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# Temporal processing dysfunction in schizophrenia as measured by time interval discrimination and tempo reproduction tasks

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ABSTRACT

*Objective:* Time perception deficiency has been implicated in schizophrenia; however the exact nature of this remains unclear. The present study was designed with the aim to delineate timing deficits in schizophrenia by examining performance of patients with schizophrenia and healthy volunteers in an interval discrimination test and their accuracy and precision in a pacing reproduction–replication test.
*Methods:* The first task involved temporal discrimination of intervals, in which participants (60 patients with schizophrenia and 35 healthy controls) had to judge whether intervals were longer, shorter or equal than a standard interval. The second task required repetitive self-paced tapping to test accuracy and precision in the reproduction and replication of tempos.
*Results:* Patients were found to differ significantly from the controls in the psychoticism scale of EPQ, the proportion of correct responses in the interval discrimination test and the overall accuracy and precision in the reproduction and replication of sound sequences ($p<0.01$). Within the patient group bad responders concerning the ability to discriminate time intervals were associated with increased scores in the Positive and Negative Syndrome Scale (PANSS) and in the Brief Psychiatric Rating Scale (BPRS) in comparison to good responders ($p<0.01$). There were no gender effects and there were no differences between subgroups of patients taking different kinds or combinations of drugs.
*Conclusions:* Analysis has shown that performance on timing tasks decreased with increasing psychopathology and therefore that timing dysfunctions are directly linked to the severity of the illness. Different temporal dysfunctions can be traced to different psychophysiological origins that can be explained using the Scalar Expectancy Theory (SET).



## 1. Introduction

Time is essential to human behavior and cognition. It allows us to determine what is occurring in our environment and when to respond to events, to sequence events, to compare their durations and the intervals between them. Pathophysiological distortions in human timing and time perception are of interest to both basic and clinical research (Haun et al., 2010).

Many theories in psychology and neuroscience aim at explaining how we judge the duration of time. In psychology, two models are of particular interest. The inference model suggests that the time of an event is inferred from information about relations between the events in question and other events whose date or time is known. The strength model of time memory proposes that an event produces a memory trace and as a consequence time perception is the comparison of this memory with the strength of its trace (Friedman, 1990).

The need to clarify the neurobiological mechanisms involved in time estimation stimulated research based on behavioral, pharmacological, lesion, electrophysiological and brain imaging studies. A very promising framework was set by Gibbon (1977) in his Scalar Expectancy Theory (SET), which suggests a temporal processing system integrating a pacemaker-switch-accumulator (or clock) stage, memory stage including working memory operation and reference memory, and decision stage (see Fig. 1). According to this view differences in time perception are attributable to changes in the operation of clock, memory or decision stages of the system. Temporal decisions

*Abbreviations:* SET, Scalar Expectancy Theory; DA, dopamine; BPRS, Brief Psychiatric Rating Scale; PANSS, Positive negative Syndrome Scale; EPQ, Eysenck Personality Questionnaire; SPL, sound pressure level; ITS, inter-tap intervals.

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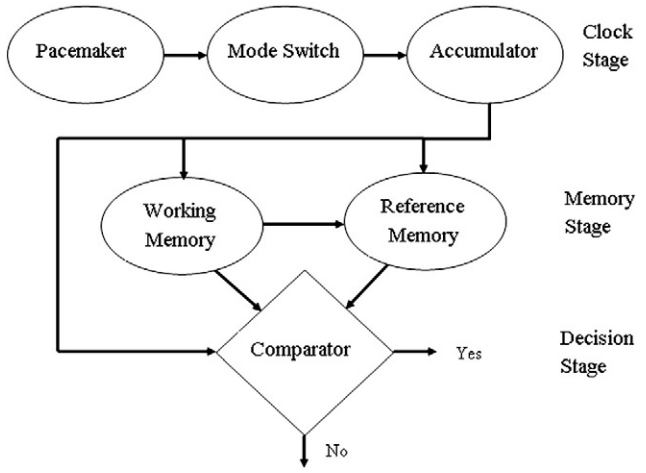


**Fig. 1.** Information-processing model of interval timing derived from the three stages (clock, memory, and decision) described by Gibbon (1977).

imply that memorized representations of time follow Weber's law (Dahaene and Brannon, 2010), which states that the intensity of the internal perception (sensation) is linearly related to the magnitude of external stimulation. The model gives special emphasis on scalar variability which states that increases in the magnitude of a physical stimulus produce proportional increases in the variance of the perception, i.e. timing of a longer duration is less precise (Allman and Meck, 2011; Gibbon, 1977; Lejeune and Wearden, 2006; Zarco et al., 2009).

