ARTICLE IN PRESS

Journal of Physiology - Paris xxx (2011) xxx-xxx

Contents lists available at SciVerse ScienceDirect

ELSEVIER

Journal of Physiology - Paris



journal homepage: www.elsevier.com/locate/jphysparis

Are impairments of time perception in schizophrenia a neglected phenomenon?

Olivier Bonnot^{a,*}, Marie de Montalembert^b, Solenn Kermarrec^c, Michel Botbol^d, Michel Walter^e, Nathalie Coulon^e

^a Child and Adolescent Department, Reference Center for Rare Disease with Psychiatric Expression, Groupe Hospitalier Pitié Salpêtrière, Assistance Publique Hôpitaux de Paris, 47-83 Boulevard de l'hôpital, 75013 Paris, France

^b Laboratoire Psychologie de la Perception, CNRS UMR 8158, Université Paris Descartes, Groupe Hospitalier Pitié Salpêtrière, AP-HP, Paris, France

^c Hospitalo-University Department of Child and Adolescent Psychiatry, Université de Rennes 1, CHGR, Rennes, France

^d Hospitalo-University Department of Child and Adolescent Psychiatry, Université de Brest (UBO), CHU de Brest, Brest, France

^e Hospitalo-University Department of Adult Psychiatry, Université de Brest (UBO), CHU de Brest, Brest, France

ARTICLE INFO

Article history: Available online xxxx

Keywords: Time Schizophrenia Psychoanalysis Phenomenology Neuroscience

ABSTRACT

Based on clinical, phenomenological and neurobiological observations, psychiatrists often report a deficit in time estimation in patients with schizophrenia. Cognitive models of time estimation in healthy subjects have been proposed and developed for approximately 30 years. The current theory in the field of time perception, which is supported by a connectionist model, postulates that temporal judgement is based upon a pacemaker–counter device that depends mostly upon memory and attentional resources. The pacemaker emits pulses that are accumulated in a counter, and the number of pulses determines the perceived length of an interval. Patients with schizophrenia are known to display attentional and memory dysfunctions. Moreover, dopamine regulation mechanisms are involved in both the temporal perception processes and schizophrenia. Thus, it is still unclear if temporal impairments in schizophrenia are related to a specific disturbance in central temporal processes or are due to certain cognitive problems, such as attentional and memory dysfunctions, or biological abnormalities. The authors present a critical literature review on time perception in schizophrenia that covers topics from psychopathology to neuroscience. Temporal perception appears to play a key role in schizophrenia and to be partially neglected in the current literature. Future research is required to better ascertain the underlying mechanisms of time perception impairments in schizophrenia.

© 2011 Elsevier Ltd. All rights reserved.

1. Introduction

Schizophrenia is a severe and complex psychiatric disorder. The core symptoms are hallucinations and delusions associated with disorganised thoughts (Andreasen, 1999). Despite several decades of research, the pathogenesis of schizophrenia remains widely unknown. For the majority of authors, it is a neurodevelopmental disorder with impairment in cognitive processes, such as attention, memory, executive functions and perception (Uhlhaas and Mishara, 2007; van Os and Kapur, 2009).

Impairment in time perception is observed in individuals with schizophrenia, but this is a poorly studied field and possibly a neglected phenomenon. This neglect might be explained by the difficulty involved in understanding time perception. As Saint Augustine, a philosopher and theologian of the 5th century wrote: "What then is time? If no one asks me, I know what it is. If I wish to explain it to him who asks, I do not know" (Saint Augustine, Confessions, 1993). Furthermore, the physicist Stephen Klein wrote: "Time is no

E-mail addresses: olivier.bonnot@psl.aphp.fr (O. Bonnot), solennkermarrec@ yahoo.fr (S. Kermarrec), michel.botbol@wanadoo.fr (M. Botbol), michel.walter@ chu-brest.fr (M. Walter).

0928-4257/\$ - see front matter © 2011 Elsevier Ltd. All rights reserved. doi:10.1016/j.jphysparis.2011.07.006

matter for any of our five senses". For sight, we have our eyes, and for hearing, we have our ears. For each of our five senses, we could describe the physical characteristics of the stimuli, the receptors, and the pathways between the receptors and the brain. However, time is not a stimulus. We do not know of any time receptors. Time perception is also subjective, and subjectivity is difficult to evaluate. Time perception is different indeed from the physical and objective measurement of time that is related to a distance or a speed.

More recently, the field of cognitive neuroscience has proposed an original time perception and estimation model, in which impairment could be associated with psychiatric disorders or could even be a part of their pathogenesis. These models involve attention and memory, two cognitive processes that are impaired in schizophrenia. Perceptual dysfunctions, including time perception, are observed in schizophrenia, but it is still unknown whether they are related to a secondary core mechanism.

The aims of this article are to present an overview of the literature regarding time estimation and schizophrenia, to discuss specific issues related to how perceptual dysfunction in schizophrenia may lead to abnormalities in time perception, and to propose new perspectives towards an integrative approach between psychoanalysis, phenomenology and neuroscience.

