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# Time, psychosis, and diagnostic frontiers

## Temps, psychose et frontières diagnostiques

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Chapter 1

# General introduction

## 1.1. Psychosis and the schizo-affective continuum

*"It is becoming increasingly obvious that we cannot satisfactorily distinguish these two diseases (dementia praecox and manic depression)."*

*Emil Kraepelin, 1920*

Psychosis is defined as a loss of contact with reality. Individuals suffering from psychosis usually present hallucinations, which are percepts in the absence of physical stimulation, and delusions, or false beliefs that are resistant to disconfirmation despite logical evidence of the contrary. Psychosis is not one psychopathological entity on its own, but rather a feature shared by several psychiatric conditions.

Schizophrenia (SZ) is an archetype of psychotic illness, affecting about 1% of the population (Roy et al., 2021). It is characterized by chronic psychotic symptoms, commonly termed "positive symptoms" as they are present "in addition" to normal functioning. These are accompanied by a general disorganization affecting the individual's speech and behavior, as well as by symptoms affecting mood and cognition, called "negative symptoms" referring to a lack of functions, such as avolition (lack of motivation), apathy (lack of interest), emotional flattening, social withdrawal, and anhedonia (decreased ability to feel pleasure).

Another example is bipolar disorder (BP), which belongs to the group of mood disorders, but whose acute mood episodes frequently present with psychotic symptoms. BP is a frequent illness with a prevalence of 1% (Merikangas et al., 2007). It is characterized by a periodic/cyclic alternation between two states, depression and mania (in type I BP), or hypomania, which is a milder form of mania (in type II BP). The two states (depression and mania) are usually separated by intermittent periods of "normal" mood and cognitive functioning. Diagnosis is based on the clinical observation of three facets of functioning: thoughts (content, structure, and speed), psychomotricity (energy level) and mood (affect) (Kraepelin, 1921). Lower activity in these three domains is indicative of a depressed state, while an elevated functioning is indicative of mania or hypomania. When the three aspects of functioning are not conjointly deviating toward one unique state, for example a depressed mood coupled with elevated thought production and hypermotricity (typical of mania), patients are in a so-called mixed state. The presence of mania or hypomania is the necessary criterium that distinguishes BP from Major Depression. When delusion and/or hallucinations occur in BP, the diagnosis becomes 'acute episode with psychosis'.

The distinction between SZ and BP was only introduced in 1899 by Kraepelin. He based this clinical separation of the two conditions on his careful observations of the course and outcome of patients' state. He opposed manic depression (today's BP), with its characteristic alternations of periods of pathological (manic or depressed) and normal functioning, to dementia praecox (today's SZ) which was characterized by a chronic and persistent degradation of cognitive functions and negative symptoms, and a poor clinical outcome. This Kraepelinian dichotomy is still present today in modern categorical classification systems that are commonly used in clinical psychiatry, such as the Diagnostic and Statistical Manual of Mental Diseases (DSM-5; American Psychiatric Association, 2013) and the International Statistical Classification of Diseases and Related Health Problems (11$^{th}$ ed.; ICD-11; World Health Organization, 2019). However, already Kraepelin noted the significant overlap in symptomatology between the two conditions, notably in the manifestation of negative symptoms. It was Eugene Bleuler who formalized the clinical picture of SZ as it is known today by completing the diagnostic criteria with the disorganization symptoms. But he also acknowledged that the severity of affective symptoms may be well described by a continuum. This suggests that these symptoms can be present not only in the established category of SZ, but also in other conditions and is in fact a transdiagnostic feature. This dimensional view is strongly present in current psychiatric research, in light of empirical findings on features shared by both conditions. The meaning of this overlap is still debated. One possibility is that instead of being two categorically separate disorders, SZ and BP would represent two extremes of a continuum. The schizo-affective continuum would thus span over diagnostic entities all sharing disturbances in not only mood and affect, but also thought, behavior, and cognition in varying portions. Schizo-affective disorder would represent an intermediate form of the two pathologies in the middle of the continuum. An alternative is that there are more than two categories of pathologies.

The aim of this work is not to resolve this question ("continuum vs. categorical"), but we hope to contribute to the debate by better defining patients' symptoms like the acceleration of thoughts, or the disorganization of thoughts. Those symptoms are related to the temporal structure of consciousness, and we aim at characterizing this structure using experimental psychology methods.

## 1.2. The importance of differential diagnosis

Beside similarities between the conditions that support the idea of a continuum (and will be reviewed shortly hereafter), specificities to both SZ and BP remain. One major practical aspect is medication and treatment management. On the one hand, antipsychotics have been the first-line medication of SZ since the discovery of chlorpromazine, because of their efficacy on treating positive symptoms. On the other hand, mood shifts between depression and mania typical of BP are commonly treated with mood stabilizers, such as lithium. The pharmaceutical treatment of BP can include or be replaced with anticonvulsants, such as valproic acid and lamotrigine, which have mood stabilizing properties. Antipsychotics can also be used in an acute or chronic way in case of psychotic symptoms.

As a rule of thumb, the best treatment is one with a balance between efficacy and tolerability. The main pharmaceutical treatments for SZ and BP have proven their efficacy. However, given inter-individual variability and the many factors that determine the efficacy of a given medication, some overlap may exist between SZ and BP treatments (*e.g.* benzodiazepine for the treatment of anxiety, antipsychotics in both cases).

Today, non-specific medication also concerns individuals who are at risk of developing psychosis, as the outcome of their condition is uncertain (whether it turns into SZ, BP, something else on the schizo-affective spectrum, or neither). When novel, specific preventive treatments are available in the future, it will be critical to identify as well as possible at-risk individuals' conditions and characterizing their symptoms will likely facilitate this. For these reasons, differential diagnosis between these two psychiatric conditions is a major issue, although often difficult due to shared symptomatology. Besides, characterizing and refining diagnostic frontiers by understanding symptoms will also contribute to a basic definition of the disorders. Inter-patient variability is high even inside groups of patients with the same or similar diagnosis. The urge for an improved definition of diagnostic frontiers between SZ and BP and a better understanding of the schizo-affective continuum have motivated the search for biomarkers and endophenotypes for psychotic disorders in the literature.

## 1.3. Similarities between SZ and BP

### 1.3.1. Search for markers of psychosis

A number of studies revealed similarities between SZ and BP in different domains of clinical research. These findings reinforce the idea of the schizo-affective continuum, but also show the complexity of this continuum.

Genetics studies revealed important overlaps between SZ and BP which support the idea that vulnerability factors are shared by the two conditions (Craddock et al., 2005; Lichtenstein et al., 2009; Purcell et al., 2009; Bellivier et al., 2013; Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013; Allardyce et al., 2018). Similarities were found in SZ and BP patients' (neuro)developmental trajectories (Arango et al., 2014; Bora, 2015) which are (at least partially) validated by imaging studies pointing to neuroanatomical alterations shared by the two conditions (Hulshoff Pol et al., 2012, for meta-analyses see Ellison-Wright & Bullmore, 2010 and Bora et al., 2012). Concerning cognitive functioning, deficits are present in both conditions and they are not specific enough to differentiate between the two (Bora et al., 2010). Eye movement research has proven to be a fruitful domain in the search for markers of psychosis, since it gives access to automatic, non-conscious mechanisms involved in cognition that are potentially more reliable than deficits in higher cognitive functions and are less biased by them. Thus, deficits in eye movements like smooth pursuit (Lencer et al., 2015; Trillenberg et al., 2017) and antisaccades (Reilly et al., 2014) were identified as potential markers of psychosis, but they do not always differentiate between the different types of psychoses.

The literature on biomarkers and endophenotypes of psychotic disorders is rich and out of the scope of the present thesis. We will thus focus our further review of the literature on aspects that are more closely related to our topic, namely the structural disturbances of thought and consciousness in SZ and BP.

### 1.3.2. Thought and consciousness

The loss of contact with reality that accompanies psychosis implies a problem in the way the psychotic individual's environment is detected, perceived and reconstructed mentally. We all have different perceptual experiences of the world, but the changes in patients' percepts and experiences appear to impair their ability to adapt to their environment. Inasmuch as the subjective experience of the world is strongly disturbed in psychotic disorders, one cannot ignore the contribution of phenomenological observations to the understanding of these conditions.

Interestingly, phenomenological accounts of SZ and BP both concern an altered sense of time and the temporal structure of conscious thought. In the following sections we will describe alterations in phenomenological aspects of consciousness and conscious thought whose distortions have been described in both disorders. Interestingly, these abnormal experiences concern different aspects of the sense of time in SZ and mood disorders (Vogel et al., 2020; see also Vogel et al., 2018, and 2019) and phenomenology may provide valuable insights into divergent mental and neural processes in SZ and BP.

### 1.3.3. The phenomenology of SZ: a disturbed sense of self and time

Already in early clinical descriptions, SZ has been characterized by an alteration of consciousness. Kraepelin (1913, cited in Parnas & Henriksen, 2014) considered that a "disunity of consciousness" represented a core feature of dementia praecox. Healthy individuals experience their conscious percepts from their own, unique first-person perspective, whereas this "unity" would be disrupted and lost in patients. Later, (Bleuler, 1911) included "ego disorders" and "loosening of associations" in the diagnostic criteria of SZ. Wolfgang Blankenburg, (1971) talked about a loss of the "natural evidence of the world", referring to SZ patients' incapacity to pre-reflexively experience and extract meaning from their environment. For Minkowski (1927), the core problem in SZ was the lack of "vital contact with reality", a problem of bonding to the environment and others, or an "incapacity to resonate with the world".

These anomalies of subjective experience in SZ described in the 20th century did not make it to the list of diagnostic criteria in current clinical classification systems with the gradual rejection of phenomenology from psychiatry in the second half of the last century (Andreasen, 2007). However, phenomenological psychiatry's insights into the patients' reality have regained an influence on today's clinical research. Phenomenologists especially focus on the definition of "self-disorders", or disorders of "ipseity" (from the Greek "ipse" meaning "self" or "itself") (Sass & Parnas, 2003). Self-disorders are considered a core symptom of SZ. They refer to an anomalous first-person perspective, characterized by an abolition of the "mineness of experience", that is the tacit, pre-reflective feeling of "I am here and now immersed in my environment, and I am the subject of my own experiences". For self-disorder patients, "experience is more observed than lived" (Parnas, Bovet & Zahavi, 2002) and the feeling of "presence" is replaced by a feeling of depersonalization or a sense of inner void. Alterations of self-demarcation (illustrated by out of body experiences), derealization (where the world feels strange or unreal), and alterations of the stream of consciousness and a fragmentation of the sense of time are also characteristic of self-disorders. Interestingly, alterations of the sense of time have been described early by Minkowski in *Le temps vécu* (1933)as a potential etiology of SZ:

> "Moreover, given the fact that the schizophrenic process attacks, as we have seen, to the vital dynamism itself, the perturbations in the phenomenon if lived time will be particularly profound. Here, time collapses in its entirety, contrary to what is observed in other disorders where a modification occurs in the domain of time itself"[1]

Other phenomenological psychiatrists have also noted a fragmentation of temporality in SZ (Binswanger, 1965; Blankenburg, 1971; Fuchs, 2007; Stanghellini et al., 2016; Wiggins et al., 1990). This observation is well illustrated by a patient's report (in Kimura 1994, cited in 2), describing a fragmented and discontinuous sense of time and self:

> "Time splits up and doesn't run forward anymore. There arise uncountable disparate now, now, now, all crazy 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."

