

Short Communication

Positive symptoms and time perception in schizophrenia: A meta-analysis

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ABSTRACT

Positive symptoms of schizophrenia may be related to distortions in time perception. To examine this issue, we conducted a meta-analysis to determine whether positive symptoms are associated with deficits in time processing performance. MEDLINE and Web of Science were searched from January 1980 through March 2017, and all related articles and their references were scrutinized to find relevant studies. Studies were selected if they included participants with a diagnosis of schizophrenia, and reported data from behavioral measures of interval timing (e.g. duration discrimination and temporal order judgement). The results indicated that positive symptoms of schizophrenia are related with overestimation of interval timing (i.e., acceleration of the “internal clock”), and suggest that time perception may be associated with psychosis.

1. Introduction

There have been many attempts to identify cognitive/behavioral indicators linked to positive symptoms (delusions, hallucinations, and etc.) of schizophrenia (Bark et al., 2003; Bear et al., 2017; Graham-Schmidt et al., 2016; Giersch et al., 2016; Horga et al., 2014). Specifically, temporal information processes are essential to all aspects of behavior, such as walking, speaking and engaging in physical activity. Recently, disturbances of temporal information processes have been suggested to contribute to the generation of positive symptoms (Carroll et al., 2009; Gómez et al., 2014; Lošák et al., 2016; Stevenson et al., 2017; Ward et al., 2012). Therefore, attempts to integrate these behavioral manifestations deserve considerations.

The nature of time perception is different from that of the other sensory modalities, e.g. visual and auditory processing, in that it is not paired to specific receptors, e.g. eyes and ears. It is generally agreed that attention and arousal may be important in temporal information processes (Merchant et al., 2013). Specifically, the pacemaker-accumulator model has been proposed as one of the main internal timing models (Treisman, 1963). This model is based on a multi-process theory that assumes three levels of timing processes common to animals and humans (Fig. 1; modified from Hartcher-O'Brien et al., 2016). The first level consists of a pacemaker and accumulator. The pacemaker generates pulses that are gated via a switch controlled by attention. In this level, a lack of attention leads to a deficiency in pulses in the

accumulator. In the second level, the pulses reach the working memory module. The final level represents the decision mechanism. During this stage, the contents of the working memory module are compared to those of the reference memory of the pulse-duration on previous occasions, to which the subject responds accordingly (e.g., see Carroll et al., 2008; Hartcher-O'Brien et al., 2016).

There are also some indications that altered time perception may be present in schizophrenia. Traditionally, the pathophysiology of schizophrenia has been associated with abnormalities in dopamine (DA) transmissions (e.g., Seeman et al., 2006), which in turn, have been linked to the speed of the internal clock (Cheng et al., 2007). In fact, several studies have demonstrated DA receptor agonists accelerate the internal clock, while antagonists decelerate it (e.g., Frederick and Allen, 1996; Meck, 2006).

Indeed, behavioral studies have reported overestimation (e.g. participants estimate the interval longer than objective time) in temporal durations ranging from milliseconds to several minutes in patients with schizophrenia (Jonson and Petzel, 1971; Volz et al., 2001; Carroll et al., 2009). The overestimation of time has been suggested to be caused by accelerated time processing (Droit-Volet and Meck, 2007).

Acceleration of the internal clock may be linked to the hypervigilance state that has been implicated in positive symptoms of schizophrenia (Lošák et al., 2016; Peterburs et al., 2013). Specifically, Dodgson and Gordon (2009) proposed that hypervigilance enhances responding biases and produces errors in cognitive processing, leading

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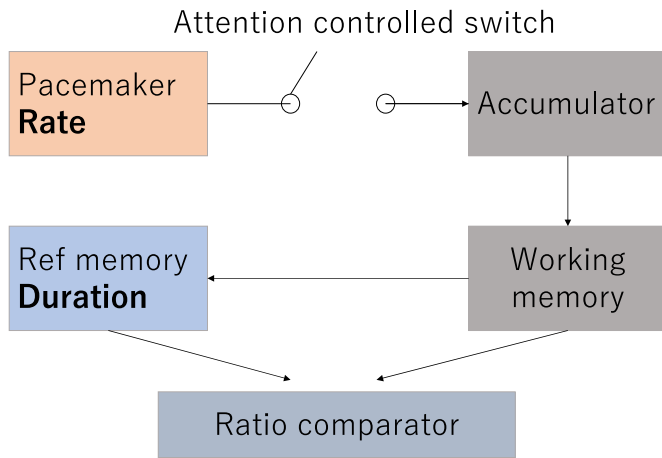


Fig. 1. The pacemaker accumulator model. Pulses are produced by the pacemaker and are gated via an attention-controlled switch. In this stage, the lack of attention leads to deficiency of pulses in the accumulator. The pulses reach working memory (or short term memory). The contents of working memory are compared with the reference memory (long term memory) which acquired pulse-duration in previous occasion and made decision how to respond.

