

Self and time in individuals with schizophrenia: A motor component?

Francois Foerster, E. Joos, B. Martin, J.T. Coull, A. Giersch

► To cite this version:

Francois Foerster, E. Joos, B. Martin, J.T. Coull, A. Giersch. Self and time in individuals with schizophrenia: A motor component?. Schizophrenia Research, 2024, 272, pp.12-19. 10.1016/j.schres.2024.08.008 hal-04739317

HAL Id: hal-04739317 https://hal.science/hal-04739317v1

Submitted on 16 Oct 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés. Schizophrenia Research 272 (2024) 12–19 Available online 22 August 2024 0920-9964/© 2024 Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Self and time in individuals with schizophrenia: A motor component? Francois R. Foerster a,1, E. Joos a,2,3,4, B. Martin b,5, J.T. Coull c, A. Giersch a,* a University of Strasbourg, INSERM Unit 1329 'Strasbourg Translational nEuroscience & Psychiatry (STEP)' Team Psychiatry, University Hospital of Strasbourg, ITI Neurostra, 1 pl de l'Hopital, ^ 67000 Strasbourg, France b Centre Ressource de R'ehabilitation psychosociale et de rem'ediation cognitive, Centre R'ef'erent Lyonnais en R'ehabilitation et en Rem'ediation cognitive (CL3R) H^ opital du Vinatier, Lyon, France c Centre for Research in Psychology & Neuroscience (UMR 7077), Aix-Marseille Universit'e & CNRS, 3 Place Victor Hugo, 13331 Marseille cedex 3, France

* Corresponding author. E-mail address: giersch@unistra.fr (A. Giersch). 1 Present address: Consciousness, Cognition, and Computation Group (CO3), Centre for Research in Cognition and Neurosciences (CRCN), ULB Neuroscience Institute (UNI), Universit'e Libre de Bruxelles (ULB), Brussels, Belgium. 2 Present address: Institute for Frontier Areas of Psychology and Mental Health, Freiburg, Germany. 3 Present address: Department of Psychiatry and Psychotherapy, Medical Center – University of Freiburg, Freiburg, Germany. 4 Present address: Faculty of Medicine, University of Freiburg, Germany. 5 Present address: Centre Hospitalier Drome [^] Vivarais, 26760 Mont'el'eger, France.

Contents lists available at ScienceDirect Schizophrenia Research journal homepage: www.elsevier.com/locate/schres <u>https://doi.org/10.1016/j.schres.2024.08.008</u> Received 26 February 2024; Received in revised form 23 July 2024; Accepted 14 August 2024 i

An update to this article is included at the end Schizophrenia Research 272 (2024) 12–19 13

ARTICLE INFO Keywords: Time prediction Sense of self Motor preparation Passage of time Phenomenology

ABSTRACT Phenomenology suggests a disruption in the experience of time in individuals with schizophrenia, related to disorders of the sense of self. Patients themselves relate a fragmentation of their temporal experience and of their sense of self. Temporal expectations help relate the present moment to the future and we have previously shown that temporal expectations are fragile in patients, and relate to disorders of the self. Here, we investigate whether patients' performance is still impaired when the motor response to the expected event can be prepared in advance. In two different experiments participants (41 patients vs. 43 neurotypicals in total) responded to a visual target occurring at a variable interval (or "foreperiod") after an initial warning signal. Moreover, in Experiment 1 we measured the sense of self with the EASE scale. We observed the usual benefit of the passage of time: the longer the waiting period, the better the preparation, and the faster the responses. However, this effect also comprises sequential (surprise) effects, when a target occurs earlier than on the preceding trial. We evaluated the effect of the passage of time, by isolating trials that followed a trial with the same foreperiod. The benefit of long, versus short, foreperiods was still observed in controls but disappeared in patients. The results suggest that the benefit of the passage of time is diminished in patients and relates

to self disorders, even when the task allows for motor preparation. The results suggest that a non-verbal impairment sub-tends disorders of the sense of self. 1.