Conscious experience is inherently dynamic, which means that time is a constitutional element of consciousness. A stability of the temporal structure of experience seems to be a necessary condition for the stability of the self and our feeling of immersion in the world. Our experiences and our sense of self are defined in relation to and by our interactions with our environment. This interaction with the external world is made possible via perception. Normally, we do not question our sense of self, since we are in a permanent, continuous contact with our environment and our interaction with it is efficient. Questions about the sense of self emerge in pathologies like schizophrenia, where the contact with the environment is affected and is not a "natural evidence" anymore. Thus, an alteration of the temporal structure of experience may explain an instability of one's sense of self (Martin et al., 2014; Giersch &

[1] Author's translation of "De plus, étant donné que le processus schizophrénique s'attaque, comme nous l'avons vu, au dynamisme vital lui-même, les perturbations du phénomène du temps vécu seront ici particulièrement profondes. Ici le temps s'effondre, s'il est permis de s'exprimer ainsi, en entier, contrairement à ce qui a lieu dans d'autres troubles mentaux où une modification se produit dans le domaine du temps lui-même."

Mishara, 2017) and represents a promising working hypothesis for pathophysiological research of SZ (Seeman, 1976; Vogeley & Kupke, 2007).

### 1.3.4. The phenomenology of time in BP

Abnormalities in temporality reported in BP have been proposed to be associated to a shift between the patient's "inner time" and the external "world time". Bleuler (1911) proposed that mania and depression are associated to an impaired "affective contact", or an inability to synchronize with the emotional atmosphere of the environment. Phenomenologists described these anomalies as a desynchronization with the external, social world: patients would be out of tune with their environment (Fuchs, 2013). It has been proposed that the biological implementation of this desynchronization between "inner" and "outer" time would be an abnormal neural variability balance between somatomotor and sensory networks (Northoff et al., 2018).

Even though patients with schizophrenia also seem to be disconnected from their environment, psychiatrists made a distinction between the different pathologies. (Minkowski, 1933) compared experiences of BP patients to that of SZ patients as follows:

> "It is evident that the manic, as well as the one with melancholic depression, when compared to the schizophrenic and even the schizoid, remain in contact with the ambient atmosphere, however it is equally evident that this contact is not increased, but, on the contrary, degraded, deformed compared to the true syntony."[2]

Minkowski characterized the acceleration of the sense of time which seemed to him to be restricted to mania. According to Minkowski, manic patients do not present an accelerated functioning which could be beneficial in their everyday life, but they are accelerated to the point where the temporal structure of consciousness collapses. Interestingly, manic patients do not lose their sense of reality as SZ patients do, but their contact with reality becomes superficial and time "shrinks", with the frontiers between past, present, and future disappearing. Manic patients' existence becomes thus instantaneous, as if they were continuously living in the present moment. Binswanger (1964, cited in Moskalewicz & Schwartz, 2020) similarly described a

[2] Author's translation of "Il est évident que le maniaque aussi bien que le déprimé mélancolique, si nous les comparons au schizophrène et même au schizoïde, restent en contact avec la vie ambiante, mais il est tout aussi évident que c'est un contact non pas accru, mais, au contraire, dégradé, déformé, par rapport à la syntonie vraie."

shrinkage of time in mania where time becomes "punctual". The patient finds himself/herself in a sort of momentary present where past and future disappear, as illustrated by the following first-person account by a patient on his/her experience of mania (quote in Moskalewicz & Schwartz, 2020):

> "It's like having this awareness, an almost physical sense of just having something that is not changing, that is just present. I mean it sounds maybe overly blunt to describe it as some sense of eternity, but that feels accurate. So there is no past, there is no future, you are just in the nowness, and that's so terrifying because I think it's so rare as most of us aren't in that most of the time".

The phenomenological examination of patients' mental lives and thought flows thus suggests that psychotic disorders are linked to aberrant temporal experiences, albeit qualitatively different in SZ and BP. SZ is associated to an aberrant sense of self and time continuity (*i.e.* fragmentation of time and self), while manic BP patients rather describe a shift between inner time and external time, and their conscious thoughts are focused on and constrained to a timeless present. Can these anomalous subjective experiences related to the structure of time be linked to objective deficits of timing and time processing revealed experimentally? Before reviewing impairments in timing and time perception which are potentially relatable to phenomenological accounts of time disturbances in psychosis patients, in the next section we first describe how psychology and cognitive science tackle the question of time in general and how the structure of time is studied from an empirical standpoint.

## 1.4. The psychology of time

We are living and evolving in a dynamic world where events take place and follow one another over the course of time. Consequently, we need to be able to follow events that unfold in our surroundings. Our perceptual systems have been adapted to process information coming from our external world and translate it into an internal, mental world with its spatial and temporal characteristics. Thus time, just like space, is represented in our mind. This representation of time allows us to estimate the duration of an elapsed time period, tell the order of two consecutive events, relive past events and plan future ones. This ability to process and organize information in time is essential for our survival and our daily functioning in the world. However, this ability to perceive time raises an issue: we do not have receptors that detect and transduce time, as we do have, for example, light-sensitive photoreceptors that detect and transduce photons allowing vision.

Our relationship with time is in fact threefold (van Wassenhove, 2009). Physical or objective time (or "clock time") is the time that we can measure with a stopwatch. Neuronal time is the time that is coded by neural activity in our brains and that neuroscientists measure and record using various tools. Finally, psychological or subjective time refers to our subjective experience and our mental representation of time. Although subjective in nature, psychological time can be assessed objectively with tools of experimental psychology and psychophysics.

### 1.4.1. Perception of time vs. time of perception

Our notion of time can be broken down to its two main constituents: duration and succession (Fraisse, 1967).

Duration concerns our ability to quantify how long a given event lasted, or how much time has elapsed between two events. The duration to be judged can be attended to prospectively (*e.g.* "for how long will the following stimulus appear on the screen?"), or retrospectively (*e.g.* "how much time has elapsed since you started reading this paragraph?"), depending on the instructions. Our judgment of a duration can be expressed either verbally (in temporal estimation tasks) or reproduced physically (in temporal reproduction tasks). A concept close to duration is passage of time. It refers to our subjective experience of the flow of time, our feeling of how fast or slow time goes by.

In the case of duration (and passage of time), time becomes the object of our consciousness. Our judgment of duration will correspond to the content of our consciousness: in time perception tasks the duration of a perceived stimulus (expressed in psychological time) is either accurate, but more often over- or underestimated compared to the actual physical duration of the stimulus (measured in physical clock time).

Succession is concerned with the structure of time and our ability to discriminate and localize events in time. Did two events take place simultaneously (*i.e.* at the same time) or successively? Time processing tasks evaluate our ability to detect succession (and will be reviewed hereafter), and our performance in these tasks depends on the temporal acuity of our sensory and perceptual systems. Thus, when judging the successiveness of two stimuli, we are essentially looking at the structure of our conscious perception.

Duration and succession can be boiled down to the concepts of *content* and *structure* of time respectively. While one is concerned with the perception *of* time, the other one relates to perception *in* time (or the time of perception). Duration and succession are not only functionally distinguishable, but the cognitive models describing them are also different. The internal clock model proposed by Treisman, 1963) has become an influential model for duration estimation and reproduction. It also formed the basis of other models for duration, such as the Scalar Timing Theory (Gibbon et al., 1984). More recently, rivalling, "non-clock models" were proposed for duration, such as the State Dependent Network Theory (Karmarkar & Buonomano, 2007; Buonomano & Maass, 2009).

These models do not account for how the brain distinguishes the positions of events in time. Stroud (1956) proposed the perceptual moments model which describes psychological time as structured into discrete units, or moments. This model influenced Pöppel (1997, 2009) for his temporal windows model for time perception (which we will develop in section 1.4.6.), in which the incoming continuous information flow is divided into small windows, or temporal system states implemented by neuronal oscillations.

### 1.4.2. Neural substrates of timing

These separate models for duration and succession are complemented by neuroscientific evidence suggesting that the processing of duration and succession rely on separate neuroanatomical structures and neurochemical pathways.

Neuroimaging studies identified several different brain regions which would underpin the perception of duration, however there is a big variability in the stimuli, paradigms and instructions used in the studies (*e.g.* estimation, motor reproduction, tapping synchronization to a rhythm, *etc*…). Thus, a distinction can be made for processing of durations in a direct manner (*i.e.* explicit instructions to evaluate a duration) vs. indirect manner (*i.e.* time is used implicitly in the task and no instructions refer to it, such as in the variable foreperiod task) (Coull & Nobre, 2008; Coull et al., 2013). Neural regions have been shown to be activated differently for these two types of duration perceptions (right fronto-striatal network involving basal ganglia, prefrontal and premotor areas for explicit timing tasks and left inferior parietal and left premotor cortices, cerebellum in implicit timing tasks). Similarly, a distinction can be made for tasks involving durations below the 1-sec range (*i.e.* sub-second timing tasks) which correlate with activations in subcortical regions (such as the basal ganglia and cerebellum), and supra-second tasks which involve more cortical areas (supplementary motor area -SMA-, prefrontal cortex) (Wiener et al., 2010).

A few meta-analyses compared neuroimaging studies on duration perception and pinpointed the bilateral SMA, the right inferior frontal gyrus, and the basal ganglia as regions that are active in all duration perception tasks independently of specific task parameters (Wiener et al., 2010; Nani et al., 2019; Teghil et al., 2019). These areas were proposed to be the neural substrates of the internal clock model (Coull & Nobre, 2008; Teghil et al., 2019).

As for succession processing, studies on patients with cerebral lesions noted a left-hemispheric lateralization of regions involved in temporal order processing (von Steinbüchel et al., 1999; Wittmann et al., 2004; Wencil et al., 2010). Several neuroimaging studies confirmed this observation and highlighted left-lateralized regions such as areas of the parietal, premotor, frontal cortices as neural correlates of temporal order processing in the visual (Davis et al., 2009), tactile (Takahashi et al., 2013; Miyazaki et al., 2016) and multisensory (audiovisual) modalities (Binder, 2015; Love et al., 2018). Intriguingly, this left lateralization of order processing was contradicted by a few studies that found correlates of order processing in the right hemisphere (albeit still highlighting a strong involvement of the parietal cortex) (Battelli et al., 2007; Snyder & Chatterjee, 2004; Woo et al., 2009). Thus, a consensus has not been reached yet concerning the neural substrates of succession and temporal order processing. These inconsistencies may be due to differences in experimental design and stimulus parameters which confound with the identification of the core region(s) or network underlying the processing of succession.

Duration and succession have been shown to be dissociated from a neurochemical standpoint. The role of the dopaminergic system in duration perception was evidenced in studies on Parkinson's disease patients (Pastor et al., 1992; Rammsayer & Classen, 1997). Patients' poor performance in duration estimation and reproduction tasks could be restored with L-DOPA administration. The implication of the dopaminergic system in duration perception was confirmed by studies on healthy volunteers by manipulating the bioavailability of dopamine precursors (Coull et al., 2012). Studies directly manipulating neurotransmitter systems as a way to investigate their involvement in the processing of succession are scarce. Only recently, Chassignolle et al. (2021b) compared the role of dopamine in duration and succession using such an approach. They reproduced an effect of dopamine depletion on participants' performance at temporal duration tasks (Coull et al., 2012), however no effect was found on succession processing (subjects had to determine the order of two consecutive stimuli), indicating different neurochemical substrates for duration perception and succession processing.

The present thesis addresses temporal disturbances in the structure of conscious thought in psychiatric conditions. As such, time as content (*i.e.* duration) is out of the scope of our review and from hereafter we will focus on time only from its structural point of view. We will first review what is known about how we judge simultaneity and order, and why this leads to several questions about the structure of consciousness, like *e.g.* the sense of time continuity. We will explain how this difficulty is addressed in the literature and how the temporal windows model can account for phenomenological and experimental data on time disturbances in SZ and BP. This leads us to question the processing of temporal order and the temporal structuring of conscious thought.

### 1.4.3. Psychophysics of succession

Tackling the question of succession, *i.e.* our ability to discriminate events in time can be equated to: what is the minimally sufficient and necessary time interval to distinguish two events from one another? Several psychophysics methodologies exist to answer this question.