^{*} Corresponding author. Tel.: +33 1 42 16 23 90.

2

2. Evidence for a timing misperception in schizophrenia based on phenomenology and psychopathology

Time perception is a complex concept. Phenomenology proposes an understanding of phenomena, the science of "life experiences", and it was a very active thinking trend in the late 19th century, following work by Heidegger and Merleau-Ponty. Analysing time perception in schizophrenia through phenomenology and psychopathology might help us to better understand this concept.

2.1. Phenomenology

Philosophy proposes a distinction between physical time (which can be measured) and subjective time. Theories that the subjectivity of time requires a conscience emerge in modern philosophy following Kant's notion of the *"inner sense"*. Henri Bergson redefined time perception along the same lines. Bergson's thesis was that human eyes can only see, on a clock, the juxtaposition of unrelated positions, but in contrast, the self is able to perceive time, the essence of which is to last (Bergson, 1995).

Minkowski found "lived time", which was also the title of one of his main books, to be severely impaired in schizophrenia. Minkowski, 1933 For him, "lived time" was closely related to "life force", the creative impulse of life (another concept developed by Henri Bergson; (Bergson, 1995)). In the line of Bleuler (1911), Minkowski thought that patients with schizophrenia suffer from a lack of perception of reality; they live in their own world. Regarding time, he explained that patients are lost in time because they are unable to segment duration and, consequently, to imagine or to picture the passing of time. The resulting state is called "geometrism", "morbid rationalism", or a "frozen, ultra logical and incommunicable" state. Furthermore, for him, there was a lack of lived time that led to a time freeze where the dynamic perception of time could no longer occur. This theory may be closer to that of Jean Sutter's works on "anticipation". For Sutter, "anticipation" was the result of everyone's necessity to fit the surrounding world, which is possible by anticipating what will happen. (Sutter, 1956) Delusion and hallucination create misunderstandings and false anticipations. Reality has lost its power of anticipation, leading to transitivism, which is an attribution lapse. In the same vein, Heidegger talked about "Dasein" or "Being"; Heidegger used a contraction of the German "da sein", which literally means "being there". Binswanger continued to coin the term "daseinanalysis". A contemporary Japanese author makes time perception a central element in several psychiatric diseases, especially in schizophrenia (Kimura, 2000, 2003). Time perception in schizophrenia is called "ante festum" (before the fest), contrary to bipolar disorder patients, where it is called "post festum". "Post festum" is the idea of something definitively passed but leading to regrets, whereas "ante festum" marks a thing that is ahead of the present time. This phenomenon is the inability to live in the present, a kind of dissolution of the natural experience (Binswanger). Anticipation obviously exists, but it is inefficient and based on misjudgements.

Unfortunately, there is no other clinical diagnostic criterion concerning time than the imprecise measurement of *disorientation in time and space* (DTS), which is mainly associated with confusion or dementia. There is no DTS in schizophrenia, but there is an impaired perception of time, which is also called *temporal syndrome* (Le Guen, 1958), and some authors have noticed clinically an inaccurate perception of time in patients (Crow and Stevens, 1978; Ehrentheil and Jenney, 1960; Mariategui and Flores, 1966; Pearl and Berg, 1963; Stevens et al., 1978). In particular, these authors noticed disorganisation and impairments in time estimation.

To conclude, for phenomenologists, the *"lived time"* is frozen (Le Guen, 1958), broken (Fernandez Zoila, 1976) or collapsed (Minkowski, 1995, original ed., 1933), while the future is either not

anticipated or is wrongly anticipated (Kimura, 2000; Sutter, 1956). Phenomenologists, such as Eugene Minkowski and Ludwig Binswanger, were interested in time processes during the exact same period when psychoanalysis indicated that the unconscious was timeless.

2.2. Psychopathology

From a psychopathological point of view, le Guen thought that patients with schizophrenia were not themselves able to figure out the passage of time (Le Guen, 1958). This is a regressive (from a psychodynamic point of view) state to avoid psychic destructuration. The relationship to time is considered to be the core symptom. Some authors have proposed that impairment in time perception could lead to a schizophrenic state and symptoms. Lost in time, the patient could elaborate delusions of two modalities. The first modality is a neo-creation of symbolic time, leading to an adaptive state that lowers mental pain. The second modality is an alteration of real time with hallucination and delusion. These two modalities lead to time misperception in patients with schizophrenia.

This concept of time without movement is close to the idea of a timeless unconscious (Freud, 1915) and the open sky unconscious in psychosis. For psychoanalysis, subjective time (which was not specifically studied by Freud) is created by the meeting of memory and perception. During early developmental stages, infants start to distinguish between before and after, and by this distinction, they develop a perception of time (e.g., Friedman, 2008; Piaget, 1969). According to Diatkine, time perception is stressful. The intrusion of time into a timeless word may be considered to be an early trauma (Diatkine, 1995).

Although the primary state of time perception impairments is still debated, psychoanalysts suggest that this function may play a key role in the psychopathology of schizophrenia.