Given the possible impact of temporal processing dysfunction on cognition and daily behavior, researchers have attempted to understand the role of time perception in schizophrenic patients. From a phenomenological and neuroscientific view, a fundamental structural disturbance consciousness appears in schizophrenia (Vogeley and Kupke, 2007). The model of "cognitive dysmetria" correlates the dysfunction of a circuit of all proposed nodes that engage in schizophrenia with "poor mental coordination". This is the fundamental cognitive disturbance that leads to an extended range of symptoms (Andreasen et al., 1998). The so called "poor mental dysfunction" seems to arise from the impairment of the "timing or sequencing component of mental activity" (Andreasen et al., 1999).

Neuroimaging studies have shown that cortico-cerebellar-thalamic-cortical circuit involving the bilateral supplementary motor area, the right middle frontal, the right inferior parietal, the insula, the left putamen, the right posterior cerebellum, the superior temporal gyrus, the right thalamus, the right middle frontal gyrus and the left superior temporal brain areas engaged in time perception has also been implicated in the pathophysiology of schizophrenia (Ivry and Spencer, 2004; Ortuño et al., 2011; Stevens et al., 2007; Volz et al., 2001). Furthermore, altered time perception in schizophrenia results in an excessive production of mental associations between unrelated events and gives rise to the expression of clinical symptoms resulting in an abnormal sense of agency in patients with hallucinations and delusions (Franck et al., 2005). Accordingly, classic symptoms of schizophrenia, such as thought disorder and disorganized behavior may be manifestations of a time dysfunction (Franck et al., 2005).

Individuals with schizophrenia have consistently displayed temporal disturbances across a variety of timing tasks (Ameller et al., 2007; Caroll et al., 2008, 2009; Davalos et al., 2003; Lee et al., 2009). In most cases the interpretation of the results was successfully based on the Scalar Timing Theory.

Schizophrenia is also of interest for investigations in interval timing because it has been linked to dysfunctions of the dopamine (DA) system and a relationship between brain dopaminergic systems and interval timing has been postulated. Research provides evidence indicating that schizophrenic patients exhibit deficits in temporal processing possibly related to abnormal dopaminergic activity in frontal–striatal circuits, which contribute to faster clock speeds and underproduction of intervals (Penney et al., 2005; Volz et al., 2001). Similar findings were discussed in relation to patients with Parkinson's disease (Malapani et al., 1998).

At the same time, pharmacological studies indicate that time perception performance is highly sensitive to dopaminergic modulation. Dopamine agonists such as cocaine and methamphetamine produce lengthening of perceived time, whereas the dopamine antagonist haloperidol causes subjective shortening of time (Meck, 1996). However, there are contradictory results showing that distinct drugs selectively interfere with perception of different time intervals. For instance, Rammsayer (1999) showed in human psychophysical experiments that the dopaminergic antagonist, haloperidol, significantly impaired discrimination thresholds of 100 ms and 1 s intervals. Remoxipride, a dopamine antagonist that is more selective for D2 receptors, impaired processing on the scale of a second but not for 50 ms intervals (Rammsayer, 1997). Experiments with benzodiazepines also support the dissociation between millisecond and second processing, by showing that performance in a 50 or 100 ms task is unaffected, whereas performance on a 1 s task is made significantly worse (Rammsayer, 1992, 1999).

In a very recent review (Bonnot et al., 2011) the authors in the very title wonder "Are impairments of time perception in schizophrenia a neglected phenomenon?" In view of the above considerations, this study was designed with the aim to delineate timing deficits in schizophrenia by examining performance of patients with schizophrenia and healthy volunteers in an interval discrimination test and their accuracy and precision in a pacing reproduction–replication test.

## 2. Methods

### 2.1. Participants

Participants were 60 patients (41 males, age range: 23–55, 42.1 ± 8.8; 19 females, age range 26–50 years, 38.2 ± 5.9) who met the ICD-10 criteria for schizophrenia and 35 controls (20 males, age range: 28–55 years, 38.3 ± 7.3; and 15 females, age range 25–46 years, 37.2 ± 5.0) healthy participants volunteered for the present study. The patient group had secondary education at a percentage of 64.33% and the 89.71% of the control group had tertiary education. Patients were hospitalized to the 'Psychiatric Hospital of Attika'. Almost all patients with the exception of two were prescribed with atypical antipsychotic drugs. In addition ten patients were also taking anticholinergics and another ten were taking typical antipsychotic drugs.

### 2.2. Measures

Current symptoms in the patient group were assessed using Brief Psychiatric Rating Scale (BPRS) (Ventura et al., 1993) and Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). The BPRS contains 24 Symptom constructs, that are scored between 1 (not present) and 7 (extremely severe). The PANSS contains 30 items, that are scored between 1 (absent) and 7 (extreme). Symptom ratings were categorized into a three subscale structure (Positive, Negative and General Subscale distribution).

Eysenck Personality Questionnaire (EPQ) was administered to all participants to evaluate the three dimensions of personality: psychoticism, extraversion, neuroticism and lie score (Eysenck and Eysenck, 1975). The EPQ is an 84 item self- report, yes/no questionnaire.

Between groups differences in the four subscales of EPQ were tested with MANOVA followed by post-hoc comparison and step-down procedures.