- Gap detection

Two stimuli belonging to the same sensory modality (e.g. auditory, visual, or tactile) are repeatedly presented to the participant at the same location with different temporal intervals, or Inter Stimulus Intervals (ISIs) separating them. Over a considerable number of trials, the participant reports whether he/she detected the interval between the two stimuli, or he/she detected one single, continuous stimulus. The ISI corresponding to a given performance level at which the stimuli are distinguished reliably (*e.g.* 70% correct responses) is considered the fusion threshold which informs about the resolution of the participant's sensory system.

- Simultaneity judgment (SJ)

Two stimuli belonging to the same or different sensory modalities (in case of multisensory integration studies) are repeatedly presented to the participant with several SOAs (Stimulus Onset Asynchronies) separating them. This time, the stimuli are displayed in different locations, and what is important is the moment of the onset of the stimuli. In many studies, the stimuli (when visual) then stay on the screen until the response of the participants: there is no offset before the response. In each trial, the participant has to answer whether he/she sensed the two stimuli as occurring simultaneously (at the same time), or asynchronously (*i.e.* successively). Responses can vary between 100% "simultaneous" to 0% "simultaneous" (*i.e.* 100% asynchronous) and the simultaneity threshold can be defined as the SOA at which the participant's responses are 50% "asynchronous" and 50% "simultaneous".

- Temporal order judgment (TOJ)

In the TOJ like in the SJ task, two uni- or multimodal stimuli are repeatedly presented to the participant who this time has to judge which of the two stimuli occurred first (*e.g.* "left or right stimulus first?" for unimodal stimuli, "sound or light first?" in case of audio-visual stimulation). When the stimuli belong to the same modality, responses can be described by a sigmoid function ranging from 50% correct responses (*i.e.* chance level) to 100% correct responses. The temporal order threshold will correspond to the SOA for which the participant can reliably report the order of the stimuli with *e.g.* 75% accuracy.

When we consider unisensory tasks (*i.e.* the successive stimuli belong to the same modality), it has to be noted that there is a fundamental difference between gap detection and the other two tasks. In gap detection the stimuli activate the sensory system at the exact same location, *i.e.* the same sensory neurons (*e.g.* in case of visual stimuli the same photoreceptors are activated successively), while in SJ and TOJ tasks stimuli are presented at distinct locations and activate different sensory neurons of the same modality (*e.g.* different photoreceptors at different parts of the retina). This way, gap detection does inform about the temporal resolution of a given sensory system, but the judgments may be biased due to refractory effects specific to the system (especially for short intervals between stimuli). Hence, in our review we will focus on SJ and TOJ as tools for the study of succession.

### 1.4.4. The temporal limits of perception

The technical advances of the 19th and 20th century allowed the development of precise experimental setups for psychology and psychophysics, and researchers had the opportunity to study the limits of human perception.

In the auditory modality, the threshold for segregating two successive stimuli was described to be around 5-10 ms (Lackner & Teuber, 1973) and the threshold to identify the order of the two stimuli to be around 20-45 ms (Exner, 1873; Hirsh, 1959; Pastore & Farrington, 1996; Szymaszek et al., 2006; Simon et al., 2020). This might suggest that in audition there is a range of SOAs between 5-10 ms and 20 ms where two successive stimuli can be discerned in time, however they cannot be ordered (Love et al., 2013).

In vision, the threshold for simultaneity detection is around 20-50 ms (Elliott et al., 2007; Foucher et al., 2007). This value is very similar to the temporal order threshold found for visual stimuli (Exner, 1873; Hirsh & Sherrick, 1961). With highly trained participants, Hirsch (1959, Hirsch & Sherrick 1961) found that the temporal order threshold could be as low as 20 ms in both auditory, visual, and tactile stimuli (on index fingers).

It is important to note that although these simultaneity and temporal order threshold values seem to be similar or different depending on the sensory modality, stimulus parameters are not always comparable between studies. The parameters like fatigue (Simon et al., 2020), presentation duration, whether there is an offset or not, the possibility of apparent motion in visual tasks (Cass & Van der Burg, 2014, 2019), the pitch of auditory stimuli (Zwislocki, 1960; Fink et al., 2005; Fostick & Babkoff, 2013) and other factors likely influence the findings. For example, if the pitch changes between two successive sounds, the subjects may use this information to determine the order of the two sounds.

Despite these methodological considerations, it appears that ordering is a particular aspect of temporal processing. Although the auditory and somatosensory systems might have a higher temporal acuity than vision, the temporal order threshold's value has been found to be consistent across sensory modalities. The range of 20-60 ms SOA interval as a lower limit for temporal order processing has been confirmed by other studies across modalities, both in unisensory (Wittmann, 1999; Kanabus et al., 2002; Ulbrich et al., 2009; Wittmann, 2011; Capa et al., 2014) and multisensory temporal order judgment tasks (Hirsh & Fraisse, 1964).

### 1.4.5. Discrete perception and consciousness

What do these findings on succession and the limits of our sensory systems say about perception and the structure of consciousness?

They show that we do not access information from the world in a perfectly continuous manner. If this were true, detecting the successiveness of sensory stimuli should be possible for the smallest of asynchronies separating them. Instead, information about the successiveness or the order of stimuli in the environment becomes difficult to integrate when the temporal delay is short. This entails that our perception and the way sensory information is integrated in time are rather based on a discrete sampling mechanism, comparable to a movie which is composed of a series of snapshots that are successively projected onto a screen.

Several recent studies complement the previously described psychophysics experiments in supporting the notion of discrete perception.

A first argument for discrete perception can be found in eye movements. Saccadic eye movements are semi-automatic actions which allow us to fixate objects and scan our surroundings with high visual acuity. However, performing a saccade, *i.e.* shifting our gaze from one target to another, takes up a certain time (approx. 100ms) and during saccades perception is interrupted (Deubel, 2008; Krekelberg, 2010). This means that stable visual information can only be acquired at discrete moments in time.

Another argument for a discontinuous perception involves cyclic attention. Our ability to detect a target at a given location was shown to fluctuate over time (Fiebelkorn et al., 2013; VanRullen, 2016). A faint visual target stimulus appearing after a cue can be detected better if its moment of appearance coincides with the optimal phase of an oscillatory pattern with a frequency of around 4 Hz. This result was interpreted as evidence for a cyclic fluctuation of attention which influences the way information is integrated over time. Interestingly, this fluctuation in detection performance was linked to oscillations in neural activity following the same frequency band (beta band, 4-8 Hz) (Fiebelkorn et al., 2018; Helfrich et al., 2018; VanRullen, 2018).

### 1.4.6. The specious "now"

The notion of discrete perception, evidenced by several experimental findings, raises a paradoxical issue: if perception is discrete, how can we experience time and our consciousness as continuous? In normal conditions, we have a subjective feeling of a continuous flow of time, consciousness, and self. Answering this paradox is of paramount importance if we want to understand abnormal experiences related to a feeling of discontinuity of time and consciousness reported by psychosis patients. We will see that it is this questioning that ultimately leads to the questions addressed in our thesis.

In his work on time consciousness, Edmund Husserl (1928/1991) proposed a phenomenological explanation to the sense of time continuity while defining the notion of "now". From a phenomenological standpoint, "now" is not a point on the line that represents the arrow of time. Subjectively, "now" is not a snapshot of perceived elements, but rather it has a duration. Husserl (1991) thus developed the notion of the "specious now", inspired by William James (1890). This extended now encompasses and binds together elemental percepts into a conscious whole and is based on a retentional-protentional mechanism. Retention refers to the mechanism by which we are still aware of things "just passed" and protention refers to the mechanism underlying our expectation of the "yet to come" in the near future. Elements from the near past and near future meet in the spacious now, but all belong to the present moment of "now". Husserl illustrated his thesis with the example of a melody. When we listen to a piece of music, we hear and are aware of the note being played. However, we concurrently still have in mind the previous note that has just been played (retention). Moreover, we already expect and have in mind the note to be played next (protention). It is by this retentional-protentional mechanism by which a series of notes becomes a melody in the mind of the listener.

Close to Husserl's spacious present, Fraisse (1967) described his notion of the "présent perceptif" (or "perceptual present") as follows:

> "But there is also a perceived present which can only have the duration of the organization that we perceive in a unit. My present is a "tick-tock" of the clock, the three beats of the rhythm of the waltz, the sentence that I hear, the cry of the bird that passes by… All the rest is past or still belongs to the future. In this present, there is order, intervals between its constituting elements, but also a form of simultaneity which belongs to the very unity of my act of perception."[3]

### 1.4.7. A hierarchical model for perception in time

These phenomenological descriptions of the spacious now which binds together perceptual elements over an extended period of time, served as an inspiration for cognitive science to model time processing and temporal consciousness. Pöppel (1997) proposed the temporal windows model, a hierarchical model of perception involving information integration at different temporal scales. Information is integrated in temporal windows of different lengths at different levels of the hierarchy, and windows from a lower level are nested into windows at the level above.

In the model, "functional moments" are the elementary units of perception. They have a duration of a few tens of milliseconds and inside these temporal windows all detected stimuli are perceived as co-temporal. This means that two successive stimuli occurring inside the same functional moment will be perceived as synchronous, and successiveness can only be perceived if the stimuli belong into two different functional moments. A pragmatic definition for the limit of the functional moment can be the simultaneity threshold measured in SJ and TOJ tasks.

One level up the hierarchy, successive functional moments are integrated into the "subjective present", also called the "experienced moment" (Wittmann, 2011). With a duration

[3] Author's translation of "Mais il existe aussi un présent perçu qui, lui, ne peut avoir que la durée de l'organisation que nous percevons en une unité. Mon présent est un « tic-tac » de la pendule, les trois temps du rythme de la valse, la proposition que j'entends, le cri de l'oiseau qui passe… Tout le reste est déjà passé ou appartient encore au futur. Dans ce présent, il y a ordination, intervalles entre les éléments qui le constituent, mais aussi une forme de simultanéité qui tient à l'unité même de mon acte de perception."

of a few seconds (around 0.5-3 s) this window of integration structures our perception and actions at a subjective level: its length corresponds to the duration that we consciously experience as belonging to the present moment. This corresponds to the necessary time to perform a motor action, to utter a sentence, or to carry out a conscious thought. The definition of the limits of the subjective present are based on empirical data: performance in duration reproduction tasks decreases above the threshold of 0.5-3 s, and it is also the average duration of stable percepts in bistable perception (Pöppel 1997) (more on the utility of alternation rates in bistable perception paradigms will be provided in Chapters 2-4). This subjective present would equate with the "specious now", as it is closely linked to our subjective experience of being in the present moment.

Finally, "mental presence" integrates the 2-3 s perceptual units of "experienced moments" into a long-term experience (3 s and above) involving the feeling of self as an acting and perceiving agent. This level of information integration is proposed to be based on memory.

The hierarchical model of temporal windows gives a framework for how information is integrated *in* time, and thus a basis for the study of the structure of time and consciousness. This is also the theoretical framework in which we formulate the hypotheses of the present thesis with regard to the anomalous temporal experiences of different psychosis patient groups and the temporal structure of their conscious experience. More specifically, the elementary time disturbances supported by a sense of fragmentation of time and self described in SZ may be related to disturbances at the level of the functional moment. Conversely, reports of an extended, timeless present moment and accelerated mental activity in BP fit well rather with alterations at the level of the subjective present. In the next section we review alterations in the structure of time from an empirical standpoint in those two pathologies, and we will see how these findings can rejoin phenomenological accounts of time disturbances in the framework of the temporal windows model. We will show how remaining questions led to our own work.

## 1.5. Empirical accounts of time processing disturbances in psychosis

Here we review psychophysics studies on succession (*i.e.* structure of time) in psychotic populations.