3. How to objectively evaluate the impairment of timing perception?

Experimental psychology emerged in the 1950s, and several experiments have of course been conducted on time perception because of clinical and phenomenological observations (Bonnot et al., 2000; Carlson and Feinberg, 1968; Clausen, 1950; Densen, 1977; Dilling and Rabin, 1967; Fraisse, 1984; Goldstone and Lhamon, 1956; Johnson and Petzel, 1971; Lhamon and Goldstone, 1973; Orme, 1966; Rammsayer, 1990; Rammsayer and Lima, 1991; Tracy et al., 1998; Tysk, 1983a,b; Wahl and Sieg, 1980). These studies are difficult to compare as they used different methods, ranging from simple to complex, had different durations; most lasting just a few seconds, but some lasting minutes, and used different stimuli modalities, such as visual or auditory. Moreover, these experimental studies were based upon different experimental paradigms. Some authors used methods of the reproduction of a time interval, asking the subject to reproduce (vocally or physically, for example, by tapping with a finger) a sound they had just heard (Bonnot et al., 2000; Johnson and Petzel, 1971; Tracy et al., 1998); other researchers used comparison and discrimination methods (Lhamon and Goldstone, 1973; Rammsayer, 1990) or direct verbal estimation (Densen, 1977; Wahl and Sieg, 1980), while still others compared different experimental procedures (Elvevag et al., 2003; Tysk, 1983). To summarise, many methods have been proposed for assessing mean estimates and variability, and the appropriateness of a method may well depend upon the range of duration under investigation (for a review, see Grondin, 2010). A distorted perception of time or problems in time processing have been reported in people suffering from various psychiatric or neurological disorders, and some recent studies have focused on the misperception of time in schizophrenia. Interestingly, as we are going to illustrate in this paper, all of the results

show a tendency for patients with schizophrenia to overestimate the elapsed time and to be less accurate in time estimation tasks than healthy participants (e.g., Carroll et al., 2009; Davalos et al., 2005; Elvevag et al., 2003).

These experiments confirm the clinical observation of impaired time perception in patients with schizophrenia, but they are not able to explain the processes involved. We will therefore briefly present cognitive theories of time perception.

4. Arguments from neuroscience

4.1. An overview of cognitive theories of time perception

In the field of cognitive neuroscience, time perception has frequently been studied, especially in healthy subjects. Despite many unanswered questions and discussions, a consensual model of time perception exists.

Early experiments focused on situations where the subject did not know that he would have to estimate the amount of time that had passed, and he had to estimate it retrospectively. This method is the well-known "retrospective paradigm". In this case, which is common in real life, the participant must look backward in his memory for a "trace" of the length of the event. The first idea is simple and suggests that the longer the event is, the larger the trace in an analogical model will be (Ornstein, 1969). This model was too simple and could not explain the differences between estimations of the same durations under, for example, different environmental conditions. A second model postulates that an estimation of the same duration of time is shorter during a blank interval (no mental task) when compared to an active interval. Experiments with participants performing attentional tasks of differing complexities during a constant time period confirm this hypothesis (Elvevag et al., 2000). This result leads to the segmentation model. The cognitive processes that are activated during the period leave traces at regular intervals, which are counted by the subject to estimate time. The more processes activated, the longer the final time estimation (Povnter, 1983). Following this work, the model was improved. During the interval period, the mental task is always performed by creating a "cognitive context" (Block, 1989). This cognitive context generates modifications, mainly temporary, which are traces of changes. The time estimation will be correlated to the types of processes that are activated during the period of estimation or to the number of processes/changes (Block, 1989). This retrospective model did not solve the question of a blank interval, and many authors have thought that such a common activity should have been generated by a specific cognitive tool.

The intentional model is based upon a cognitive processor, as described by Thomas and Weaver in 1975. The original experimental procedure compared performance in time estimation (i.e., patients were aware that the experiment was about time estimation) in three groups while simultaneously performing attentional tasks: (i) looking at a simple item picture with no specific task to perform; (ii) looking at a complex picture with many items and being asked to count them; and (iii) looking at a complex picture with few items and being asked to count them. The results showed that the time estimation (in seconds) was proportionally longer when the items to count were few or zero. The memory model, presented below, would predict the exact opposite. The authors suggested two major hypotheses. First, they proposed that attentional resources are defined as fixed, meaning that, in a multitask situation, there should be a sharing process. This phenomenon explains why performance is lower for an attentional task when the subjects are performing tasks simultaneously. Second, supported by a connectionist model (Brown, 1995; Gibbon and Church, 1990), they postulated the existence of a cognitive

temporal processor (Pt), which is supposed to stock Subjective Time Units (STU), mostly depending upon allocated attentional resources. This temporal processor hypothesis, also called the temporal module or pacemaker, was confirmed in several studies and has an extensive literature (e.g., Block, 1989; Brown, 1995; Fortin et al., 1995; Predebon, 1995; Zakay et al., 2004; Zakay et al., 1994; Meck, 2005). The stream of pulse from the pacemaker results in a linearly increasing accumulator value (Alan and Gibbon, 1991; Gibbon, and Church, 1984), and the accurate estimation of time is also based on memory and thus depends upon the subject's cognitive performance (Fortin and Couture, 2002). Such a pacemaker-counter device forms the basis of many theoretical propositions, and this view can be summarised as follows: the pacemaker emits pulses that are accumulated in a counter, and the number of pulses that are counted determines the perceived length of an interval. The exact role of cognitive processes, the number of pacemaker(s) and accumulator(s) and the type of memory activated in time estimation remains contested (see Grush, 2005; Rubia and Smith, 2004).