Introduction

The relationship between self and time was originally proposed in phenomenology (Husserl, 2012), which in turn inspired psychiatrists (Minkowski, 2013). The sense of self has been proposed to involve several components, and among them a narrative self, which allows us to explicitly define our personal identity (Gallagher, 2000). The sense of self also includes a bodily component, or 'minimal' self. The bodily self is based on non-verbal information from the body, e.g. proprioception, vestibular information, tactile and interoceptive information (Blanke and Metzinger, 2009). It includes the borders and location of the body, agency (the feeling of being at the source of our actions), body ownership (the feeling that we own our body), and interoception (e.g. heartbeats). In this study we focus on one specific property of the 'minimal' sense of self, i.e. its phenomenological continuity. We refine and extend prior work and propose an experimental approach to evaluate the experience of time by measuring the incidental influence of the passage of time on response speed in a simple target detection task. We relate time continuity to the feeling of self-continuity by using a phenomenological scale, the EASE. Indeed, we do possess a feeling of self that is continuous over time and that matches our feeling of time continuity. Furthermore, our experience of time and self as being continuous refers to our everyday first-hand experience of the world, i.e. our self, for which time never seems to stop, jump, or disappear. Time is thus intimately related to our experience of one unique and continuous sense of self. Consistent with the relationship between time and self, disorders of the sense of self in schizophrenia have been related to a disordered experience of time (Fuchs, 2007; Vogeley and Kupke, 2007; Vogel et al., 2019). Patients' own reports suggest a relationship between the sense of self and time disorders: 'Time splits up and doesn't run forward anymore. There arise uncountable disparate now, now, now, all crazy and without rule or order. It is the same with myself. From moment to moment, various 'selves' arise and disappear entirely at random. There is no connection between my present ego and the one before' (Kimura, cited in Fuchs, 2007). Many aspects of timing are impaired in patients with schizophrenia (Giersch and Mishara, 2017; Thoenes and Oberfeld, 2017). Here we evaluated the incidental influence of the passage of time on response speed in a reaction time task with variable intervals (or "foreperiods"). We have already shown a link between disrupted performance on the variable foreperiod paradigm and disorders of the sense of self in individuals with schizophrenia (Martin et al., 2017; see also Ciullo et al., 2018), as evaluated with the phenomenological scale EASE (Parnas et al., 2005). In the variable foreperiod paradigm, individuals are instructed to respond as quickly as possible to a target, which can be presented in any sensory modality. Crucially, the target is presented after a warning cue with the interval (or "foreperiod") between cue and target being varied from one trial to the next. Since time flows inexorably forward ("time's arrow" and "passage of time"), the probability of target occurrence increases with the amount of time elapsed since cue presentation, and the sense of expectation grows with this probability (Elithorn and Lawrence, 1955; Luce, 1986). As the trial unfolds, the probability of target occurrence is progressively updated, which translates into faster reaction times (RTs) for targets occurring after longer intervals (Niemi and N" aat " anen, " 1981). This effect of foreperiod duration on response speed is known as the "variable foreperiod" effect. An advantage of this paradigm is that it invokes an increasing sense of temporal expectation that the target will soon occur,

which may help construct a sense of time continuity. The sense of time continuity is necessary to feel oneself as a continuous being in time, and conversely a disruption of the sense of time continuity may disrupt the phenomenological continuity of self in time (Martin et al., 2014). As a matter of fact events are discrete and how we go from a series of disconnected events to the perception of a continuous flow is not as straightforward as it seems. It has long been proposed that events are related to one another by means of memory ('retention') and prediction ('protention') mechanisms (Husserl, 2012). A famous example is the one of music, during which distinct notes are played successively, but interpreted as an integrated melody, thanks to past, present and future notes being simultaneously present in mind, i.e. phenomenologically perceived. However if, for example, prediction mechanisms are impaired, it may disrupt the phenomenological continuity of time and self. Our previous results are in agreement with this hypothesis (Martin et al., 2017). A pending question is whether our results are due to perturbed cognitive expectations (waiting for the target) or to poor motor preparation. The latter would suggest a more basic motor impairment. In Martin et al. (2017), individuals had to respond with the left or right hand according to the presentation side of the target. This meant they could not prepare their motor response ahead of target presentation. Instead, they had to wait for presentation of the target to know on which side it appeared and then to initiate their response. The preparation thus concerned mainly temporal expectation of the moment at which they would process the location of the target. The benefit of time preparation is observed in many different settings (Nobre and van Ede, 2018), and preparing to process a target location certainly entails time expectation. However, it has been suggested that time preparation may also involve motor preparation in neurotypicals (Hasbroucg et al., 1999; Nobre et al., 2007; Thomaschke et al., 2011; Volberg and Thomaschke, 2017). In addition, motor preparation has been suggested to be impaired in individuals with schizophrenia (Delevoye-Turrell et al., 2006). As already emphasized, a growing literature suggests an impaired sense of bodily self in individuals with schizophrenia (Gallese and Ferri, 2014; Lee et al., 2021a, 2021b). Planning when to contract muscles in a motor sequence or when to expect sensory feedback is integral to action, and their impairment relates to agency disorders (Foerster et al., 2021; Frith, 2005). It thus makes sense to verify whether performance on a variable foreperiod reaction time paradigm that allows for motor preparation is also impaired in individuals with schizophrenia. In Ciullo et al. (2018), the same response effector (i.e. the same hand) was used to respond to the target whatever the location of the target. As in Martin et al. (2017), the variable foreperiod effect appeared to be preserved in individuals with schizophrenia in the absence of attention or changes in target occurrence probability. However, the variable foreperiod effect was not fully distinguished from sequential effects (see below), which were also preserved, and which could contribute to the pattern of performance observed. In the present study we therefore analyzed the variable foreperiod effect separately from sequential effects, in a reaction time paradigm in which motor preparation was possible. The variable foreperiod effect represents the speeding of response times when the cuetarget interval is long rather than short and reflects performance benefits of the passage of time. However, response times (RTs) are not only influenced by the current cue-target delay, but also depend on what happened on the preceding trial. When the target occurs after a long foreperiod on trial t – 1, a long foreperiod is expected again on trial t. As a consequence, if the foreperiod is short on trial t, the target comes as a surprise, participants are not prepared, and response times are lengthened (Correa et al., 2006; Los and Agter,