### 1.5.1. Time processing disturbances in SZ

SJ tasks conducted with SZ patients showed a bigger tolerance for audio visual asynchronies: SZ patients present a longer window of integration (*i.e.* temporal window for which two multimodal stimuli are perceived as simultaneous) for simple audiovisual stimuli such as a flash and a beep (Foucher et al., 2007; Stevenson et al., 2017) and more ecological stimuli involving speech, such as in the McGurk illusion (Martin et al., 2013). A recent study by Di Cosmo et al. (2021) found impaired simultaneity thresholds in unisensory SJ tasks in the tactile and the auditory domains, as well as in multisensory audio-tactile SJ tasks in both SZ patients and schizotypal individuals. Interestingly, increasing levels of schizotypy, as measured via a schizotypal personality questionnaire, showed a linear relation with increasing simultaneity thresholds, suggesting that impairments in temporal processing are linked to the schizotypal phenotype. An impaired temporal sensory acuity was also found in visual unimodal tasks, with similarly extended simultaneity thresholds: SZ patients needed a longer SOA to reliably detect the asynchrony between two successive visual stimuli (Giersch et al., 2009; Schmidt et al., 2011; Lalanne, van Assche, et al., 2012; Zhou et al., 2018). Interestingly, (Lalanne, van Assche, et al., 2012; Lalanne, Van Assche, et al., 2012) found additional anomalies in the detection of successiveness for subthreshold asynchronies. In trials with SOA=17 ms, participants' performance (both healthy controls and SZ patients) was comparable to that in SOA=0 ms trials, meaning they perceived the two types of trials similarly. However, when looking at the side of the response (left or right button press) relative to the sequence of presentation of the stimuli (left-right vs. right-left) healthy control participants presented a motor bias toward the second stimulus. This result has since been reproduced (Poncelet & Giersch, 2015). This was interpreted as a manifestation of automatic, non-conscious temporal processing mechanism. A Simon effect was also found in SZ patients, however this group presented a bias toward the first stimulus. This set of results was interpreted as evidence for impairments in not only the conscious detection of the most basic form of temporal processing (*i.e.* simultaneity detection), but also disturbance in non-conscious mechanisms of temporal processing and information integration in time (Lalanne, van Assche, et al, 2012a,b; Giersch & Mishara, 2017).

Logically, detecting the asynchrony between two successive stimuli is a necessary condition for the detection of their order. Hence, no order should be detected without the detection of an asynchrony. How do the previously reviewed impairments in SJ relate to SZ patients' performance in order detection? Only few studies investigated temporal order processing in SZ. Although data on TOJ tasks in patients is sparse, they all point toward an impairment in the processing of temporal order, with a higher temporal order threshold in patients compared to healthy controls in unisensory visual or auditory stimulation (Tenckhoff et al., 2002; de Boer-Schellekens et al., 2014; Capa et al., 2014; Stevenson et al., 2017; see Thoenes & Oberfeld, 2017; Zhou et al., 2018 for reviews). Interestingly, temporal order seems to involve difficulties which extend beyond those predicted by impairments in SJ (Capa et al., 2014; Stevenson et al., 2017). The question of whether the underlying mechanisms of SJ and TOJ are shared or different in healthy volunteers is a vividly ongoing discussion in the literature (van Wassenhove, 2009; Arstila et al., 2020). However, studies comparing measures from both tasks found no correlation between the two, suggesting separate underlying mechanisms (Recio et al., 2019). Whether order processing deficits observed in SZ are specific to this disorder and manifest a basic temporal integration deficit which can be a psychopathological cause of clinical symptoms is still an open question. Moreover, it is unknown whether disturbances in automatic, non-conscious processing mechanisms (as evidenced by implicit measures at SJ tasks) have a link with deficits at simultaneity and order judgment tasks for SOAs corresponding to the conscious processing. The level of processing at which these order deficits are rooted in SZ (*i.e.* conscious level or more automatic processing level) is all the more intriguing that the origin of order processing is still unknown today in healthy individuals. In other words, does order processing emerge already at an automatic non-conscious level, or is ordering specific to consciousness?

Note that most studies checked a potential effect of medication that may explain the observed temporal processing disturbances; however, the impairments in SZ patients seem to be independent of medication.

### 1.5.2. Time processing disturbances in BP

To our knowledge, no data has been published on the processing of succession (SJ, TOJ) in BP. Most studies on timing or time perception in BP individuals looked at duration estimation, duration reproduction or the experience of passage of time. In these studies on the content of time, an underestimation of clock time was found in reproduction tasks, and an overestimation in duration judgment tasks (Tysk, 1984). Concerning the passage of time, the common findings involve a subjective slowing of time in depressive states and a subjective speed up in mania (Bschor et al., 2004; Northoff et al., 2018).

However, these studies on the perception *of* time do not inform about perception *in* time or the structure of the conscious experience in BP. A phenomenon close to an altered temporal structure of the consciousness is racing thoughts described in BP (Piguet et al., 2010). Racing thoughts correspond to the feeling of an increased production and subjective acceleration of thoughts. Described as a primarily manic symptom, it can also be found in mixed states where symptoms of mania and depression are intertwined (Weiner et al., 2019a). Interestingly, this symptom is based on patients' subjective reports and objective experimental measures of racing thoughts, independent of patients' subjective descriptions, do not exist (although see Weiner et al., 2019b). Yet, racing thoughts represent an incapacitating aspect of BP patients' mental activity and a better understanding of its underlying mechanisms has clinical relevance (see Chapter 3).

Other observations that may be relevant to the structure of perception and action in time can be found in studies employing implicit timing measures. A study by Bolbecker et al. (2011) investigated sub-second (500 ms interval) anomalies in euthymic and manic BP patients in a finger tapping task. Participants had to synchronize their movements (*i.e.* tapping with a finger on a surface) to the sound of a metronome, then maintain the tapping rhythm without the metronome. This task involves an automatic, fine tuning of movements and sensory information processing in time. BP patients presented a heightened variability in their tapping performance compared to healthy controls. This finding is in line with other time perception tasks showing heightened timing variability (Bolbecker et al., 2014). Although the study by Bolbecker et al. (2011) did not investigate succession or the structure of perception in time directly, it indicates impaired (motor) timing abilities and the structuring of action in time in BP. Whether these impairments generalize to the structure of perception and conscious thought, and whether they are related to the altered sense of being in an extended "now" reported in BP is yet unknown.

### 1.5.3. Deficits in different temporal windows in SZ and BP?

The findings of our review can be summarized in the context of the temporal windows model by Pöppel (1997). More specifically, temporal disturbances based on phenomenological and empirical observations in SZ and BP point to alternations at distinct levels of information integration in the two conditions.

On the one hand, patient reports involving a fragmentation of time and the sense of self were interpreted as manifesting an elementary disturbance in the way information is integrated in time in SZ (Minkowski, 1933; Fuchs, 2007; Stanghellini et al., 2016). These phenomenological considerations coincide with empirical findings on impaired time processing in SZ, with alterations at the level of automatic, non-conscious, as well as conscious processing (Giersch & Mishara, 2017). Based on these findings, we hypothesize that altered experiences related to time may be explained by disturbances at the most elementary level of information integration in time affecting the "functional moment", *i.e.* at the millisecond level. Additionally, specific disturbances concern temporal order processing in SZ. Are alterations at the millisecond-level related to deficits in ordering conscious thoughts and percepts, or do order deficits emerge only at the level of conscious perception? This question is all the more intriguing that it is unknown even in healthy individuals whether order processing is rooted at the millisecond-level or if it is a purely conscious process. Whether or not order processing exists at a millisecond-level will change how we understand the conscious ability to order information, and why it is disturbed in patients. Clarifying this potential link between disturbances at automatic, non-conscious processing level and order deficits at a conscious level could help unravel the pathophysiological origin of altered sense of time continuity in SZ.

On the other hand, disturbed temporal experiences described in BP seem qualitatively different from those in SZ. To our knowledge, there is no evidence in the literature supporting the idea that the basic structure of time and self would be altered in BP. Subjective reports by BP patients are not pointing towards low level alterations like in SZ with *e.g.* time fragmentation. In addition, empirical data concerning the temporal structure (*i.e.* succession at the second or millisecond level) are lacking in the literature. However, disturbances have been reported at the level of conscious thought. The disturbed feeling of "being in an extended present moment" and symptoms such as racing thoughts, point toward impaired information integration at a larger temporal scale in the model, *i.e.* at the level of the "subjective present" (or "experienced moment") (0.5-3 s). Deficits described in implicit and explicit timing and temporal perception tasks concern the same temporal scale as subjective reports (*i.e.* the second and sub-second level). However, a link between altered subjective experiences related to time in BP and objective, empirical measures of timing have not yet been tested directly.

## 1.6. Objectives

The aim of the present thesis is to better understand the temporal structure of consciousness and to improve the characterization of temporal disturbances described in SZ and BP. We seek to attain this goal by using objective measures of time processing and comparing patient groups with healthy control groups, but also comparing SZ and BP groups with each other.

Our first objective concerns finding a potential objective neuropsychological equivalent of racing thoughts, a symptom often associated to BP, and which has mainly been evaluated subjectively until now. Evaluating racing thoughts in both BP and SZ and comparing our objective measure between the two groups will inform us about the extent to which alterations at the level of the "subjective present" (sub-second and second scale) are shared by the two conditions.

In Chapter 2, we describe a new method to study temporal processing related to the "subjective present" based on eye movements in a bistable perception paradigm. The alternation rate of percepts during bistable perception has been associated to the "subjective present", and the measure of eye movements offers an appealing additional objective measure which has clinical relevance. In Chapter 3, we apply our measure based on eye movements to a mixed group of BP patients and healthy controls reporting different levels of racing thoughts. With our novel measure we seek to find an objective correlate of racing thoughts. This is verified in Chapter 4, where we compare a BP population to a group of SZ patients and a group of healthy controls. Both psychiatric groups are evaluated on their reported level of racing thoughts. The comparison of our objective measure of temporal processing relating to the "subjective present" will give insight into whether the mechanism underlying racing thoughts is shared or different between the two psychosis populations.

A second objective of the thesis is to verify to what extent disturbances in temporal order processing are specific to SZ. No experimental data has been reported on the processing of succession in BP. Moreover, SZ patients seem to have a particular difficulty to order information in time. In Chapter 5 we compare SZ patients with BP patients and healthy controls in a TOJ task. This study will inform whether alterations in temporal ordering are specific to SZ or shared by other psychotic conditions.

Our final objective is also related to temporal order. SZ patients present alterations in the detection of succession as measured directly with SJ and TOJ tasks. However, they also present altered information processing at an automatic level, as measured via an indirect measure, the Simon effect in SJ tasks (Lalanne et al., 2012a,b; Giersch et al., 2015). Whether temporal order processing deficits, which seem to be selectively altered in SZ (Capa et al., 2014), are rooted in deficient processing mechanisms at the level of conscious perception or the level of non-conscious, automatic processing is yet unknown. This is all the more a mystery that the processing level at which temporal order processing emerges is still unknown in healthy individuals. The objective of Chapter 6 is to check in a group of healthy volunteers whether temporal order processing is possible at a non-conscious, automatic processing level. We designed an original study in order to answer this question. The results of the study are relevant to the orientation of future research, as they will give a hint on the level at which temporal order processing deficits in SZ may be rooted and should be investigated.