Consensual theories postulate the activation of different cognitive processes depending on the paradigmatic condition. The STU attentional model (Gibbon and Church, 1990) is accurate for prospective time estimation, and the memory model is proposed for retrospective conditions. However, both processes (pacemaker and memorybased) are activated in any case. According to this model, time perception involves two successive steps. The first step - the storage of the temporal pulse in an accumulator - is a time-specific process. The second step leads to a decision through a comparison between the pulse level estimated in the working memory and samples of previous time durations from the reference memory (Gibbon and Church, 1990). Obviously, beyond specific timing processes, accurate time estimation requires attentional and memory resources (Fortin and Couture, 2002; Meck, 2005; Rammsayer and Lima, 1991). Cognitive experiments in this field have indicated that the accurate processing of temporal intervals in the range of seconds requires increased attentional and mnesic demands (Fortin and Couture, 2002).

4.2. Neuroscience approach of time perception in schizophrenia

The investigation of time perception is pertinent to the understanding of neurobiological and cognitive abnormalities in schizophrenia. First, brain lesion and neuroimaging studies have shown that the critical brain structures engaged in time perception include the prefrontal and parietal lobes (lateralised to the right), thalamus, basal ganglia and cerebellum (Mattel and Meck, 2000). These brain areas have been implicated in the pathophysiology of schizophrenia in that there is impaired coordination of activity among these regions (Andreasen et al., 1999). Second, pharmacological studies indicate that time perception performance is highly sensitive to dopaminergic modulation (Davis et al., 1991).

Clinical and experimental data strongly suggest that patients with schizophrenia are less accurate in their ability to estimate time than healthy subjects. The specificity of this clinical and behavioural impairment is still in question, however, as time estimation requires memory and attentional resources. Memory impairments in schizophrenia are well known, both in working and episodic memory (Forbes et al., 2009; Ranganath et al., 2008; Wang et al., 2009), and attention deficits are also well documented (Millan and Brocco, 2008; Rund, 1998). Moreover, episodic memory was also studied in naturalistic experiments, which suggest that patients with schizophrenia remember that an event occurs but do not know when it occurred (Franck et al., 2005; Rizzo et al., 1996). These results are in line with previous observations and experiments showing that patients are not clinically suffering from a lack of memory capacity but rather from a disorganisation of their timeline (Jenkins and Winkelman, 1966; Mo et al., 1978). However, as for sub-clinical memory and attention processes,

4

episodic memory is known to be impaired in schizophrenia, and this may not be related to a specific deficit in the timing mechanism (Elvevag et al., 2000). Elvevag et al. (2000) found that patients with schizophrenia were less accurate than controls at recognising a standard duration on a temporal generalisation task. The performance of patients was also significantly different from controls on a temporal bisection task, in which participants categorised durations as either short or long. They also found that a patient's working memory did not correlate significantly with their performance on the duration judgment tasks. They concluded that patients with schizophrenia were less accurate at estimating brief time periods and that this deficit may reflect the dysfunction of biopsychological timing processes. The dysfunction in episodic memory is mostly the result of a failure in strategic processing at the encoding stage, although an impairment of strategic processing at the retrieval stage cannot be ruled out. Some authors suggest that it is not the execution of the encoding strategies that is defective but rather their self-initiation (Danion et al., 2007). Consequently, it is difficult to delineate deficits of temporal perception from generalised impairments of attention or memory, especially in schizophrenia.

Lee et al. (2009) investigated time perception dysfunction and its neuropsychological correlates in patients with schizophrenia. In their study, thirty-eight patients and thirty-eight age- and sex-matched healthy volunteers were compared in an auditory temporal bisection paradigm using two interval ranges (a 400/800 ms condition and a 1000/2000 ms condition). In the temporal bisection, the subjects were required to categorise a probe duration as short or long based upon the similarity with two reference durations. All of the subjects also completed a battery of neuropsychological tests that measured their sustained attention, short- and long-term memory and executive function. In the 400/800 ms condition, the patients judged durations to be significantly shorter than did control subjects. They also found that patients exhibited decreased temporal sensitivity in both conditions. Furthermore, they found in both groups a negative association between temporal sensitivity and sustained attention for the 400/ 800 ms condition and between temporal sensitivity and long-term memory for the 1000/2000 ms condition. In patients, short-term memorv performance was negatively associated with duration judgment in both conditions, while executive dysfunction was correlated with a general performance deficit in the 400/800 ms condition. They conclude that time perception abnormalities in schizophrenia might be a part of neuropsychological dysfunction.