2005). This 'sequential' or 'trial-to-trial' effect is extremely robust. It is independent of the effects of the passage of time itself (Tal-Perry and Yuval-Greenberg, 2022) and was observed in individuals with schizophrenia in both Ciuollo's and Martin's studies. So far however, when analyzing the benefit of the passage of time on RTs, an influence of sequential effects has not been systematically ruled out. Thus, the slowing down of RTs when a trial with a short foreperiod is preceded by a trial with a long foreperiod may contribute to the apparent benefit of the passage of time, by artificially increasing RTs at short foreperiods, independent of the benefit of the passage of time itself (see Los et al., 2014 and Salet et al., 2022 for discussion of this point). In the current study, we isolated the effect of the passage of time from sequential effects. Since sequential effects are observed when foreperiods differ on two successive trials (more specifically when a trial with a long foreperiod precedes a trial with a short foreperiod i.e. longshort), our solution was to measure the benefit of the passage of time selectively on trials that were preceded by a trial with an identical foreperiod (e.g. short-short or long-long). If participants benefit from the passage of time, an RT advantage for long foreperiods over short foreperiods should still be observed in such trials. In contrast, if patients do not benefit from the passage of time then response times for short-short or long-long trials should be similar. A possible difference between patients and neurotypicals in this study would thus help assess the extent to which timing information can be dynamically updated in individuals with schizophrenia when motor preparation is made possible. 2.

Methods

Participants in Experiment 1 were a sample of 24 outpatients and 22 matched controls. They are almost the same participants as described in Martin et al. (2017) (characteristics of the present group are summarized in Table 1, columns 1-3), although we describe here the results of a different paradigm than that in Martin et al. (2017). Patients were recruited in a rehabilitation center in Lyon. Participants in Experiment 2 are a different group of 17 outpatients and 19 matched controls recruited and tested in the University Hospital of Strasbourg (1 patient was excluded from the initial dataset due to a difference in RTs between short and long foreperiods more than 2SD above the average; characteristics of this group are summarized in Table 1, columns 4–6). Details on inclusion and exclusion criteria, as well as the description of the phenomenological scale (the EASE), can be found in supplementary material. In addition to typical clinical scales, the EASE scale was administered by the 3rd author of the paper (MB), who is trained on its use. This scale was used only in Experiment 1, because Experiment 2 was conducted in a different town (Strasbourg), where psychiatrists are not trained in phenomenology. The EASE is a semistructured interview designed to evaluate disorders of the minimal self (Parnas et al., 2005). The minimal self is a non-verbal type of self that includes, among others, the sense of bodily self. It entails five domains, including the sense of mineness of mental experience, selfawareness and presence, bodily experiences, demarcation between oneself and the environment, and existential reorientation. A full description of the five domains can be found in supplementary material. Although the lack of phenomenological evaluation in Experiment 2 is a limitation, Experiment 2 allowed us to generalize the results obtained in Experiment 1 to a different group of slightly older patients, with slightly less symptoms, and with a different experimental setting. In addition, the target was displayed laterally in Experiment 1, whereas it was always presented in the center in Experiment 2. Experiment 2

therefore allowed us to discard any possible role for conflict between the side of the target and the response in the pattern of data since this conflict was possible only in Experiment 1.

2.1. Stimuli Details on the apparatus can be found in supplementary material. In Experiment 1, the background display consisted of a central fixation point ("+") surrounded by two circles, and two peripheral boxes left and right of the center (Fig. 1). The trial started when both circles were briefly (100 ms) highlighted, indicating the beginning of the trial. Next, the screen remained blank for a variable foreperiod of 400 or 1000 ms. The target was then displayed in either the left or right box for 100 ms. If no response to the target was made, the next trial began after a randomized foreperiod of 1600 or 2000 ms. The target was either the letter 'X' or the symbol '+'. The two targets appeared with a probability of 0.50, and were varied only to avoid boredom. Crucially, the response was the same whatever the form of the target, and whatever the side of the target. In Experiment 2, a light in the center of a virtual robot was the central fixation point used to deliver the visual cue and target stimuli. This light could be either on or off and have either a red (cue) or green (target) color. The trial started with the light off for a random interval between 2000 ms and 3000 ms. Then, the light turned red for a variable foreperiod of 900 or 1500 ms. At the end of the foreperiod, the light turned green and remained on screen until the participant's response. The task of the participant was to respond as quickly as possible to the onset of the green target light (correct response), and refrain from responding beforehand (incorrect response) while the light was still red. In case of an incorrect response, negative feedback (i.e. a buzz sound) was delivered, the red light turned off and the next trial was initiated. The participants provided their motor response by pressing the button pad of a virtual reality controller placed in their right-hand, using their thumb.