Chapter 2

# Novel method to measure temporal windows based on eye movements during viewing of the Necker cube

The following chapter contains the original manuscript that appeared as: Polgári, P., Causin, J.-B., Weiner, L., Bertschy, G., & Giersch, A. (2020). Novel method to measure temporal windows based on eye movements during viewing of the Necker cube. *PLOS ONE*, *15*(1), e0227506. https://doi.org/10.1371/journal.pone.0227506

## Abstract

Bistable stimuli can give rise to two different interpretations between which our perception will alternate. Recent results showed a strong coupling between eye movements and reports of perceptual alternations with motion stimuli, which provides useful tools to objectively assess perceptual alternations. However, motion might entrain eye movements, and here we check with a static picture, the Necker cube, whether eye movements and perceptual reports (manual responses) reveal similar or different alternation rates, and similar or different sensitivity to attention manipulations. Using a cluster analysis, ocular temporal windows were defined based on the dynamics of ocular fixations during viewing of the Necker cube and compared to temporal windows extracted from manual responses. Ocular temporal windows were measured also with a control condition, where the physical stimulus presented to viewers alternated between two non-ambiguous versions of the Necker cube. Attention was manipulated by asking subjects to either report spontaneous alternations, focus on one percept, or switch as fast as possible between percepts. The validity of the ocular temporal windows was confirmed by the correspondence between ocular fixations when the physical stimulus changed and when the bistable Necker cube was presented. Ocular movements defined smaller time windows than time windows extracted from manual responses. The number of manual and ocular windows both increased between the spontaneous condition and the switch condition. However, only manual, and not ocular windows, increased in duration in the focus condition. Manual responses involve decisional mechanisms, and they may be decoupled from automatic oscillations between the two percepts, as suggested by the fact that both the number and duration of ocular windows remained stable between the spontaneous and focus conditions. In all, the recording of eye movements provides an objective measure of time windows, and reveals faster perceptual alternations with the Necker cube and less sensitivity to attention manipulations than manual responses.

## Introduction

Our perception of the outer world is usually stable: objects and persons do not change abruptly from one moment to another. Yet, when we look at a bistable figure, such as the Necker cube (Fig 1), our perception changes after a while and we perceive the figure differently despite the unchanged sensory input. The Necker cube can be perceived in two different ways and the two interpretations of the picture alternate, each one dominating our consciousness for a few seconds before giving way to the other percept [1]. Perceptual bistability has become a widely used experimental tool to study the mechanisms associated to consciousness, and especially the dynamics of mental and neural activity linked to conscious perception [2,3]. One limit is that alternations rely on the subjects' explicit reports, which include decision criteria and self-monitoring, and can bias results [4–6]. This becomes critical when exploring alternations in clinical populations [7], especially as in those populations, experimenters often privilege short-duration evaluations, due to the fatigability of the patients [8,9]. It has recently been suggested that it may be possible to measure alternations by means of eye movements and fMRI, which were found to be strongly coupled to explicit reports [10,11]. However, these studies relied on moving plaids or gratings and the recording of optokinetic nystagmus. Hence, it can be questioned whether ocular movements are entrained by the motion specifically. As a matter of fact, the tight coupling between perception and eye movements has been recently questioned [12], and dissociations between eye movements and conscious reports have been described even with moving stimuli [13]. Interestingly, dissociations have been reported mainly when the task requires continuous evaluation of the stimuli rather than alternative force-choice tasks [12]. Here we use the bistable and static Necker cube to study the temporal characteristics of alternations over a short, continuous period. We check to which extent changes in ocular fixations define temporal windows that are similar, or not, to the subjective alternations reported by the subjects.

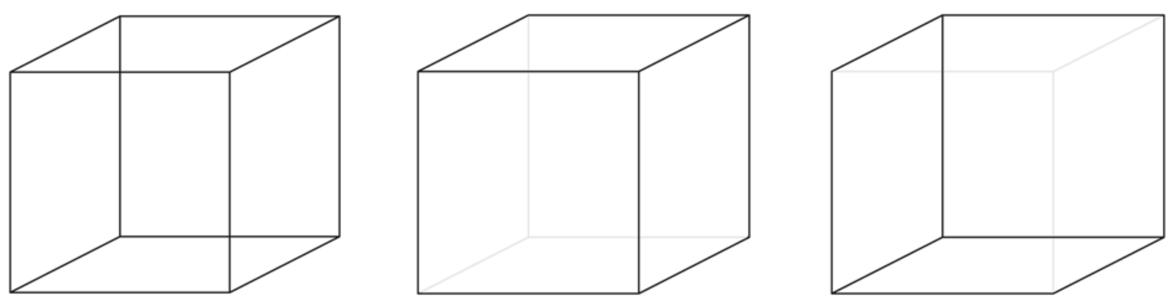

**Figure 1.** The Necker cube, an example of ambiguous figure (left), and its two non-ambiguous versions (middle, right).

### Why measure time windows?

The definition of time windows is a critical issue to understand how conscious perception is structured in time. Despite the fact that time seems to flow continuously, we have a sense of present moment, corresponding to our subjective experience of being here and now. It has been proposed that the present moment, or 'subjective present', corresponds to the time required to accomplish a mental act in perception, cognition or action [14–16]. The 'subjective present' has no fixed period, but its duration would be between a few hundreds of milliseconds and a few seconds. The Necker cube has been proposed as an operationalization of the concept of the 'subjective present', each percept corresponding to a moment. As a matter of fact, the mean duration of each percept range between 2.0 and 3.2 seconds [17,18]. It has been used in the context of bipolar disorder to evaluate the possibility that there is either a slowing down or an acceleration of thought, depending on the state of the patients [8,9,19]. The dynamics of perceptual alternations during viewing of the Necker cube have also a neurobiological counterpart, since they have been found to be correlated with endogenous brain dynamics [3]. However, whether or not perceptual alternations actually reflect a rhythmicity of our perception has been questioned [20]. Moreover there is more to the temporal structure of consciousness than only the sense of subjective present. Pöppel has proposed that temporal windows of different lengths are embedded in one another, leading to a hierarchical organization of mechanisms characterized by different rhythmicities [14]. When we perceive and interact with our environment, essentially we integrate information at different time scales into a coherent whole, and measuring time windows solely with subjective reports might be misleading. It may thus be useful to collect additional responses to subjective reports.

### Why track eye movements?

Experiments studying spontaneous perceptual reversals of bistable figures are often conducted with the figure remaining on the screen for a certain period of time (for the sake of simplicity from now on we will take the example of the Necker cube) (but see *e.g.* [1] for a two-alternative forced choice procedure). The participant is instructed to look continuously at the figure and to press a response button each time his/her perception of the Necker cube changes. Hence these measures reflect the viewer's subjective perception, as approximated by his/her explicit manual responses. We call this response explicit, because subjects are explicitly instructed to give a manual response each time they detect a perceptual change. This means that after a perceptual reversal has taken place, the viewer has to make a conscious decision of pressing a button. This subjective response, like any manual response to a subjective phenomenon, includes a response bias that is entirely dependent on the viewer. A growing body of research has shown that the rate of perceptual reversals and reversal times of ambiguous figures are associated to important interindividual differences in healthy individuals [21–24]. This variability might index either the individual temporal characteristics of the perceptual alternation itself, or the individual biases related to the need to give an explicit, subjective response. Here we develop an additional, more implicit measure by means of ocular movements. We call this measure implicit because the instructions do not require the subjects to make any specific eye movements during the task. The subjects are only asked to give their manual responses as reliably as possible while looking passively at the figure. In the present work, the main aim is to have an additional measure of time windows to test whether all measures lead to the same result or not.

### Eye tracking and perceptual bistability in the literature

Some studies combining eye tracking measurements and perceptual bistability have been conducted with static stimuli, but these focused on short periods around the moment of perceptual reversals in order to determine whether ocular movements cause perceptual reversals or vice versa [25–27]. It has been shown that during perceptual reversals the position of fixations are different for the two percepts [26] and fixation coordinates have extreme values at the moment of the reversals [28]. A few other studies have also queried whether it is possible to entrain perceptual reversals via controlled ocular oscillations [29]. To the best of our knowledge, however, research has been mainly conducted on the periods around the perceptual alternations, and it has not been checked whether for static stimuli ocular movements can be used to measure a spontaneous oscillation akin to the manual windows. Hancock et al. (2012) [30] used binocular rivalry, which also leads to perceptual alternations, this time between the information conveyed by one or both eyes. Hancock et al. (2012) found a positive correlation between the rate of perceptual reversals and the rate of saccadic eye movements, pointing toward shared underlying mechanisms. The absolute rate of the two measures differed, however, since saccadic eye movements occurred more frequently than perceptual reversals. It is possible that successive saccades relate to the same subjective perception, but this possibility cannot be checked in the results of Hancock et al. (2012). By using a relatively large picture of the Necker cube and a clustering method to classify saccades, we aimed to measure the frequency of ocular-related time windows relative to the frequency of manual-related time windows. Our approach is directly inspired by the temporal windows model [14]. We noticed an oscillatory pattern in the positions of eye movements between the left and right part of the figure (Fig 2), and we defined temporal windows based on the dynamics of ocular fixations during viewing of the Necker cube. These calculations define 'ocular temporal windows' which are compared to temporal windows based on manual responses. First we checked the validity of the ocular temporal windows in a control condition, during which the physical stimulus presented to the viewer oscillated between two non-ambiguous versions of the Necker cube (Fig 1). In addition, we checked whether ocular and manual time windows have the same duration and vary in the same way in different experimental conditions. After a first condition where subjects were asked to report spontaneous reversals (spontaneous condition), two conditions were used to test the impact of attentional control. In one condition subjects were asked to focus on the same preferred percept as long as possible (focus condition), whereas in the other they were asked to switch as fast as possible between the two percepts (switch condition). It has already been shown in the literature that these instructions yield significant changes in manual windows [25,31,32]. If ocular and manual measures index the same phenomena, then they should be similarly sensitive to attention manipulations, whereas if they reveal different types of windows, they should be affected differently by attention manipulations.

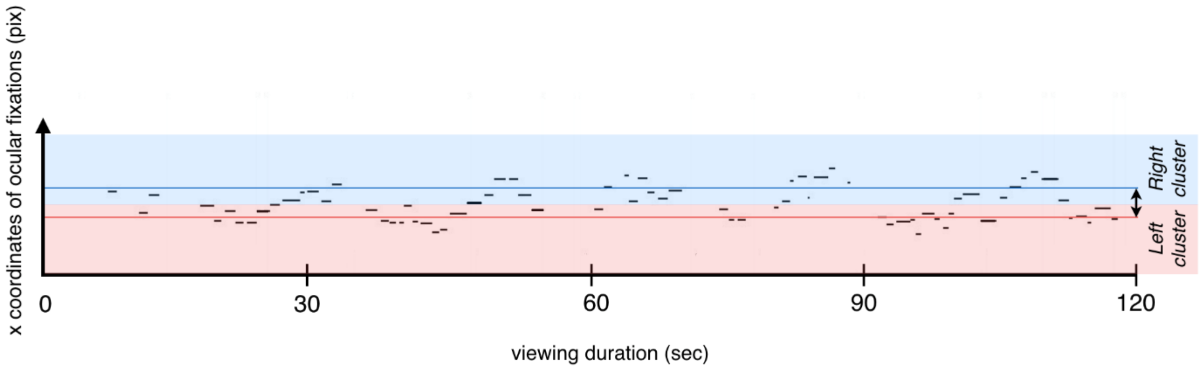


**Figure 2.** Illustration of the oscillatory pattern of ocular fixations during viewing of the Necker cube.
The graph represents the x coordinates of ocular fixations as a function of time for one individual participant during the spontaneous condition. The horizontal strips correspond to ocular fixations. The length of each strip is proportional to the corresponding fixation's duration. The closer the value of an x coordinate is to zero, the closer the fixation is to the left side of the screen. The blue shaded part (above) corresponds to the right cluster, whereas the red one corresponds to the left cluster. The blue and red lines correspond respectively to the median of the x coordinates of the right and left clusters. The difference between these medians represents the distance between the clusters (the black arrow on the right part of the graph).