Others recent studies try to address this problem (i.e., is time misperception a single or a more generalised disorder?) with brief visual or auditory stimuli in the range of milliseconds (50–100 ms), which puts minimal demands upon non-temporal processes. Researchers have used discrimination tasks and shown that patients with schizophrenia were less accurate in their timing judgment than healthy controls (Carroll et al., 2009; Elvevag et al., 2003; Rammsayer and Lima, 1991). The role of attentional resources is more important when patients with schizophrenia must evaluate a specific duration by a reproduction method in two different conditions (one blank situation, with no task, and one with an attention-consuming task). These results confirm previous works and support a deficit in a specific timing process.

Bonnot used retrospective and prospective conditions as defined by Zakay with schizophrenic patients in a time reproduction task (Zakay, 1993; Zakay et al., 1994). The results showed less accuracy for time estimation in patients with schizophrenia compared to healthy participants and an overestimation in both conditions (Bonnot et al., 2000). These results suggest that a defect of the time processor may not be the only impairment that is involved in time misperception in schizophrenia. Attention and memory, which are impaired and involved in time estimation, are confounding factors in schizophrenia (Bonnot and Georgieff, 2000; Carroll et al., 2009) and time perception itself (Meck, 2005). Moreover, the biological mechanisms involved in schizophrenia and cognitive processes of time estimation are similar. Thus, the biological approach to time perception and research in humans and animals in this field suggest that timing mechanisms are affected by the functioning of dopamine (Harrington et al., 1998; Maricq and Church, 1983; Maricq et al., 1981; Rammsayer, 1990, 1993). Dopamine dysregulation is involved in schizophrenia pathogenesis, and recent research provides evidence for (i) a subcortical hyperstimulation of D2 receptors underlying positive symptoms and (ii) cortical hypodopaminergia-mediating cognitive disturbances and negative symptoms (for a review, see (Guillin et al., 2007; Howes and Kapur, 2009). Finally, antipsychotics are known to be associated with impairment in the estimation of time intervals, and several studies have shown that the discrimination of sound duration is affected by psychotic treatment (for a review, see (Meck, 1996).

The dimensional approach to schizophrenia suggests that three dimensions account for the inter-relationships among the symptoms of schizophrenia (positive, negative and disorganisation). The hypothesis of "cognitive dysmetria" is the cognitive or mental equivalent of motor dysmetria: a disruption in the fluid coordination of mental activity that is the hallmark of normal cognition. This model contributes to a neurodevelopmental approach to schizophrenia (Andreasen, 1999; Andreasen et al., 1999). The core idea is that cognitive defects are the key symptoms: they play an important role in the pathogenesis of the disorder and may be mediated by dysfunction in the cortico-cerebellar-thalamic-cortical circuit (CCTCC). Evidence from neuroimaging and neuroanatomy (Antonova et al., 2004; Picard et al., 2008) suggests that the CCTCC performs a similar function in monitoring and coordinating the fluid execution of mental activity (synchrony) and that a disruption in the activity of this circuit leads to cognitive dysmetria and, ultimately, to the disordered cognition and clinical symptoms of schizophrenia (Andreasen and Pierson, 2008). The role of the CCTCC is to facilitate the smooth planning and execution of both motor and cognitive activities. When these activities become dysmetric, the vast range of symptoms that characterise schizophrenia may occur.

5. Conclusion

Clinical evidence associated with psychopathological, biological and cognitive theories strongly suggests that patients with schizophrenia have a deficit in time perception. Discrimination and the reproduction of durations have been found to be constantly consistently impaired and disorganised. While psychopathological and phenomenological work strongly suggests that time perception disturbance may be the key or core symptom in schizophrenia, neuroscience studies have failed to do the same. The question of specificity of temporal perception impairments in schizophrenia remains contested.

This question goes beyond time perception mechanisms. Neuroscience studies suggest that time symptoms in patients with schizophrenia are only secondary to thought disorders and primary cognitive impairments. This debate refers to the etiologic/organic versus psychogenesis/psychological dichotomy and may be overtaken. Developmental psychology is one way to allow for an integrative approach that bypasses the nature or nurture controversy. Indeed, it is now well known that development involves the contribution of both genes and environment (for a complete overview, see (Karmiloff-Smith, 2009). This perspective, called neuroconstructivism or probabilistic epigenesis (Gottlieb, 2007) goes beyond simple causality; it postulates that there are constant interactions between the environment (physical, social or cultural), behaviour, neural and genetic activity. Moreover, these authors strongly insist on the fact that interactions take place between these domains and are time sensitive. Development is a systemic dialectic process. These models open new perspectives for research

and understanding. Therefore, time perception impairment may be related to attentional and memory processes, as underlined by neuroscience, but it also plays a role by itself in other domains.