2.2. Procedure In both Experiments (see Fig. 1), patients and controls were instructed to respond to the target as quickly and accurately as possible. Experiment 1 included two experimental blocks in which the cue indicated the upcoming foreperiod (temporal cue), as in Martin et al. (2017). The results for these experimental blocks can be found in the supplementary material, along with methodological details. The results did not show any difference between groups when this temporal cue was presented prior to the target. Here, we consider only the two blocks of 100 trials in which the initial cue was neutral, i.e. it contained no information regarding the cue-target foreperiod (those blocks were displayed separately from blocks with temporal cues). There were 100 trials for each cue-target foreperiod (400 and 1000 ms) displayed in random order, leading to around 50 trials for each sequential order (trials with a short foreperiod followed by a long foreperiod, i.e. shortlong, or short-short, long-short and long-long). Experiment 2 included distinct experimental blocks manipulating the presence or absence of (1) an optical flow displayed in the background, and (2) visual distractors (orange lights) displayed on the vertical light display in the visual periphery during all foreperiods (at 500 ms). Given the scope of this article, only data recorded in pairs of trials without the optical flow and without the distracting lights were used. There was one block with a static optical flow, which showed similar results to those reported here, but we discarded these results due to numerous static lights in the visual field. The trials without an optic flow and without distracters were mixed with trials with distracters. However, the effect of distractors was marginal (if any it rather improved performance in patients), and the task and foreperiods were similar across conditions. We included only those trials without distracters for the present analysis. There

was a total of 240 trials composed of 120 trials per foreperiod (900 and 1500 ms), displayed in random order. The number of trials per sequential order was thus around 60.

2.3. Statistical analysis

Trials with correct responses faster than 150 ms or slower than 1000 ms were excluded from the RT analysis in both Experiments and then averaged for each participant and condition. Mean RTs were normally distributed in Experiment 1 but not in Experiment 2. The two experiments differed in the foreperiods used and in the experimental setting. To make results more comparable between experiments and to take into account the lack of normality of the data in Experiment 2, we calculated two normalized indices (the distribution normality of the indices for each experiment and group was verified with a Shapiro-Wilk test).

- We estimated the benefit of the passage of time by calculating for each participant the difference in RTs when the trial had a short foreperiod versus when it had a long one. For this index, we considered only trials preceded by a trial with an identical foreperiod i.e., short-short minus long-long. The difference was divided by the sum of the averaged RT across both conditions.

- We estimated the typical slowing in RT that occurs when the target occurs earlier than expected by subtracting for each participant the RT observed when the trial with a short foreperiod was preceded by an identical trial, from the RT observed when the trial with a short foreperiod was preceded by a trial with a long foreperiod i.e. longshort minus short-short. The difference was again divided by the sum of the averaged RT in the two conditions.

We conducted repeated-measures ANOVAs separately for those indices with the factors foreperiod/sequential effect as independent within-subject variables, and group (controls/patients) as the betweensubject variable. Given the differences between Experiment 1 and 2, we analyzed each index first separately and only then compared the index between experiments, which was included as an additional betweensubject variable. In addition, we used t-tests to verify if the indices differed from 0. We correlated the two indices with PANSS and EASE scores. For the sake of clarity, in the graphs (Fig. 2) we represent data as average RT for each condition rather than the value of the calculated index.

3. Results

An analysis of variance was conducted for Experiment 1, with foreperiod (400 ms/1000 ms), and sequence type (similar vs. different on trials t and t – 1) as independent within-subjects variables, and group (controls/patients) as a between-subject categorical variable. There was a significant interaction between the three factors (F[1,44] = 4.4, p < .05, partial η 2 = 0.09. We did not conduct this analysis for Experiment 2, as data was not normally distributed. The following analyses were conducted on the normalized indices. Given the experimental differences between Experiments 1 and 2, we analyzed each index separately for each experiment. The index evaluating the benefit of the passage of time in trials with a foreperiod identical to the one in the preceding trial (i.e. short-short minus long-long) was smaller in patients than in controls in both Experiment 1 (– 0.01 vs. 0.015, F[1,44] = 5.1, p < .05, partial η 2 = 0.1) and Experiment 2 (0.004 vs. 0.02 F[1,34] = 4.7, p < .05, partial η 2 = 0.12). In controls, the index tended to differ from 0 in Experiment 1 (tvalue = 1.9, p = .06) and significantly differed from 0 in Experiment 2 (tvalue = 3.6, p < .005). In patients the