## Materials and methods

### Participants

Twelve subjects (mean age ± SD : 30.8±7.6; 9 females and 3 males) with normal or corrected-to-normal vision participated in the experiment. The project was approved by the local ethics committee (People Protection Committee "Est-IV"). All subjects gave their informed written consent in accordance with the declaration of Helsinki.

Exclusion criteria included a history of substance abuse, and a history of neurological or psychiatric disorders.

One subject had to be excluded from the analysis of the ocular clusters' spatial coordinates due to technical problems during data acquisition in the control condition. Data presented in the corresponding section are thus averaged over 11 subjects. The rest of the results remained identical whether or not this subject's data were taken into account in the analyses.

### Equipment and stimuli

The experiment was conducted in a quiet room with reduced illumination. Stimuli were generated by a Hewlett-Packard Compaq 8100 Elite 2 computer using programs written on MATLAB software (2007) by MathWorks and PsychToolbox [33]. The visual stimuli were generated on a 21" Sony Triton CRT screen.

During each experimental trial the Necker cube was presented on the screen for 60 seconds. Each side had a length of 12° of visual angle, consisting of black lines (0.008 cd/m$^2$ and 0.18° thick) on a white background (41.5 cd/m$^2$).

### Eye tracking

Right eye movements were measured continuously throughout the experiment using an infrared video-based eye tracking system (EyeLink CL 1000, SR Research) with a sampling frequency of 1000 Hz, and a spatial resolution of 1024 x 768 pixels. Before each experimental condition, the eye tracker was calibrated by asking participants to repeatedly fixate a 9-point grid. Participants' heads were stabilized using a chin-rest at a distance of 70 cm from the computer screen in order to minimize head movements and errors of measurement.

We registered and analyzed the number of ocular fixations and the mean duration of each fixation. Fixations were defined by stable eye position coordinates for at least 90 ms, and they were excluded if their mean duration was longer than 1000 ms. This eye tracking data processing was carried out using programs written on MATLAB software and Statistica 13.0 software.

### Experimental task and procedure

The experiment consisted of four conditions: spontaneous, focus, switch, and control conditions. In the first, spontaneous condition participants were instructed to manually report the perceptual reversals of the cube that occurred spontaneously, by pressing one of two buttons on a keyboard, each corresponding to a perceived orientation of the cube (left response button for the downward left-facing orientation, right response button for the upward right-facing orientation).

In the focus condition participants were asked to focus on and mentally hold their preferred orientation of the cube and go back to this orientation as quickly as possible in case of reversal. In the *switch* condition participants were instructed to switch as quickly as possible between the two orientations. Just as in the spontaneous condition, participants had to report the perceptual reversals of the cube with button presses. The order of the focus and switch conditions was randomized between subjects, but the experiment was designed so that the spontaneous condition always came first, thus minimizing the effect of voluntary control on perceptual reversals in this condition.

A final control condition was designed to make sure that the subjects were able to detect and reliably report the perceptual reversals. To that aim two modified, non-ambiguous versions of the Necker cube (Fig 1) were presented alternately at the same location, each figure presented for a duration of 3 seconds. Participants were asked to press a response button each time they perceived an alternation and to choose the key corresponding to the current orientation. The response time recorded in this condition was used to estimate time between the perceptual reversals and the subject's reaction. The key press is necessarily delayed relative to the occurrence of the perceptual reversal, and the reaction time in the control condition was used in the other three conditions, in which there was no physical reversal, to evaluate the time of occurrence of the perceptual reversals.

### Behavioral and eye tracking data processing and analysis

For each subject the preferred and non-preferred percepts of the cube were identified based on the median duration of the reversal times, *i.e.* intervals of transiently stable percepts based on the subjects' manual responses. It has been shown elsewhere [7,27] that everyone has a preferred percept of the Necker cube, that is one orientation (bottom-left or top-right) is perceived for longer periods than the other, despite the continuous alternation of the two. We extracted the total number of perceptual reversals and the median duration of the reversal times (referred to hereafter as "manual windows"). Preferred and non-preferred percepts were respectively defined by the orientation corresponding to the longer and shorter manual windows.

In parallel we identified ocular fixations, and we quantified them for each subject. Fixations were analyzed using a cluster analysis. The graphic representation of the changes in x and y fixation coordinates over time indeed suggested an oscillation between two positions (Fig 2). Y coordinates appeared to be redundant with x coordinates, hence we focused on ocular displacements on the horizontal axis. It is to be noted that an analysis performed on y coordinates led to similar but less clear results, probably because the two perceptual interpretations of the Necker cube differ more in their horizontal orientation (see similar observations in [26]). Considering the two alternating mental representations of the Necker cube we decided to separate the fixations into two groups, so called "ocular clusters", based on their spatial coordinates. To this aim we used the Expectation-Maximization (EM) algorithm [34] which permits to find for any data the maximum likelihood of belonging to a previously specified number of clusters. Each fixation was classified into one of two clusters (left or right) and each cluster was composed of one or several successive fixations. "Ocular windows" were defined as temporal windows corresponding to the summed duration of ocular fixations inside each cluster. We extracted the total number and the median duration of ocular windows.

In order to confirm the validity of our cluster analysis, we compared ocular windows in the control and in the three main conditions. To this aim, we analyzed the spatial coordinates of fixation clusters in all four conditions (spontaneous, focus, switch, and control). In the control condition we separated the fixation clusters corresponding to the two non-ambiguous versions of the Necker cube. We calculated the median of the x coordinates of fixation clusters corresponding to each non-ambiguous version of the cube. In the other three conditions, we calculated the median x coordinates of the left and right fixation clusters, and the spatial distance between the left and right fixation clusters (median x coordinate for the right cluster − median x coordinate for the left cluster, see Fig 2). The aim was to check whether the x coordinates of the left and right clusters corresponded to the coordinates observed in the control condition.

### Statistical analysis

Data analyses consisted of repeated measures ANOVA and were performed using Statistica 13.0 software by Statsoft©. We added the partial eta-squared ($\eta^2$) as a measure of effect size. Tukey HSD post hoc analyses were used to localize the differences. Correlations were conducted by computing Pearson's correlation coefficients. The significance level throughout the analyses was set at $\alpha=0.05$.

We checked the effect of order between the *focus* and *switch* conditions in separate analyses, and found no significant effect. The results presented hereafter are thus averaged over the order between the *focus* and *switch* conditions.

## Results

### Spatial coordinates of ocular clusters

In the first analysis we distinguished the fixation clusters based on their left/right location on the screen with the aim to see if a correspondence in the x axis coordinates of ocular clusters could be found between the control condition and the other three main conditions. We conducted a repeated-measure ANOVA on the coordinates of the ocular clusters with the abscissa of the clusters (left or right) and condition (spontaneous, focus, switch and control) as within-group variables. Left and right clusters had statistically different x coordinates [$F(1, 10)=112.63$, $p<0.001$, partial $\eta^2=0.92$] (with x(left)=612 vs x(right)=684 in pixels). We found an interaction between cluster location and condition [$F(3, 30)=3.84$, $p<0.05$, partial $\eta^2=0.23$]. Decomposing the interaction using HSD Tukey's post hoc analysis showed that the coordinates of left and right clusters were separated by a significant distance in all four conditions. Coordinate values are detailed in Table 1.

To understand the origin of the interaction, we calculated the distance between the right and left clusters in each condition (median x coordinates for the right cluster −median x coordinates for the left cluster) (Table 1, also illustrated in Fig 2). This analysis revealed that the distance varied over the four conditions [$F(3, 30)=3.84$, $p<0.05$, partial $\eta^2=0.28$]. Tukey's post hoc analysis showed that the distance between the left and right clusters was larger in the switch condition (108) than in the spontaneous condition (50, $p<0.05$). No other significant difference was revealed between the conditions.

| Condition | Left coordinate | Right coordinate | p-value | Right − Left coordinates |
|---|---|---|---|---|
| Spontaneous | 610 | 660 | **<0.05** | 50 |
| Focus | 643 | 703 | **<0.005** | 60 |
| Switch | 599 | 707 | **<0.001** | 108 |
| Control | 596 | 665 | **<0.001** | 69 |

**Table 1.** Coordinates of left and right fixation clusters in the four experimental conditions. The first two columns in the table show the left and right x coordinates of the fixation clusters in pixels (x=0 pix corresponds to the left border of the screen), and the third column the p value corresponding to the comparison of the left and right coordinates for each condition. The column on the right shows values of the distances between left and right fixation clusters in the four conditions.

## Number of manual and ocular windows

In the following analyses fixation clusters were distinguished based on their correspondence to the preferred and non-preferred percepts of the Necker cube and were used to define ocular windows.

A one-way ANOVA conducted on the number of manual responses (*i.e.* button presses reflecting perceptual switches), with experimental condition as a within-group variable, revealed an effect of the condition (spontaneous vs. focus vs. switch) [$F(2, 22)=6.48$, $p<0.01$, partial $\eta^2=0.37$] (Fig 3). Tukey's post hoc test showed that the number of manual responses increased in the switch condition (23.67) compared to the spontaneous (14.75, $p<0.05$) and focus (13.83, $p<0.01$) conditions.

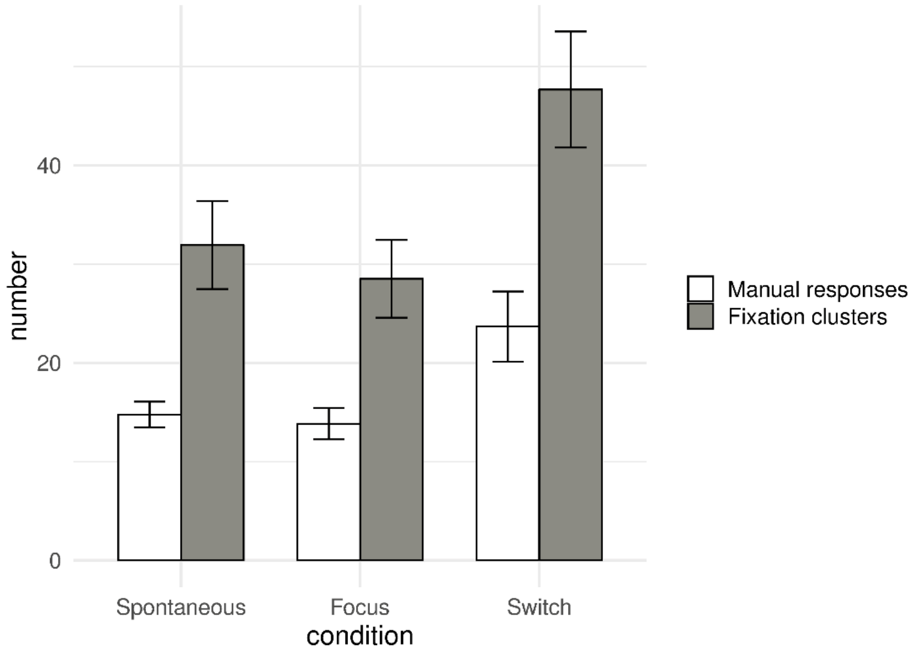


**Figure 3.** Illustration of the results for the number of manual responses and fixation clusters. Number of manual responses (white) and ocular fixation clusters (grey), as a function of the experimental conditions (spontaneous, focus, switch). Error bars represent ± SEM.

A similar analysis revealed an effect of the condition also on the number of fixation clusters [$F(2, 22)=9.78$, $p<0.001$, partial $\eta^2=0.47$] (Fig 3). Tukey's post hoc analysis showed that the number of ocular clusters, similar to the number of button presses, increased in the switch condition (47.67) compared to the spontaneous (31.92, $p<0.01$) and focus (28.50, $p<0.005$) conditions.