In another field of medicine, patients with microdeletion 22q11 are considered to present a genetic visuo-spatial impairment. This impairment is probably present at an early age and leads, in some cases, to dyscalculia, logical thinking disorders and dyspraxia (Simon et al., 2005). Interestingly, microdeletion 22q11 is related to schizophrenia (Horowitz et al., 2005). It would be interesting to study patients with this genetic defect in a longitudinal manner and see if they show will impairment in time perception. Current cognitive research does not use a diachronic approach and has not studied the developmental aspects of time estimation or its interactions with non-cognitive domains. Schizophrenia is a neuro-developmental disorder and requires longitudinal studies with a dynamic approach.

There is still much work to be done to identify the exact sources of variability in temporal judgments in schizophrenia, and the study of the developmental course of time perception could be an interesting route. Regardless of the role of temporal deficits in the pathogenesis of schizophrenia (as a general cognitive disorder or a core role), clinical and phenomenological data encourage us to conduct further studies, especially in the field of developmental psychology.

References

- Andreasen, N.C., 1999. A unitary model of schizophrenia: Bleuler's "fragmented phrene" as schizencephaly. Arch. Gen. Psychiatry 56 (9), 781–787.
- Andreasen, N.C., Pierson, R., 2008. The role of the cerebellum in schizophrenia. Biol. Psychiatry 64 (2), 81–88.
- Andreasen, N.C., Nopoulos, P., O'Leary, D.S., Miller, D.D., Wassink, T., Flaum, M., 1999. Defining the phenotype of schizophrenia: cognitive dysmetria and its neural mechanisms. Biol. Psychiatry 46 (7), 908–920.
- Antonova, E., Sharma, T., Morris, R., Kumari, V., 2004. The relationship between brain structure and neurocognition in schizophrenia: a selective review. Schizophr. Res. 70 (2–3), 117–145.
- Allan, L.G., Gibbon, J., 1991. Human bisection at the geometric mean. Learn. Motiv 22, 39–58.
- Bergson, H., 1995, original ed., 1903 L'évolution créative. Presses Universitaire de France, Paris.
- Block, R.A., 1989. Experiencing and remembering time: Affordance, context, cognition. In: Levin, I., Zackay, D. (Eds.), Time and human cognition: A life span perspective. North-Holland Edition, Amsterdam, pp. 333–364.
- Bonnot, O., Georgieff, N., 2000. Processus cognitifs de la temporalité: Apport dans l'étude de la schizophrénie. Annales Médico-Psychologiques 158 (6), 475–482.
- Bonnot, O., Georgieff, N., Dalery, J., 2000. Etude clinique des troubles de la temporalité chez les schizophrènes. Revue française de Psychiatrie et de Psychologie Médicale (7), 76–80.
- Brown, S.W., 1995. Time, change, and motion: The effects of stimulus movement on temporal peception. Percept. Psychophys 57 (1), 105–116.
- Carlson, V.R., Feinberg, I., 1968. Individual variations in time judgment and the concept of an internal clock. J. Exp. Psychol. 77 (4), 631–640.
- Carroll, C.A., O'Donnell, B.F., Shekhar, A., Hetrick, W.P., 2009. Timing dysfunctions in schizophrenia span from millisecond to several-second durations. Brain Cognit. 70 (2), 181–190.
- Clausen, J., 1950. An evaluation of experimental methods of time judgment. J. Exp. Psychol. 40 (6), 756–761.
- Crow, T.J., Stevens, M., 1978. Age disorientation in chronic schizophrenia: the nature of the cognitive deficit. Br. J. Psychiatry 133, 137–142.
- Danion, J.M., Huron, C., Vidailhet, P., Berna, F., 2007. Functional mechanisms of episodic memory impairment in schizophrenia. Can. J. Psychiatry 52 (11), 693– 701.
- Densen, M.E., 1977. Time perception and schizophrenia. Percept. Mot. Skills 44 (2), 436–438.
- Diatkine, R., 1995. Intemporalité et coordonnées temporelles. Revue Française de Psychanalyse LIX (4), 993–997.
- Dilling, C.A., Rabin, A.I., 1967. Temporal experience in depressive states and schizophrenia. J. Consult. Psychol. 31 (6), 604–608.
- Ehrentheil, O.F., Jenney, P.B., 1960. Does time stand still for some psychotics? Arch. Gen. Psychiatry 3, 1–3.
- Elvevag, B., Egan, M.F., Goldberg, T.E., 2000. Memory for temporal order in patients with schizophrenia. Schizophr. Res. 46 (2–3), 187–193.
- Elvevag, B., McCormack, T., Gilbert, A., Brown, G.D., Weinberger, D.R., Goldberg, T.E., 2003. Duration judgements in patients with schizophrenia. Psychol. Med. 33 (7), 1249–1261.
- Fernandez Zoila, A., 1976. Le temps brisé des schizophrènes. L'Evolution Psychiatrique 41 (4), 975–991.

