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Patients with schizophrenia selectively impaired in temporal order judgments

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ABSTRACT

The ability to order events in time plays a pervasive role in cognitive functions, but has only rarely been explored in patients with schizophrenia. Results we obtained recently suggested that patients have difficulties following events over time. However, this impairment concerned implicit responses at very short asynchronies, and it is not known whether it generalizes to subjective temporal order judgments. Here, we make a direct comparison between temporal order judgments and simultaneity/asynchrony discrimination in the same patients. Two squares were displayed on the screen either simultaneously or with an asynchrony of 24 to 96 ms. In one session 20 patients and 20 controls made a temporal order judgment and in the other they discriminated between simultaneous and asynchronous stimuli. Controls recorded similar performances in the two tasks at asynchronies above 50 ms, whereas patients displayed a sizeable impairment in temporal order judgment selectively. This impairment occurred in the easiest conditions, with the largest SOAs (Stimulus Onset Asynchronies) and only in the temporal order judgment. The results are the first evidence that patients with schizophrenia have a selective difficulty determining temporal order, even for asynchronies producing a clear perception of asynchrony. This impairment may mediate difficulties engaging oneself in everyday life events.
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1. Introduction

Time has a special status in cognition. There is no one single area that processes time information, and time is only rarely the target of our thoughts, but nonetheless it plays a pervasive part in human cognition. This is especially true for temporal order. In general, speaking, reasoning, and thinking all imply the ordering of thoughts, words, and syllables. It is the ordering which allows us to consider things as past, and it is also at the root of our ability to look ahead (van Wassenhove, 2009; Wittmann, 2011).

Because temporal order has such a special status, it is a good candidate for explaining a series of impairments in schizophrenia. Even though a number of studies have focused on time in schizophrenia (Foucher et al., 2007; Giersch et al., 2009; Lalanne et al., 2012a,b,c; Giersch et al., 2013), hardly any have addressed the question of whether time ordering represents a particular difficulty for patients. In the present study, we compare the ability to detect asynchronies and to judge temporal order in both patients with schizophrenia and control subjects.

Several psychiatrists have suggested that time plays a central role in the pathophysiology of schizophrenia. One of them, Minkowski (1933), used his clinical experience to describe a loss of 'vital dynamism', signifying a difficulty following events in time. A disrupted sense of time continuity, i.e. a fragmentation of the normal flow of events (Fuchs, 2007; Vogeley and Kupke, 2007), has also often been described at a clinical level. Finally, Andreasen (1999) described the concept of a cognitive dysmetria, which may be regarded as essentially temporal in nature, and which as Andreasen proposed was a basic deficit sub-tending secondary cognitive difficulty. On an experimental level, several difficulties pertaining to time have been reported in patients with schizophrenia, but the link with clinical descriptions is still unclear. Patients are often described as having disturbances when it comes to determining the duration of events (Volz et al., 2001; Elvevåg et al., 2003; Davalos et al., 2005; Allman and Meck, 2012; Roy et al., 2012), but it is unclear how these difficulties relate to other cognitive difficulties or clinical symptoms. Our own results suggest indirectly that it is difficult for patients to follow events over very short periods. In the course of our procedure, two spatially-separate visual stimuli are presented on a computer screen either simultaneously or with very brief onset asynchronies, and subjects decide whether the two stimuli are simultaneous or asynchronous. They must answer by pressing a left response key for simultaneity and a right response key for asynchrony. For patients to detect an asynchrony between the stimuli the asynchrony has to be longer than

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for healthy participants, a result replicated in four studies (Giersch et al., 2013). However, when the procedure is as straightforward as described above, i.e. two successive visual stimuli, the impairment in patients is relatively small. For example, several studies have reported a shift in the threshold of only 10 ms. The patients were thus impaired relative to controls when the asynchrony was close to threshold, i.e. around 50 ms, but performance was very similar between patients and controls at the largest asynchronies, i.e. around 100 ms (Foucher et al., 2007; Lalanne et al., 2012a).