We conducted an additional analysis to compare the number of manual and ocular windows, with experimental condition and window type (manual vs. ocular) as within-group variables. The results showed that the number of ocular windows was significantly higher than the number of manual windows [$F(1, 11)=18.59$, $p<0.005$, partial $\eta^2=0.63$] (36.03 vs. 17.42 respectively). The analysis also revealed an effect of the condition [$F(2, 22)=18.72$, $p<0.001$, partial $\eta^2=0.63$]. No interaction was found with the window type.

## Durations of manual and ocular windows

A repeated measures ANOVA was conducted on the median duration of manual windows, with condition (spontaneous vs. focus vs. switch) and preference (preferred vs. non-preferred percepts) as within-group variables. An effect of preference was revealed [$F(1, 11)=36.26$, $p<0.001$, partial $\eta^2=0.77$] with a longer median window duration for the preferred percept compared to the non-preferred percept (4.35 s vs 2.59 s, $p<0.001$). This effect is trivial since preference was defined by the length of the temporal windows. The critical result concerned the impact of the condition (spontaneous vs. focus vs. switch) on the windows' length. We found an interaction between condition and preference [$F(2, 22)=8.65$, $p<0.005$, partial $\eta^2=0.44$]. Decomposing the interaction by means of Tukey's post hoc analysis showed that the median manual window duration for the preferred percept in the focus condition (6.04 s) was longer than all the other durations (preferred/spontaneous 4.12 s, $p<0.05$; non-preferred/spontaneous 2.94 s, $p<0.001$; non-preferred/focus 2.54 s, $p<0.001$; preferred/switch 2.89 s, $p<0.001$; non-preferred/switch 2.28 s, $p<0.001$) (Fig 4a).

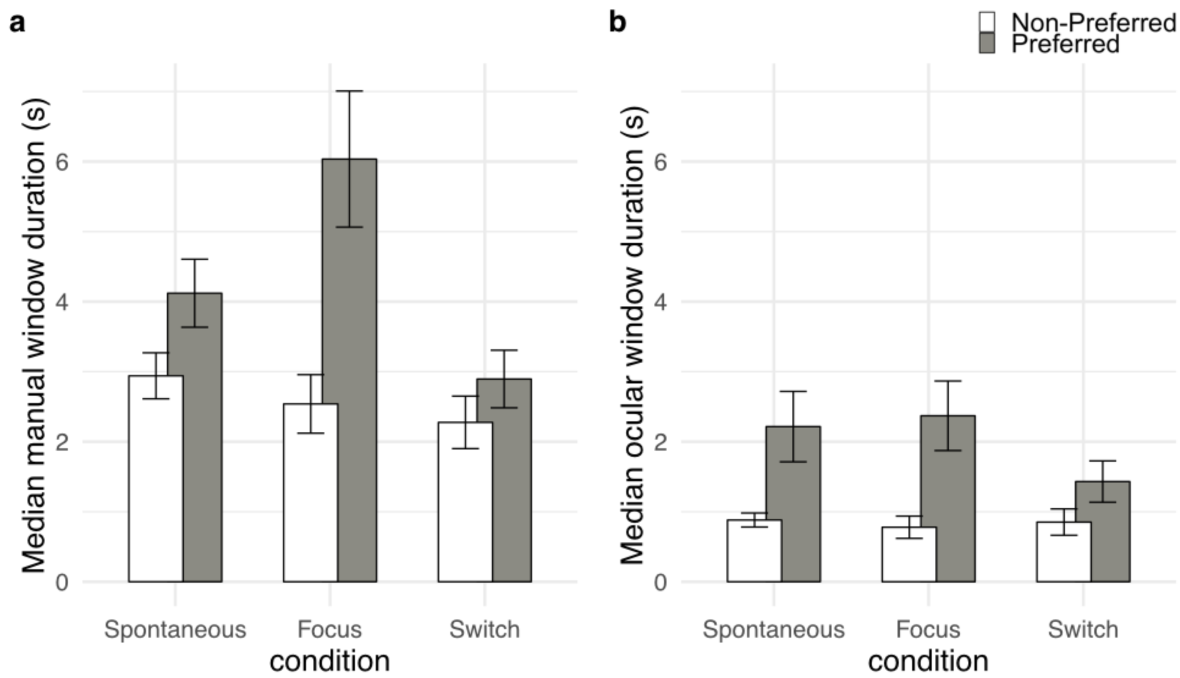


**Figure 4.** Illustration of the results for the median duration of manual and ocular windows. Median duration of preferred and non-preferred (in grey and white respectively) manual (a) and ocular windows (b) as a function of the experimental conditions (spontaneous, focus, switch). Error bars represent ± SEM.

A similar analysis of the median duration of the ocular windows, with condition and preference as within group variables, revealed a main effect of preference [$F(1, 11)=21.89$, $p<0.001$, partial $\eta^2=0.67$] with a longer median ocular window duration corresponding to the preferred percept (2.00 s) compared to the non-preferred percept (0.84 s) (Fig 4b). There was no significant effect of condition or interaction between the two factors.

We compared the median duration of manual and ocular windows, with window type (manual vs. ocular), preference and experimental condition as within-group variables. The results showed that ocular windows had a shorter median duration than manual windows [$F(1, 11)=37.01$, $p<0.001$, partial $\eta^2=0.77$] (1.42 vs. 3.47 respectively). No interaction was revealed between the window type and the other factors.

### Correlations

No correlation was found between ocular and manual windows.

## Discussion

The main results are, firstly, the correspondence between the ocular fixation clusters when the Necker cube is ambiguous and when the cube changes physically in the control condition. Second, ocular fixation clusters alternate much more frequently than manual responses. Nevertheless the number of temporal windows changes in the same way between the spontaneous and switch conditions, whether measured with eye fixations or manual responses. In contrast, in the focus condition the durations of manual windows change without being accompanied by a corresponding change in the durations of ocular windows, indicating that ocular and manual time windows are not always sensitive in the same way to attention manipulations.

The difference between ocular and manual time windows can hardly be attributed to the way we calculated ocular windows. Our choice of the "EM" cluster analysis on ocular fixation measurements was validated by the findings on the ocular fixation clusters' spatial coordinates. We found similar coordinates for fixation clusters in the spontaneous, focus and control conditions. This implies that the fixation clusters are located in the same locations on the screen when the two versions of the cube are physically distinct (control condition) and in the spontaneous condition, where the Necker cube stays physically the same and only the subjective perception changes over time. The spatial correspondence between ocular fixations in the two conditions suggests that the spatial locations of the fixations in the spontaneous condition are linked to changes in perception. The correspondence between ocular fixations and percepts is also supported by the fact that manual and ocular windows that correspond to the preferred version of the Necker cube both had longer durations than those corresponding to the non-preferred version of the cube. These results validate the use of the spatial coordinates of fixation clusters to study the dynamics of ocular windows and compare them with that of manual windows.

It can thus be affirmed that ocular clusters alternate much more frequently than the manual windows. This result suggests that the percept does not change each time eyes change position. It may be possible that changes in ocular positions correspond to oscillations between distinct percepts that do not reach consciousness. Such an interpretation would be consistent with observations that eye movements can respond to invisible stimuli [35], *i.e.* a dissociation between eye movements and perceptual awareness [12]. Regarding studies on bistable stimuli, our results are consistent with those reported by Brascamp et al. (2015) [36], or Kornmeier et al. (2019) [37] who showed in fMRI or EEG evidence of alternations that occur faster than the behavioral responses. As suggested by these authors sensory alternations may occur without reaching consciousness. The possibility that changes in ocular positions reflect an unconscious oscillation between percepts is plausible in the light of models by Logothetis (1998) [38] and Grossberg et al. (2008) [39] which posit that different interpretations for visual information compete for consciousness. Several interpretations of the information would be made available by automatic and unconscious perceptual mechanisms, leading to relatively fast alternations on a non-conscious level, as suggested by ocular movements.

Additional volitional and attentional mechanisms may be needed to decide about the percept and give a manual response. This may contribute to some of the dissociations between ocular and manual windows. For example, the duration of the manual windows that correspond to the preferred percept of the Necker cube increased in the focus condition, suggesting that subjects succeeded in maintaining their preferred orientation of the Necker cube for longer periods. However, neither the number nor the duration of the ocular windows corresponding to the preferred percept in the focus condition were significantly different from the results in the spontaneous condition. This means that the increase in size of the preferred manual windows was not associated with a corresponding ocular change. These results suggest a decoupling between the manual and ocular windows in the focus condition. The literature suggests that a range of factors influence alternations and perception in general [40]. For example, it has been demonstrated that top-down factors, or volitional control [7,25,27,31,32,41,42] can modify the rate of perceptual alternations, as also observed in our focus and switch conditions. As repeatedly observed in focus conditions [43], it is however impossible to completely suppress alternations, confirming the conjoint influences of sensory competition and volitional control. In our study one possible explanation may thus be that the ocular temporal windows reflect an irrepressible sensory alternation, whereas manual responses would be more susceptible to volitional control. The latter may be used to refrain from perceptual alternations, by vetoing sensory influences, or may be necessary to transform a sensory alternation into a conscious one.

Both explanations would account for the ocular fixation clusters' lack of sensitivity to the focus condition, contrasting with the increase in length for the manual time windows.

Contrary to the focus condition, in the switch condition both ocular and manual windows change in parallel. The number of manual responses (*i.e.* number of perceptual reversals) and the number of fixation clusters both increased in the switch condition in comparison to the spontaneous and the focus conditions. These results suggest that when subjects try to speed up the perceptual reversals of the Necker cube, they do succeed, and this is accompanied by an increased number of ocular movements. In the switch condition changes in ocular positions, *i.e.* voluntary eye movements may be used to increase the rate of perceptual alternations. This possibility is supported by the analysis of the distances between the left and right cluster coordinates. This analysis revealed that subjects tend to fixate two locations on the screen that are more distant in the switch condition than in the spontaneous condition. We can speculate that this finding reflects the subjects' effort to voluntarily alternate between the two percepts. Caution is required when interpreting these results however, since the duration of ocular windows remains smaller than that of manual windows even in the switch condition. Even in this condition, there is no perfect match between eye movements and manual responses.

In conclusion, we propose a new way of measuring temporal windows with the clustering of ocular fixations. We do not claim that eye movements analyzed the way we did could substitute explicit reports, but instead we believe that eye movements could serve as a complementary measure to explicit reports, inasmuch our ocular temporal windows (ocular clusters) seem to reveal dynamic perceptual mechanisms at a different, more automatic level than the one of conscious perception and perceptual alternations. The ocular temporal window measure is validated by the similarity of the coordinates of the fixation clusters for ambiguous and non-ambiguous versions of the Necker cube, and by the parallelism of the effects of preference and switch on ocular and manual windows. The ocular windows suggest that there is a spontaneous rhythm at an implicit level, which might reflect perceptual alternations between possible interpretations of sensory information. These alternations are faster than alternations at the conscious level, confirming that alternations occur at different time scales. It remains to be checked whether the partial parallelism between ocular and manual windows indexes a temporal coupling between different mechanisms involved in perception [44], but some conclusions can already be tentatively derived. Sensory alternations are supposed to trigger conscious alternations in perception [45] and the fact that there are faster alternations in the case of ocular temporal windows is consistent with the idea that sensory alternations are primarily driving perceptual switches. Top-down volitional control would have a role in gating these alternations by affecting their potential to reach consciousness. This interpretation, which is consistent with the current literature, implies that the ocular and manual windows are not independent but rather hierarchically organized. Caution is required, though, since ocular movements are not a pure measure of unconscious mechanisms, inasmuch they can be voluntarily controlled. Also, it remains to be investigated whether similar results, and especially the dissociation between ocular and manual temporal windows would be found with other types of static bistable figures.

