clock speed" or other cognitive processes known to influence the perception of longer durations (Densen, 1977; Johnson & Petzel, 1971; Lhamon & Goldstone, 1956; Tracy et al., 1998; Tysk, 1983a; Tysk, 1983b; Tysk, 1990; Wahl & Sieg, 1980). The absence of group differences in the location of the bisection point under both millisecond and several-second conditions in the present study suggests that temporal judgments were not influenced by intervening cognitive factors, and that such factors did not significantly influence the timing of longer durations.

This inference is further supported by the absence of group difference in anchor retention across the span of the task. Specifically, all participants were found to maintain initial memory of the anchor durations throughout both millisecond and several-second bisection tasks, supporting the contention that memory disturbances did not differentially affect patient performance in the timing of longer durations. Furthermore, the lack of relationship between anchor memory and temporal precision indicates that the greater timing variability observed in the schizophrenia group cannot be attributed to a more generalized memory deficit.

As mentioned previously, a primary aim of including both millisecond and several-second duration tasks was to assess the effects of higher-level cognitive processes on temporal performance, as the majority of timing studies in schizophrenia have employed several-second durations that require additional mnemonic and attentional resources for proper encoding. In the few studies that have used millisecond durations to investigate temporal bisection in schizophrenia, participants with schizophrenia have shown less temporal precision than non-psychiatric controls (Carroll et al., 2008; Elvevåg et al., 2003). In addition, performance differences were not attributable to mnemonic failure across the tasks (Carroll et al., 2008; Elvevåg et al., 2003). However, in contrast to the present findings and those of Carroll and colleagues (2008), Elvevåg and colleagues (2003) found that participants with schizophrenia had significantly higher bisection points than the non-psychiatric comparison group, which were proposed to result from distortions in reference memory. A formal assessment using quantitative modeling may have helped locate the source of bisection differences, because, as acknowledged by the authors, the upward shift

Table 4
Pearson product-moment correlation coefficients between symptom ratings and behavioral indices of temporal precision for individuals with schizophrenia.

Temporal bisection		Positive and negative symptom scale factors				
		Positive	Negative	Cognitive	Hostility	Emotion
Difference limen	Short	0.10	0.40	0.23	0.13	0.00
	Long	−0.19	−0.13	0.26	−0.01	−0.06
Weber fraction	Short	0.01	0.16	0.01	0.04	0.15
	Long	−0.29	−0.01	0.31	0.06	−0.06

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in patients' bisection points may have been due to a simple bias against responding long (Elvevåg et al., 2003).

Finally, it should be noted that no relationships were found between symptom measures as assessed using the PANSS and any of the bisection measures. Total PANSS scores in the present patient sample ranged from 36 to 115, with an average score of 64. It has been reported that stable outpatients generally score between 60 and 80, with more severely impaired inpatients scoring between 80 and 150 (Opler, Opler, & Malaspina, 2006). Given the lower range of scores obtained for individuals with schizophrenia in the present study, it is possible that no relationships were found due to the fact that the majority of patients scored within or below the range commonly seen in outpatients. Thus, to better account for the role of symptom severity and/or symptom type in temporal performance, it will important for future studies to include individuals at different phases of schizophrenia as well as individuals with different symptom profiles.

In summary, the primary aim of the duration bisection tasks was to delineate deficits of temporal perception from generalized mnemonic and attentional difficulties commonly associated with schizophrenia. The absence of group differences in the location of the bisection point in the millisecond and several-second duration tasks suggests that many of the timing deficits previously reported in schizophrenia are due to perceptual, or "clock," processes. Contrary to prediction, comparable bisection points between the schizophrenia and non-psychiatric groups in both duration conditions indicate that the higher attentional demands required for the timing of longer durations did not have an effect on temporal encoding in the schizophrenia group. Although timing variability was greater in schizophrenia overall, the absence of a group by condition interaction suggested a common source of variance affecting temporal processing in both the millisecond and several-second conditions.

Application of the SKE model to the bisection data revealed that increased response variance in the schizophrenia group may be partially due to greater variability in reference memory. However, the absence of a significant relationship between behavioral and model indices of temporal precision in participants with schizophrenia implicates variance at other stages of the response process that is not accounted for by the SKE model. Despite this limitation, the successful application of the SKE model to patient data supports the use of the model in the formal assessment of temporal bisection in schizophrenia.

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