- Forbes, N.F., Carrick, L.A., McIntosh, A.M., Lawrie, S.M., 2009. Working memory in schizophrenia: a meta-analysis. Psychol. Med. 39 (6), 889–905.
- Fortin, C., Breton, R., 1995. Temporal interval production and processing in working memory. Percept. Psychophys 57 (2), 203–215.
- Fortin, C., Couture, E., 2002. Short-term memory and time estimation: beyond the 2second "critical" value. Can. J. Exp. Psychol. 56 (2), 120–127.
- Fraisse, P., 1984. Perception and estimation of time. Annu. Rev. Psychol. 35, 1–36. Franck, N., Posada, A., Pichon, S., Haggard, P., 2005. Altered subjective time of events in schizophrenia. J. Nerv. Ment. Dis. 193 (5), 350–353.
- Gibbon, J., Church, R.M., 1990. Representation of time. Cognition 37 (1-2), 23-54.
- Gibbon, J., Church, R.M., 1984. Sources of variance in an information processing theory of timing. In: Roitblat, H.L., Bever, T.G., Terrace, H.S. (Eds.), Animal Cognition, Lawrence Erlbaum Associates. Hillsdale, NJ, pp. 465–488.
- Goldstone, S., Lhamon, W.T., 1956. The time sense: estimation of one second durations by schizophrenic patients. AMA Arch. Neurol. Psychiatry 76 (6), 625–629.
- Gottlieb, G., 2007. Probabilistic epigenesis. Dev. Sci. 10 (1), 1-11.
- Grondin, S., 2010. Timing and time perception: a review of recent behavioral and neuroscience findings and theoretical directions. Atten. Percept. Psychophys 72 (3), 561–582.
- Grush, R., 2005. Internal models and the construction of time: generalizing from state estimation to trajectory estimation to address temporal features of perception, including temporal illusions. J. Neural Eng. 2 (3), S209–218.
- Guillin, O., Abi-Dargham, A., Laruelle, M., 2007. Neurobiology of dopamine in schizophrenia. Int. Rev. Neurobiol. 78, 1–39.
- Harrington, D.L., Haaland, K.Y., Knight, R.T., 1998. Cortical networks underlying mechanisms of time perception. J. Neurosci. 18 (3), 1085–1095.
- Horowitz, A., Shifman, S., Rivlin, N., Pisante, A., Darvasi, A., 2005. A survey of the 22q11 microdeletion in a large cohort of schizophrenia patients. Schizophr. Res. 73 (2–3), 263–267.
- Howes, O.D., Kapur, S., 2009. The dopamine hypothesis of schizophrenia: version III – the final common pathway. Schizophr. Bull. 35 (3), 549–562.
- Jenkins, S.B., Winkelman, A.C., 1966. Inverted perception of time sequence in mental disorders. Int. J. Neuropsychiatry 2 (2), 122–128.
- Johnson, J.E., Petzel, T.P., 1971. Temporal orientation and time estimation in chronic schizophrenics. J. Clin. Psychol. 27 (2), 194–196.
- Karmiloff-Smith, A., 2009. Nativism versus neuroconstructivism: rethinking the study of developmental disorders. Dev. Psychopathol. 45 (1), 56–63.
- Kimura, B., 2000. L'Entre Une approche phénoménologique de la schizophrénie. Editions Jérôme Millon, Paris.
- Kimura, B., 2003. Disturbance of timing and selfhood in schizophrenia. Seishin Shinkeigaku Zasshi 105 (6), 729–732.
- Lee, M.S.Y., Oliver P., Hutchinson, M.N., 2009. Phylogenetic uncertainty and molecular clock calibrations in legless lizards (Pygopodidae, Gekkota). Mol. Phylogenet. Evol. 50, 661–666.
- Le Guen, C., 1958. Le temps figé du schizophrène. Entretien Psychiatrique 22 (3), 701-735.
- Lhamon, W.T., Goldstone, S., 1973. Temporal information processing in schizophrenia. Arch. Gen. Psychiatry 28 (1), 44–51.
- Mariategui, J., Flores, J.R., 1966. The experience of suspended time in schizophrenia. Rev. Neuropsiquiatr. 29 (4), 301–319.
- Maricq, A.V., Church, R.M., 1983. The differential effects of haloperidol and methamphetamine on time estimation in the rat. Psychopharmacology (Berlin) 79 (1), 10–15.
- Maricq, A.V., Roberts, S., Church, R.M., 1981. Methamphetamine and time estimation. J. Exp. Psychol. Anim. Behav. Process. 7 (1), 18–30.
- Matell, M.S., Meck, W.H., 2000. Neuropsychological mechanisms of interval timing behavior. BioEssays. 22, 94–103.
- Meck, W.H., 1996. Neuropharmacology of timing and time perception. Brain Res. Cognit. Brain Res. 3 (3–4), 227–242.
- Meck, W.H., 2005. Neuropsychology of timing and time perception. Brain Cognit. 58 (1), 1–8.
- Millan, M.J., Brocco, M., 2008. Cognitive impairment in schizophrenia: a review of developmental and genetic models, and pro-cognitive profile of the optimised D(3) > D(2) antagonist, S33138. Therapie 63 (3), 187–229.
- Minkowski, E., 1995, original ed., 1933. Le temps vécu. Presses Universitaires de France, Paris.
- Mo, S.S., Kersey, R., Huang, D.D., 1978. Weakness and instability of time expectancy in schizophrenia. J. Clin. Psychol. 34 (1), 37–44.
- Orme, J.E., 1966. Time estimation and the nosology of schizophrenia. Br. J. Psychiatry 112 (482), 37–39.
- Ornstein, R.E., 1969. On the experience of time. Penguin Books, New York.
- Pearl, D., Berg, P.S., 1963. Time perception and conflict arousal in schizophrenia. J. Abnormal Soc. Psychol. 66, 332–338.
- Picard, H., Amado, I., Mouchet-Mages, S., Olie, J.P., Krebs, M.O., 2008. The role of the cerebellum in schizophrenia: an update of clinical, cognitive, and functional evidences. Schizophr. Bull. 34 (1), 155–172.
- Poynter, W.D., Homa, D., 1983. Duration judgement and the experience of change. Percept. Psychophys 33, 548–560.
- Prebedon, J., 1995. Prospective and retrospective time estimates as a function of clock duration. Percept. Mot. Skills 80 (3), 941–942.
- Rammsayer, T., 1990. Temporal discrimination in schizophrenic and affective disorders: evidence for a dopamine-dependent internal clock. Int. J. Neurosci. 53 (2–4), 111–120.
- Rammsayer, T.H., 1993. On dopaminergic modulation of temporal information processing. Biol. Psychol. 36 (3), 209–222.