index did not differ from 0 neither in Experiment 1 (t-value = -1.31, n.s.) nor Experiment 2 (t-value< .01, partial $\eta 2 = 0.1$), without interaction with Experiment. We had included five untreated patients, three in Experiment 1 and two in Experiment 2. The index measuring the benefit of the passage of time in these patients had values of 0, – 0.004, – 0.027 respectively in Experiment 1, and 0.019 and 0.006 in Experiment 2. These values were all below the average values found in controls (0.015 in Experiment 1 and 0.02 in Experiment 2); only one was close to the controls' values, in a pauci-symptomatic patient. The index measuring the surprise effect (slower RTs when a trial with a short foreperiod was preceded by a trial with a long rather than short foreperiod i.e. long-short minus short-short) was systematically different from 0 (see supplementary material) and tended to be larger in patients than controls in Experiment 1 (0.057 in patients vs. 0.03 in controls; F[1,44] = 4, p = .053, partial $\eta^2 = 0.08$). There was no group effect in Experiment 2 (F < 1) or when the two Experiments were put together (F [1,80] = 2.6, n.s., partial η 2 = 0.03). We did not find any correlation between the different indexes and chlorpromazine equivalents. The following correlation was found to be significant when pooling together data from the two experiments. The index measuring the surprise effect was negatively correlated with the positive subscale of the PANSS (N = 41, r = -0.32, p = .04). In Experiment 1, we additionally assessed patients' sense of self using EASE (see supplementary material). The index evaluating the passage of time was negatively correlated with the 'presence' sub-score of the EASE (N = 24, r = -0.42, p < .05), i.e. the subscore evaluating the patients' self-awareness and immersion in the world. The correlation did not survive correction for multiple correlations, though. As in Martin et al. (2017), we created sub-groups of patients based on a median split of EASE scores. We conducted an analysis of variance on the index evaluating the passage of time, which showed an effect of group (low EASE score patients vs. high EASE score patients vs. controls, F[2,43] = 4.4, p < .05, partial $\eta 2 = 0.17$). The HSD post-hoc test showed that only the sub-group of patients with a high presence score had a significantly lower passage of time index than controls (p < .05).

4. Discussion

We present results from two different experiments involving individuals with schizophrenia and matched controls, in which participants had to react to a target occurring at different intervals after an initial cue. The two experiments differed in terms of cue-target interval, the position of the target (left or right in Experiment 1 but centered in Experiment 2) and the mode of stimulus presentation (simple stimuli on a computer screen for Experiment 1 vs. complex visual scene in a virtual reality environment for Experiment 2). Despite these numerous differences, the results were similar across experiments. In controls, we observed the usual benefit of the passage of time on reaction time (RT), with faster RTs for targets appearing after a long interval (foreperiod) than a short one. This effect was significant in both experiments, even when isolating those trials that were preceded by a trial with an identical foreperiod. Our main result is that this benefit of the passage of time was significantly decreased in patients relative to controls, in both experiments. In addition, in Experiment 1, phenomenological evaluation of the sense of self revealed that the sense of presence, i.e. an impaired immersion of the world, was associated with this lack of benefit from the passage of time. A fragility in being able to benefit from the predictive information carried by the passage of time fits with Martin et al., 2017 and with conclusions of older studies (Galbraith et al., 1983), and extends those previous results. We used relatively short intervals (<2s) like in Martin et al. (2017) and Ciullo et al. (2018), and made it possible for

participants to prepare their motor response in advance of the target occurrence, allowing the benefit of the passage of time to be facilitated by motor preparation. Although Ciullo et al. (2018) or Zahn et al. (1963) also used a simple reaction task, here we additionally isolated the benefit of the passage of time from sequential effects. This was possible thanks to a high number of trials per foreperiod, which allowed us to differentiate the benefit of the passage of time when two consecutive trials had the same vs. a different foreperiod. Our results thus suggest that the benefit of the passage of time is fragile in patients when it is isolated from sequential effects, even when it is possible to prepare a motor response in advance. Inasmuch as schizophrenia is seen as a pathology affecting consciousness, it is not often expected that they show disturbances at the motor level. As a matter of fact, patients move, act, speak, and do not show clearcut motor deficits (but see Krebs et al., 2000; Walther et al., 2020). Moreover, those abilities are timed and require planning in time. It is thus probable that patients have some kind of compensatory strategy. The additional indexes measured in the present study shed some light on the alternative strategies used by patients and allow us to reconcile apparent contradictions in the literature, as well as the discrepancy with the fact that patients still can time their actions and thoughts. The decrease in the benefit of the passage of time cannot be attributed to an impairment in sequential effects. If any, patients tend to show a rather larger surprise effect: they are clearly slowed down when the target occurs at a short interval immediately after a trial with a long foreperiod. Those results are consistent with previous results suggesting increased sequential effects in individuals with schizophrenia (Zahn et al., 1963). They are also consistent with recent results based on motor actions (Foerster et al., 2021). In this study, participants made pointing actions on a virtual surface. The haptic (kinesthetic and tactile) feedback was artificially provided by means of the virtual setting and was deliberately delayed in some trials. Results showed that individuals with schizophrenia adapted their motor trajectory according to the moment of the haptic feedback on the previous trial, whereas controls appeared to wait for the haptic feedback whilst ignoring the recent history of actions. In this study, patients also appeared to be excessively sensitive, rather than insensitive, to sequential effects. However, part of the results might seem contradictory to the present ones, and this contradiction is actually informative. In Foerster et al. (2021), results showed that patients were exceptionally sensitive to very short delays in haptic feedback. Such results might seem at odds with patients' inability to benefit from the accumulating passage of time. The fact that patients are sensitive to short delays in haptic feedback shows that they had correctly predicted the moment of occurrence of the feedback. Similarly, the preservation of sequential effects and of the benefit of temporal cues (see supplementary material) shows that patients are able to rely on predefined time intervals to plan a response, and thus to estimate time. These apparent discrepancies can be resolved by observing that there are several possible mechanisms for predicting the time of occurrence of an event. It is possible to (1) rely either on the recent experience of various time intervals, or (2) on temporal cues, to prepare for a specific interval (Los et al., 2014). As shown by preserved or increased sequential effects, patients are able to mobilize these mechanisms, which make it possible to have equivalent reaction times for short foreperiod trials preceded by an identical trial, as when both trials have a long foreperiod. In patients, it is as if the sequential effects have similar effects than the effects of temporal cues: patients prepare for an interval defined by either a cue or the foreperiod of the preceding trial. However, such a strategy may lack flexibility since, in real life, events rarely happen at predictable moments. Temporal uncertainty is the rule rather than the exception. This leads