Modified from [Hartcher-O'Brien et al., 2016](#) with permission from ELSEVIER LISENCE (License number: 4242350830031).

to the perception of a vague signal as a distinct one. Taken together, it is hypothesized that there is an association between positive symptoms and accelerated time perception, both linked to hypervigilance. Therefore, we conducted a meta-analysis to determine if severity of positive symptoms would be correlated with degree of acceleration of time perception in patients with schizophrenia.

2. Methods

2.1. Data sources

We conducted a literature review to search for articles that investigated timing abilities in schizophrenia. MEDLINE and Web of Science were searched through January 1980 to May 2017. We used two key words *schizophrenia* and *positive symptoms* in combination with any of the following terms: *time discrimination*, *interval timing*, and *time perception*. The reference list of identified studies was also hand-searched to obtain additional articles. Inclusion criteria were as follows: (1) published in English in a peer-reviewed journal; (2) included subjects with a primary diagnosis of schizophrenia on the basis of ICD (International Statistical Classification of Diseases and Related Health Problems) or DSM (Diagnostic and Statistical Manual of Mental Disorders) classification criteria; (3) reported behavioral measures of interval timing; and (4) conducted a correlation analysis between behavioral data and measures of positive symptom severity. Studies were excluded if correlational data concerning the timing ability of patients and positive symptom severity could not be extracted from the reported information.

The literature search yielded 100 < studies, 5 of which fulfilled the inclusion/exclusion criteria. Two articles reported on acceleration or deceleration in time perception ([Waters and Jablensky, 2009](#); [Peterburs et al., 2013](#)), while three reported on the ability to detect temporal precision of duration discrimination ([Carroll et al., 2008](#); [Carroll et al., 2009](#); [Stevenson et al., 2017](#)). Multiple publications from the same investigators were examined to exclude duplication of subjects ([Carroll et al., 2008](#)). Finally, four studies ([Carroll et al., 2009](#); [Peterburs et al., 2013](#); [Stevenson et al., 2017](#); [Waters and Jablensky, 2009](#)), containing a total of 101 individuals with schizophrenia, were included in the meta-analysis (See [Table 1](#)).

Table 1
Overview of studies on timing deficits in schizophrenia.

Study	Sample size	Symptom scale	Task	Modality	Duration of the task	Findings
Carroll et al. (2009)	28	PANSS	Temporal bisection task	Audio	3–6 s	Correlation between severity positive symptoms and temporal precision was slight almost negligible or low.
Peterburs et al. (2013)	22	PANSS	Anticipation movement task (AMT)	Visual	3000 or 18,000 ms	Severity positive symptoms were associated with over estimation/under production of movement object time.
Stevenson et al. (2017)	16	SAPS	Simultaneity judgement task	Audio/visual	0, ± 10, ± 20, ± 50, ± 80, and ± 100 to 300 ms in 50 ms	Temporal precision associates with severity of hallucinations.
Waters and Jablensky. (2009)	35	FRS	Duration discrimination task	Audio	1260–1440 ms	Subjects prone to overestimate were related to higher First Rank Symptoms scores.

Note. PANSS = The Positive and Negative Syndrome Scale. SAPS = The Scale for the Assessment of Positive Symptoms. FRS = First Rank Symptom scale.

2.2. Data extraction

One of the four studies (Waters and Jablensky, 2009) examined the ability of subjects to compare the duration of a probe sensory stimulus with target stimulus previously stored in the working or reference memory (i.e., duration discrimination task). The second study (Carroll et al., 2009) used a temporal bisection task which required individuals to judge whether presented temporal stimuli were similar to the long or short standard durations previously presented. Another study (Stevenson et al., 2017) used a simultaneity judgement task to measure the smallest difference in duration between two intervals that could be detected by participants. The final study (Peterburs et al., 2013) included in the analysis examined the ability to anticipate how long it would take to move objects to reach a target position (i.e. anticipation movement task). In this study, if participants estimated the interval to be longer than objective time, the internal clock speed is assumed to be increased (Cheng et al., 2007).

If a study included two sets of empirical data and correlation analyses, we included the data that used longer than a 1 s duration (supra-second) on the basis of the assumption that the use of longer duration data would be more effective than shorter duration data in terms of detecting variability in the internal clock.