ARTICLE IN PRESS

O. Bonnot et al./Journal of Physiology - Paris xxx (2011) xxx-xxx

Rammsayer, T.H., Lima, S.D., 1991. Duration discrimination of filled and empty auditory intervals: cognitive and perceptual factors. Percept. Psychophys. 50 (6), 565–574.

Ranganath, C., Minzenberg, M.J., Ragland, J.D., 2008. The cognitive neuroscience of memory function and dysfunction in schizophrenia. Biol. Psychiatry 64 (1), 18–25.

- Rizzo, L., Danion, J.M., van der Linden, M., Grange, D., 1996. Patients with schizophrenia remember that an event has occurred, but not when. Br. J. Psychiatry 168 (4), 427–431.
- Rubia, K., Smith, A., 2004. The neural correlates of cognitive time management: a review. Acta Neurobiol. Exp. (Wars) 64 (3), 329–340.
- Rund, B.R., 1998. A review of longitudinal studies of cognitive functions in schizophrenia patients. Schizophr. Bull. 24 (3), 425–435.
- Simon, T.J., Bearden, C.E., Mc-Ginn, D.M., Zackai, E., 2005. Visuospatial and numerical cognitive deficits in children with chromosome 22q11.2 deletion syndrome. Cortex 41 (2), 145–155.
- Stevens, M., Crow, T.J., Bowman, M.J., Coles, E.C., 1978. Age disorientation in schizophrenia: a constant prevalence of 25 per cent in a chronic mental hospital population? Br. J. Psychiatry 133, 130–136.
- Sutter, J., 1956. L'anticipation des schizophrènes. L'Evolution Psychiatrique (1), 56– 63.
- Tracy, J.I., Monaco, C., McMichael, H., Tyson, K., Chambliss, C., Christensen, H.L., Celenza, M.A., 1998. Information-processing characteristics of explicit time

estimation by patients with schizophrenia and normal controls. Percept. Mot. Skills 86 (2), 515–526.

- Tysk, L., 1983a. Estimation of time and the subclassification of schizophrenic disorders. Percept. Mot. Skills 57 (3 Pt 1), 911–918.
- Tysk, L., 1983b. Time estimation by healthy subjects and schizophrenic patients: a methodological study. Percept. Mot. Skills 56 (3), 983–988.
- Uhlhaas, P.J., Mishara, A.L., 2007. Perceptual anomalies in schizophrenia: integrating phenomenology and cognitive neuroscience. Schizophr. Bull. 33 (1), 142–156.
- van Os, J., Kapur, S., 2009. Schizophrenia. Lancet 374 (9690), 635–645.
 Wahl, O.F., Sieg, D., 1980. Time estimation among schizophrenics. Percept. Mot. Skills 50 (2), 535–541.
- Wang, Y., Cui, J., Chan, R.C., Deng, Y., Shi, H., Hong, X., Li, Z., Yu, X., Gong, Q.Y., Shum, D., 2009. Meta-analysis of prospective memory in schizophrenia: nature, extent, and correlates. Schizophr. Res. 114 (1–3), 64–70.
- Zakay, D., 1993. Time estimation methods do they influence prospective duration estimates? Perception 22 (1), 91–101.
- Zakay, D., Block, R.A., 2004. Prospective and retrospective duration judgments: an executive-control perspective. Acta. Neurobiol. Exp. (Wars) 64 (3), 319–328.
- Zakay, D., Tsal, Y., Moses, M., Shahar, I., 1994. The role of segmentation in prospective and retrospective time estimation processes. Mem. Cognit. 22 (3), 344–351.