us to regularly check for the occurrence of an event, allowing expectations to be updated, checking again for the event, and so on. Although patients with schizophrenia clearly benefit from fixed a priori temporal expectations (temporal cues or sequential effects), they find it more difficult to adapt when temporal information is unreliable (Coull and Giersch, 2022) or, as we have shown here, changes dynamically with the very passage of time itself. Furthermore, we have shown in previous studies that patients with schizophrenia have difficulty planning for the time of occurrence of sequences of visual stimuli at the level of milliseconds (Lalanne et al., 2012a, 2012b; Margues-Carneiro et al., 2021; reviewed in Coull and Giersch, 2022). This difficulty may underpin a more general difficulty in benefiting from the passage of time: if expecting an event at the level of seconds entails checking regularly for the event at the level of milliseconds, such millisecond-level mechanisms may help time to be accumulated at a longer scale, thus leading to benefits of the passage of time. This benefit of the passage of time would entail growing expectation over time, ultimately reflected in faster reaction times after long intervals, on top of any influence of sequential effects. These are the mechanisms we hypothesise are impaired in patients. There are several limitations in the results, and some aspects that warrant discussion. First the effects are small in amplitude. However, they replicate a vast literature. Moreover, the lack of benefit of the passage of time in patients is unlikely due to response variability, since sequential and cue effects are preserved in the very same patients. Also, it might be tempting to attribute the lack of benefit of the passage of time to medication, especially as it is motor-related. Yet, with the exception of four patients in Experiment 2, all patients were treated with atypical antipsychotics, which have fewer motor side-effects, and so should minimize the motor impact of their medication, especially for the cohort in Experiment 1. In addition, low or absent benefits of the passage of time were observed in at least 4 out of 5 unmedicated patients. We have already conducted a single case analysis in an unmedicated patient (Martin et al., 2018), suggesting that the inability to benefit from the passage of time precedes medical treatment. In all, the results are consistent with studies suggesting that a diminished sense of presence precedes the emergence of psychosis (Nelson et al., 2020; Parnas et al., 2016) and is thus independent of treatment. The correlation between the lack of benefit of the passage of time and a diminished sense of presence in Experiment 1 is consistent with the idea that timing deficits relate to minimal self disorders. It might seem surprising that we find a correlation with the sense of presence rather than with the sub-scale exploring the stream of consciousness. However, incidental accumulation of temporal information throughout the passage of time is unlikely to emerge at the conscious level. Even if some patients report a disappearance of time, and a fragmentation of time, and even if those complaints seem to fit with our experimental observations, the benefit of the passage of time at the level of milliseconds mainly serves to adjust one's own behaviour to a changing environment, i.e. to immersion and presence. It has to be noted, though, that more robust correlations may be achieved with larger samples of patients. It is a limitation that we did not perform a phenomenological evaluation in Experiment 2. However, the similar results in both experiments represent an internal replication, and this similarity was observed despite the use of a different set-up in the two experiments, and slight differences in patients' symptomatology.

5. Conclusions

In all, our results generalize and extend previous ones in individuals with schizophrenia, and show an impaired benefit of the passage of time when preparing to make a motor response.

This impairment is correlated with a diminished sense of 'presence', i.e. disorders of the minimal self. These results are consistent with the phenomenological literature on self and time disorders in patients, as well as with the literature on motor disorders.

Role of the funding sources

The supporting and funding sources were not involved in the study design, collection, analysis and interpretation of the data, or in the decision to submit the article for publication.

CRediT authorship contribution statement

Francois R. Foerster: Writing – review & editing, Visualization, Validation, Software, Methodology, Funding acquisition, Data curation, Conceptualization. E. Joos: Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis. B. Martin: Writing – review & editing, Resources, Investigation, Funding acquisition, Conceptualization. J.T. Coull: Writing – review & editing, Methodology, Formal analysis, Conceptualization. A. Giersch: Writing – review & editing, Writing – original draft, Supervision, Software, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization

Declaration of competing interest The authors have no competing interest to declare.