2.3. Data synthesis

One study reported Spearman's rank correlation coefficients, while another used Kendall's rank correlation coefficients. We transformed Spearman's and Kendall's correlation coefficients to Pearson's coefficients using transformation functions (Croux and Dehon, 2010) on the assumption that the variables followed a normal distribution after applying an adequate statistical transformation (e.g., Box-Cox transformation). Another study conducted a partial correlation analysis. We treated the partial correlation as if it was a simple Pearson's correlation analysis, which tends to be a conservative approach for the assessment of correlational significance.

A meta-analysis was conducted with the R (version 3.2.3; R Core Team, 2016) Meta package (Schwarzer et al., 2015). Pooled data from the four studies suggested a low to large association between performance on timing tasks vs. total psychotic symptom severity, as assessed by Positive symptom scores from the Positive and Negative Syndrome Scale (PANSS), Scale for the Assessment of Positive Symptoms (SAPS), or First Rank Symptom scale (Waters and Jablensky, 2009).

3. Results

The meta-analysis revealed a moderate correlation between severity of positive symptoms and performance on timing tasks (Fig. 2). Correlation coefficient was $-0.54[-0.69; -0.33]$ in the random effects model ($I^2 = 0.328, \gamma^2 = 0.022, p = 0.216$). Visual inspection of peak funnel plots did not reveal potential publication bias or other gross abnormalities.

4. Discussion

In spite of the small total number of subjects included in the meta-analysis, we found a link between positive symptoms of schizophrenia and the acceleration and precision of timing. This finding may not be a result of random error, but represents an association between timing task performances and positive symptoms.

A small degree of heterogeneity was found across the studies included in this meta-analysis. This is attributable to one study (Carroll et al., 2009) that reported small correlation coefficients between temporal precision and severity of positive symptoms. That study used outpatients whose positive symptoms were not severe (with an average PANSS score of 64), probably yielding the heterogeneity.

Findings from the studies included in this meta-analysis are consistent with the concept that accelerated time perception are linked to hypervigilance (McCarthy-Jones and Longden, 2016), which may underlie the generation of positive symptoms. Hypervigilance is a mental state in which attention to external stimuli is exaggerated (Tiemann et al., 2012). The relationship between positive symptoms and dysregulation of the internal clock, observed in this study, is consistent with a role for hypervigilance in mediating these two mental events.

Altered DA transmissions have been suggested to cause positive psychotic symptoms in several psychiatric illnesses, particularly schizophrenia (Seeman et al., 2006). As discussed above, DA transmissions also regulate the speed of the internal clock (Frederick and Allen, 1996). Therefore, it is possible that dysregulation of DA activities may produce positive symptoms via modulation of the internal clock, which deserves further investigations.

The present results may have some clinical implications. Specifically, as the change in time perception has been associated with psychotic states, its measurement may add to an objective evaluation of psychosis, and possibly, early interventions (Cellard et al., 2007; de Montalembert et al., 2016; Horton et al., 2014; Reed and Randell, 2014). Accordingly, Penney et al. (2005) reported interval timing deficits in people who were at high risk for developing schizophrenia. Taken together, further efforts should be directed to determining the neural substrates underlying the altered time perception in psychotic conditions.

Limitations of this study include reproducibility problem due to the small number of trials (only 4 studies were included in this meta-analysis), suggesting a need for further study.

5. Conclusions

In this meta-analysis, positive symptoms of schizophrenia were found to be related to acceleration of timing. Further examinations of factors regulating this association may help understand the neural mechanisms underlying the pathophysiology of psychosis.

Author contributions

NU and TS wrote and revised the manuscript. KM conducted

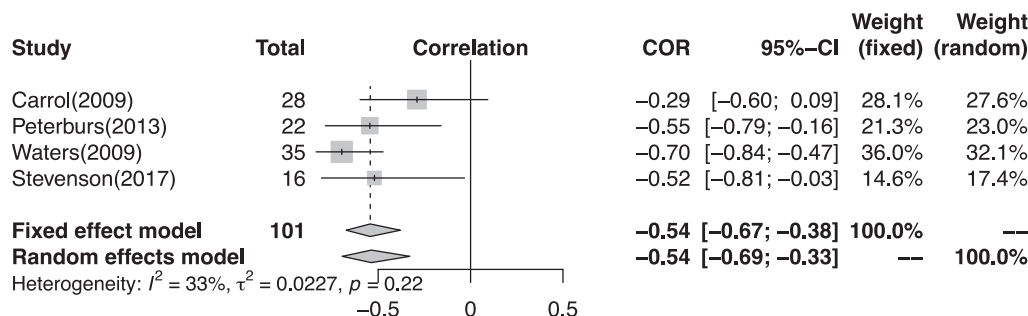


Fig. 2. Forest plot of standardized correlation coefficient between timing task performance and positive symptoms.

statistical analyses and revised it. All authors approved submission of the final draft.

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Conflict of interest

All authors report no conflict interest.

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