We also explored how patients process asynchronies automatically, i.e. implicitly, even when they were unable to report the existence of a delay explicitly. Our results showed that the asynchrony is processed in patients and controls even though participants are unable to report it (Lalanne et al., 2012a,c; Giersch et al., 2013). Interestingly, there was a qualitative difference between patients and controls (Lalanne et al., 2012a,c). Our results suggested that controls are able to follow events over time automatically and to focus on the last event to have occurred, whereas patients would be stuck on the first event (Giersch et al., 2013). It is these results that suggest that patients are impaired when it comes to following events over time. The main question at this stage is whether this impairment is confined to very short time scales, or whether it also applies with delays above 20 ms. The present study does not look at very short asynchronies below 20 ms. Rather, it explores the ability to distinguish events over larger time intervals. We already know that patients are moderately impaired when required to detect an asynchrony. When asynchronies are sufficiently long their performance is similar to that of controls. However, making judgments about temporal order may involve different or additional mechanisms compared to those involved in simultaneity/asynchrony judgments (Vatakis et al., 2008; García-Pérez and Alcalá-Quintana, 2012). Individuals are able to detect an asynchrony between two events without knowing about their temporal order (Wittmann, 2011). Until now, investigations in patients with schizophrenia have focused mainly on simultaneity/asynchrony judgments. It might therefore be worth considering whether patients have particular difficulty judging temporal order. To the best of our knowledge, there is only one study to date which has explored the ability of patients with schizophrenia to make judgments about temporal order (De Boer-Schellekens et al., 2014). It showed that patients need a larger asynchrony than controls to judge temporal order, but did not compare performance with a judgment of simultaneity/asynchrony, making it difficult to decide whether this effect is selective. In our study the two judgments are directly compared in the same patients. The simultaneity/asynchrony discrimination task is similar to the paradigm used in previous studies, and we expected to replicate the minor impairment already described. If patients are impaired specifically when it comes to following events over time, it is possible that they may be more impaired with respect to temporal order judgments (TOJs) than as regards simultaneity/asynchrony discrimination. If, on the contrary, their impairment is confined to very short time scales, similar impairments should be observed in both tasks.

2. Method

2.1. Subjects

We detail demographic characteristics in Table 1. The project was approved by the local ethics committee. All subjects gave their informed written consent prior to testing, in accordance with the recommendations laid down in the Helsinki Declaration. Patients were stabilized, with relatively mild symptoms.

Details concerning subjects, exclusion criteria, the equipment (computer and 85 Hz monitor), and stimuli can be found in Supplementary data. It should be noted that we analyzed urine samples systematically in order to make sure that no subject was a cannabis consumer.

Table 1
Demographic and clinical data of the participants.

	Patients	Controls
Gender (M/F)	14/6	14/6
Age (mean ± SD)	37.2 ± 9.2	34.3 ± 11.4
Years of education (mean ± SD)	13.3 ± 2.2	13.1 ± 2
Medication (typical/atypical/no medication)	8/10/2	–
Dose of chlorpromazine equivalents	231 mg/day	–
Antiparkinsonian treatment (tropatepine/no medication)	4/16	
Mean disease duration	12.8 ± 7.2	
Outpatients/inpatients	19/1	
PANSS positive symptoms (mean ± SD)	17.7 ± 5.9	–
PANSS negative symptoms (mean ± SD)	21.5 ± 7.2	–
PANSS general symptoms (mean ± SD)	39.1 ± 11	–
PANSS total (mean ± SD)	78.3 ± 20.4	–

2.2. Experimental task and procedure

At the start of each trial a central fixation point was displayed in the middle of the screen, followed immediately by two rectangles, displayed in gray, either simultaneously (SOA = 0 ms) or asynchronously. Five levels of Stimuli Onset Asynchrony (SOA) were used. The two rectangles remained on the screen until a response had been given.

In the temporal order judgment (TOJ) task, subjects were instructed to respond by hitting the key corresponding to the position of the second rectangle (left ‘f’ key if the second rectangle was on the left, and right ‘j’ key if the second rectangle was on the right).

In the simultaneity/asynchrony discrimination task, subjects were instructed to respond by hitting the left ‘f’ key if the rectangles were judged to be displayed at the same time (synchronously) and the right ‘j’ key if they were judged to be displayed at different times (asynchronously).

Each target order and SOA (5 levels: 0, 24, 48, 72, and 96 ms) were tested in the same number of trials in a random order. All subjects were tested first with the temporal order judgment (TOJ), and then with the simultaneity/asynchrony discrimination task. This task order was used to avoid a cost of task switching in the TOJ task. We took additional precautions to avoid an interference of learning effects. These are detailed in Supplementary data.

2.3. Complementary data

In order to check for sustained attention performance in patients and controls, we used an AX-CPT task (Cohen et al., 1999; methodological details can be found in Supplementary data).

2.4. Statistical analyses

For each task, we first conducted a repeated-measures analysis of variance (ANOVA) on the rate of simultaneous responses in the simultaneity/asynchrony task, and on the rate of errors in the TOJ. Group was used as a between-group variable and experimental conditions (SOA) as within-group variables. We report effect sizes for all significant between-group differences, in Table 2.

Secondly, we set out to compare performance in the two tasks, especially at supra-threshold SOAs. This required certain calculations that are detailed in Online supplemental material. We predicted data in TOJ based on simultaneity/asynchrony judgments. If both tasks involve the same mechanisms, the transformed curves should be superimposed. By contrast, if TOJ requires specific mechanisms, a higher error rate should be observed during the TOJ than the one predicted based on the simultaneity/asynchrony judgment. We additionally calculated thresholds for asynchrony and temporal order detection, which are presented in Supplementary data.

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