Acknowledgements We would like to thank Nicolas Franck, who made the work of Experiment 1 possible, by supervising Brice Martin at the time of the study. We would also like to thank Michel Cermolacce, who helped Brice Martin to score the EASE. We would like to thank Camille Scherer for her help in testing the patients in Experiment 2. INSERM, the University Hospital of Strasbourg and of Lyon (Le Vinatier) provided logistical support for Experiment 1, as well as a grant from the 'Conseil Scientifique de la recherche de l'Hopital ^ le Vinatier' (CSR F05, AO 2014) and an ANR grant (Autotime, ANR-16-CE37-0004). Experiment 2 was funded by the EU, Horizon 2020 Framework Program, FET Proactive (VIRTUALTIMES consortium, grant agreement Id: 824128 to A.G.), and supported by INSERM and the University Hospital of Strasbourg.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.schres.2024.08.008

References

Blanke, O., Metzinger, T., 2009. Full-body illusions and minimal phenomenal selfhood. Trends Cogn. Sci. 13, 7–13. https://doi.org/10.1016/j.tics.2008.10.003. Ciullo, V., Piras, F., Vecchio, D., Banaj, N., Coull, J.T., Spalletta, G., 2018. Predictive timing disturbance is a precise marker of schizophrenia. Schizophr. Res. Cogn. 12, 42–49. https://doi.org/10.1016/j.scog.2018.04.001. Correa, A., Lupia´nez, ~ J., Tudela, P., 2006. The attentional mechanism of temporal orienting: determinants and attributes. Exp. Brain Res. 169, 58–68. https://doi.org/ 10.1007/s00221-005-0131-x. Coull, J.T., Giersch, A., 2022. The distinction between temporal order and duration processing, and implications for schizophrenia. Nat. Rev. Psychol. 1–15. https://doi. org/10.1038/s44159-022-00038-y. Delevoye-Turrell, Y.N., Thomas, P., Giersch, A., 2006. Attention for movement production: abnormal profiles in schizophrenia. Schizophr. Res. 84, 430-432. https://doi.org/10.1016/j.schres.2006.02.013. Elithorn, A., Lawrence, C., 1955. Central inhibition-some refractory observations. Q. J. Exp. Psychol. 7, 116–127. https://doi.org/10.1080/17470215508416684. Foerster, F.R., Weibel, S., Poncelet, P., Dufour, A., Delevoye-Turrell, Y.N., Capobianco, A., Ott, L., Giersch, A., 2021. Volatility of subliminal haptic feedback alters the feeling of control in schizophrenia. J. Abnorm. Psychol. 130, 775–784. https://doi.org/10.1037/abn0000703. Frith, C., 2005. The neural basis of hallucinations and delusions. C. R. Biol. 328, 169–175. Fuchs, T., 2007. The temporal structure of intentionality and its disturbance in schizophrenia. Psychopathology 40, 229– 235. https://doi.org/10.1159/000101365. Galbraith, K.J., MacCrimmon, D.J., Steffy, R.A., 1983. Prepreparatory interval effects on redundancy deficit reaction time patterns in schizophrenic and normal subjects using the embedded-set procedure. J. Nerv. Ment. Dis. 171, 670–675. https://doi.org/ 10.1097/00005053-198311000-00005. Gallagher, S., 2000. Philosophical conceptions of the self: implications for cognitive science. Trends Cogn. Sci. 4, 14–21. https://doi.org/10.1016/S1364-6613(99) 01417-5. Gallese, V., Ferri, F., 2014. Psychopathology of the bodily self and the brain : the case of schizophrenia. Psychopathology 47 (6), 357–364. https://doi.org/10.1159/000365638. Giersch, A., Mishara, A.L., 2017. Is schizophrenia a disorder of consciousness? Experimental and phenomenological support for anomalous unconscious processing. Front. Psychol. 8, 1659. https://doi.org/10.3389/fpsyg.2017.01659. Hasbroucq, T., Osman, A., Possamaï, C.A., Burle, B., Carron, S., D'epy, D., Latour, S., Mouret, I., 1999. Cortico-spinal inhibition reflects time but not event preparation: neural mechanisms of preparation dissociated by transcranial magnetic stimulation. Acta Psychol. (Amst) 101, 243–266. https://doi.org/10.1016/s0001-6918(99) 00007-4. Husserl, E., 2012. On the Phenomenology of the Consciousness of Internal Time (1893–1917). Springer Science & Business Media. Krebs, M.O., Gut-Fayand, A., Bourdel, M., Dischamp, J., Oli'e, J., 2000. Validation and factorial structure of a standardized neurological examination assessing neurological soft signs in schizophrenia. Schizophr. Res. 45, 245–260. https://doi.org/10.1016/ s0920-9964(99)00206-6. Lalanne, L., van Assche, M., Giersch, A., 2012a. When predictive mechanisms go wrong: disordered visual synchrony thresholds in schizophrenia. Schizophr. Bull. 38, 506–513.

https://doi.org/10.1093/schbul/sbq107. Lalanne, L., Van Assche, M., Wang, W., Giersch, A., 2012b. Looking forward: an impaired ability in patients with schizophrenia? Neuropsychologia 50, 2736–2744. https://

doi.org/10.1016/j.neuropsychologia.2012.07.023. Lee, H.-S., Griffith, T., Park, S., 2021a. Bodily self-disturbances in schizophrenia: a comparative study of South Korea and the USA. Psychopathology 54, 262–274. https://doi.org/10.1159/000517933. Lee, H.-S., Hong, S.-J.J., Baxter, T., Scott, J., Shenoy, S., Buck, L., Bodenheimer, B., Park, S., 2021b. Altered peripersonal space and the bodily self in schizophrenia: a virtual reality study. Schizophr. Bull. 47, 927–937. https://doi.org/10.1093/schbul/ sbab024. Los, S.A., Agter, F., 2005. Reweighting sequential effects across different distributions of foreperiods: segregating elementary contributions to nonspecific preparation. Percept. Psychophys. 67, 1161–1170. https://doi.org/10.3758/bf03193549. Los, S.A., Kruijne, W., Meeter, M., 2014. Outlines of a multiple trace theory of temporal preparation. Front. Psychol. 5, 1058.

https://doi.org/10.3389/fpsyg.2014.01058. Luce, R.D., 1986. Response Times: Their Role in Inferring Elementary Mental Organization. OUP USA. Marques-Carneiro, J.E., Krieg, J., Duval, C.Z., Schwitzer, T., Giersch, A., 2021. Paradoxical sensitivity to sub-threshold asynchronies in schizophrenia: a behavioral and EEG approach. Schizophr. Bull. Open 2.

https://doi.org/10.1093/ schizbullopen/sgab011. Martin, B., Wittmann, M., Franck, N., Cermolacce, M., Berna, F., Giersch, A., 2014. Temporal structure of consciousness and minimal self in schizophrenia. Front. Psychol. 5, 1175.

https://doi.org/10.3389/fpsyg.2014.01175. Martin, B., Franck, N., Cermolacce, M., Falco, A., Benair, A., Etienne, E., Weibel, S., Coull, J.T., Giersch, A., 2017. Fragile temporal prediction in patients with schizophrenia is related to minimal self disorders. Sci. Rep. 7, 8278. https://doi.org/ 10.1038/s41598-017-07987-y. Martin, B., Franck, N., Cermolacce, M., Coull,

J.T., Giersch, A., 2018. Minimal self and timing disorders in schizophrenia: a case report. Front. Hum. Neurosci. 12, 132. https://doi.org/10.3389/fnhum.2018.00132. Minkowski, E., 2013. Le temps v'ecu. Etudes ' ph'enom'enologiques et psychopathologiques, Quadrige. Presses Universitaires de France, Paris cedex 14. Nelson, B., Lavoie, S., Gawęda, Ł., Li, E., Sass, L.A., Koren, D., McGorry, P.D., Jack, B.N., Parnas, J., Polari, A., Allott, K., Hartmann, J.A., Whitford, T.J., 2020. The neurophenomenology of early psychosis: an integrative empirical study. Conscious. Cogn. 77, 102845 https://doi.org/10.1016/j.concog.2019.102845. Niemi, P., N" a" atanen, " R., 1981. Foreperiod and simple reaction time. Psychol. Bull. 89, 133–162. https://doi.org/10.1037/0033-2909.89.1.133. Nobre, A., Correa, A., Coull, J., 2007. The hazards of time. Curr. Opin. Neurobiol. 17, 465–470.

https://doi.org/10.1016/j.conb.2007.07.006. Nobre, A.C., van Ede, F., 2018. Anticipated moments: temporal structure in attention. Nat. Rev. Neurosci. 19, 34–48.

https://doi.org/10.1038/nrn.2017.141. Parnas, J., Møller, P., Kircher, T., Thalbitzer, J., Jansson, L., Handest, P., Zahavi, D., 2005. EASE: examination of anomalous self-experience. PSP 38, 236–258. https:// doi.org/10.1159/000088441. Parnas, J., Carter, J., Nordgaard, J., 2016. Premorbid self-disorders and lifetime diagnosis in the schizophrenia spectrum: a prospective high-risk study. Early Interv. Psychiatry 10, 45–53.

https://doi.org/10.1111/eip.12140. Salet, J.M., Kruijne, W., van Rijn, H., Los, S.A., Meeter, M., 2022. FMTP: a unifying computational framework of temporal preparation across time scales. Psychol. Rev. 129, 911–948. https://doi.org/10.1037/rev0000356. Tal-Perry, N., Yuval-Greenberg, S., 2022. The spatiotemporal link of temporal expectations: contextual temporal expectation is independent of spatial attention. J. Neurosci. 42, 2516–2523. https://doi.org/10.1523/JNEUROSCI.1555-21.2022. Thoenes, S., Oberfeld, D., 2017. Meta-analysis of time perception and temporal processing in schizophrenia: differential effects on precision and accuracy. Clin. Psychol. Rev. 54, 44–64.

https://doi.org/10.1016/j.cpr.2017.03.007. Thomaschke, R., Kiesel, A., Hoffmann, J., 2011. Response specific temporal expectancy: evidence from a variable foreperiod paradigm. Atten. Percept. Psychophys. 73, 2309–2322. https://doi.org/10.3758/s13414-011-0179-6. Vogel, D.H.V., Beeker, T., Haidl, T., Kupke, C., Heinze, M., Vogeley, K., 2019. Disturbed time experience during and after psychosis. Schizophr. Res. Cogn. 17, 100136

https://doi.org/10.1016/j.scog.2019.100136. Vogeley, K., Kupke, C., 2007. Disturbances of time consciousness from a phenomenological and a neuroscientific perspective. Schizophr. Bull. 33, 157–165. https://doi.org/10.1093/schbul/sbl056