It can be noted that the impact of the focus and switch conditions was significant, consistent with the literature [25,31,32] despite the short duration of the experiments. Such short experiments may thus be easily used in pathological groups to explore the rhythmic alternations in perception. Additionally eye tracking may be useful by providing a measure for no-report paradigms, in which no subjective report is required from the participants [6].

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In chapter 2 we proposed a new method to study temporal processing at the level of the subjective present (or experienced moment) which is based on eye movements. Given that ocular movements are less biased by top-down, decisional mechanisms compared to manual responses, ocular windows are proposed to reflect perceptual processes at a more automatic level and thus a more objective measure of perceptual alternations of the Necker cube. Such an objective measure is especially appealing in clinical research, where patients' explicit responses may be unreliable.

In the next chapter, we apply out measure based on ocular movements to a group of healthy participants and BP patients in order to see whether ocular windows can capture the symptom of racing thoughts, a symptom related to conscious thought that has mainly been described subjectively until now.

# Chapter 3

# Investigating racing thoughts via ocular temporal windows: Deficits in the control of automatic perceptual processes

The following chapter contains the original manuscript that appeared as: Polgári, P., Weiner, L., Causin, J.-B., Bertschy, G., & Giersch, A. (2021). Investigating racing thoughts via ocular temporal windows: Deficits in the control of automatic perceptual processes. Psychological Medicine, 1–9. https://doi.org/10.1017/S003329172100259

## 3.1. Original manuscript

### Abstract

**Background**. Racing thoughts have been found in several states of bipolar disorder, but also in healthy populations with subclinical mood alterations. The evaluation of racing thoughts relies on subjective reports, and objective measures are sparse. The current study aims at finding an objective neuropsychological equivalent of racing thoughts in a mixed group of bipolar disorder patients and healthy controls by using a bistable perception paradigm.

**Method**. Eighty-three included participants formed three groups based on participants' levels of racing thoughts reported via the Racing and Crowded Thoughts Questionnaire. Participants reported reversals in their perception during viewing of the bistable Necker cube either spontaneously, while asked to focus on one interpretation of the cube, or while asked to accelerate perceptual reversals. The dynamics of perceptual alternations were studied both at a conscious level (with manual temporal windows reflecting perceptual reversals) and at a more automatic level (with ocular temporal windows derived from ocular fixations).

**Results**. The rate of windows was less modulated by attentional conditions in participants with racing thoughts, and most clearly so for ocular windows. The rate of ocular windows was especially high when participants with racing thoughts were asked to focus on one interpretation of the Necker cube and when they received these instructions for the first time.

**Conclusions**. Our results indicate that in subjects with racing thoughts automatic perceptual processes escape cognitive control mechanisms. Racing thoughts may involve not only conscious thought mechanisms but also more automatic processes.

**Key words**: Racing thoughts, temporal windows, bipolar disorder, bistable perception

### Introduction

Racing thoughts refer to a subjective acceleration and increased production of thoughts typically found in bipolar disorder (BP). Racing thoughts are frequently described as crowded, and not only as accelerated (Weiner et al., 2019a). This psychiatric symptom was originally associated to manic and hypomanic states of BP (APA, 2013). However, the phenomenon of racing thoughts can also be present in mixed states (e.g. mixed depression) when associated with other symptoms of depression (Weiner et al., 2019a). Characterizing racing thoughts is important because when they co-occur with depression in mixed states, they are associated with a higher rate of suicides (Akiskal and Benazzi, 2006; Benazzi, 2007; Dodd et al., 2010) and poor response to antidepressant medication (Stahl et al., 2017). Racing thoughts also predict a greater likelihood of conversion to BP after a first depressive episode (Fiedorowicz et al., 2011; Zeschel et al., 2013; Diler et al., 2017). It is noteworthy that racing thoughts, although primarily related to mood disorders, are not specific to BP and can be found in other psychiatric conditions which share symptoms of mood alterations, such as anxiety disorder, attention deficit/hyperactivity disorder and sleep disorders (Bertschy et al., 2020). A study on a healthy population suggests that milder forms of racing thoughts can be associated to sub-clinical mood instability (Weiner et al., 2018). These findings favor a dimensional view of racing thoughts according to which this phenomenon could be found in the general population and would reflect a continuum in mental activity ranging from “healthy” to “pathological”. Here we aim to find a neuropsychological equivalent for racing thoughts by exploring the dynamics of perceptual reversals during viewing of an ambiguous figure, both in healthy subjects and in patients with BP.

Exploring racing thoughts through perception may seem counterintuitive given that racing thoughts are supposed to be verbal. However, the mechanisms underlying racing thoughts may generalize to perception. Racing thoughts were first studied phenomenologically based on qualitative analyses of BP patients’ descriptions (Piguet et al., 2010; Bertschy et al., 2020). Since then, significant advances have been made to capture this complex phenomenon, notably via the development of the Racing and Crowded Thoughts Questionnaire (RCTQ) (Weiner et al., 2018). This self-rating scale, based on patients’ reports, allows for a quantitative clinical assessment of subjects’ experiences of racing thoughts. It has been validated in patients with BP (Weiner et al., 2019a), and in healthy volunteers (Weiner et al., 2018). Objective measures of racing thoughts however are still sparse (for a study testing a verbal fluency task see Weiner et al., 2019b), and we explored the possibility of an objective measure with the same populations for which the RCTQ had been validated.

It is in fact difficult to evidence thought acceleration, even though finding an objective neuropsychological counterpart for racing thoughts is of paramount importance if we want to understand the underlying mechanisms of this symptom and provide a tool to explore its neurobiological mechanisms. Part of the difficulty in evidencing thought acceleration may come from the fact that the spontaneous acceleration often disappears in laboratory settings, e.g. when participants are instructed to find as many animal names as possible in a limited time period (Weiner et al., 2019b; for a meta-analysis see Raucher-Chéné et al., 2017). An activation can be observed, but not directly on a measure relevant to the ongoing task. For example, when manic patients were instructed to find semantically related words (e.g. naming animals), they used additional phonological information to produce words (e.g. rhymes) (Weiner et al., 2019b). These results are particularly evocative of racing thoughts and its verbal equivalent (i.e. flight of ideas) since they are based on the exploration of verbal production, but the use of phonological information discorded with the instructions. If these findings reveal a general cognitive control difficulty, they may generalize to perception.

The measure of the perceptual reversal rate in perceptual bistability paradigms is a potential candidate to objectively capture the phenomenological symptom of racing thoughts, inasmuch as both rely on dynamic neural processes. When viewing a bistable figure, such as the Necker cube, sensory information is ambiguous and our perceptual system alternates between the two possible interpretations of the stimulus (Leopold & Logothetis, 1999; Kornmeier & Bach, 2012). Pöppel (1997; 2009; Wittmann, 2011) proposed a correspondence between the duration of stable percepts during bistable perception and one's sense of subjective present. The subjective present is defined as a temporal window within which a thought or a mental act can be completed (Wittmann, 2011). Pöppel proposed that bistable perception and the measure of perceptual reversals represent an operationalization of the concept of the subjective present, each stable percept corresponding to one temporal window. Thus, measuring the rate of perceptual reversals in bistable perception would essentially reflect the dynamics of one's flow of thoughts. Pöppel's temporal windows model and the operationalization of the subjective present via bistable perception were the rationale for the present study on racing thoughts in BP.

Studies on perceptual bistability have been conducted in the context of BP, but none of them considered perceptual alternations in relation to racing thoughts (some studies used bistable figures: Hunt & Guilford, 1933; Eysenck, 1952; Philip, 1953; Hoffman et al., 2001; Krug et al., 2008; Schmack et al., 2013; other studies used binocular rivalry, another type of perceptual bistability paradigm: Pettigrew & Miller, 1998; Miller et al., 2003; Nagamine et al., 2009; Ngo et al., 2011; Vierck et al., 2013; Ye et al., 2019). Interestingly, in a study using the Necker cube, Hoffman et al. (2001) found an increased rate of perceptual reversals in patients with manic-spectrum disorders compared to healthy controls and schizophrenia patients. Considering that racing thoughts are primarily manic-like symptoms (although not exclusive to pure mania), the finding by Hoffman et al. represents an encouraging premise for testing perceptual alternations as a means to capture racing thoughts.

In the present study we aim at investigating whether perceptual reversals of the Necker cube reflect the phenomenon of racing thoughts in a group of BP patients and healthy participants. We additionally record eye movements, based on a previous study in healthy participants (Polgári et al., 2020). In our previous study we found an oscillatory behavior between two locations on the screen for ocular fixations, which correspond to the two interpretations of the bistable Necker cube. This oscillation in ocular fixations is akin to oscillations in manual responses reflecting subjects' perceptual alternations, but at a higher temporal frequency. In the present work, temporal windows were computed from both manual and ocular measurements. Alternations reported by participants require a conscious decision, which might itself be impaired in patients. The rate of "ocular windows" is proposed to reflect more automatic and faster perceptual alternations between representations of the Necker cube than the classic "manual windows". Although eye movements are not a purely automatic behavior, compared to explicit manual responses, they are affected to a lesser extent by top-down, decisional mechanisms (Spering & Carrasco, 2015). Thus, ocular windows represent an additional objective measure for the characterization of racing thoughts during the Necker cube paradigm, and their evaluation allowed us to contrast a manual response based on a conscious decision, and a less controlled ocular response.

After they completed a self-report measure of racing thoughts (the RCTQ), participants performed the perceptual bistability paradigm where they reported manually each time their perception of the Necker cube changed spontaneously.

In order to examine how instruction-related constraints interfere with the spontaneous alternation rate, participants performed two attentional conditions in addition to the "spontaneous report" condition: one where subjects were instructed to focus on one of the two percepts of the Necker cube and inhibit the other (Focus condition), and another one where they were asked to switch as fast as possible between the two percepts (Switch condition). These instructions have been shown to have significant effects on subjects' perceptual reversals (Strüber & Stadler, 1999; Meng & Tong, 2004; van Ee et al., 2005; Mathes et al., 2006).

If the acceleration of thoughts is genuine, it should be mainly observed in the spontaneous condition. In contrast, if racing thoughts are related to a cognitive control difficulty, i.e. switching between or focusing on the interpretations of the figure, abnormal alternation rates should be shown in the attentional conditions. In both cases, rates might be affected either at the level of manual or ocular responses. Since some patients are able to report their subjective experience of racing thoughts (Piguet et al., 2010), it is a valid assumption that racing thoughts should be captured at the level of manual responses which reflect subjects' conscious perception (i.e. manual windows rate). If racing thoughts are associated to more automatic, non-conscious perceptual processes at a smaller temporal scale, the ocular windows rate may increase, either in the spontaneous condition or in the attentional conditions, again depending on the genuine vs. cognitive control-related nature of racing thoughts.

## Materials and methods

### Participants

Sixty-two patients (mean age±SD: 43.60±12.57; 40 females) with BP and 21 healthy controls (mean age±SD: 37.33±12.40; 16 females) participated in the study. Sixteen inpatients and 46 outpatients were recruited at the University Hospital of Strasbourg and fulfilled criteria for BP according to DSM-IV-TR (APA, 2000). Patients' clinical state was evaluated using the Young Mania Rating Scale (YMRS; Young et al., 1978) and the Quick Inventory of Depression Symptomatology-Clinician-Rated Version (QIDS-C16; Rush et al., 2003). The same score cut-offs previously used by Weiner et al. (2019b) were used to establish patients' mood state. Diagnostic criteria were established for each mood state as in previous studies (Favre et al., 2003; Rush et al., 2003; Suppes et al., 2005; Miller et al., 2016). The number of patients per group is presented in Table 1. Healthy controls were recruited by advertisement and had no current or past personal or family history of mood disorder or psychosis. Control subjects were originally matched to the sub-groups of BP patients in a previous study using the same participants, hence the imbalance between the patient and healthy control groups. For all participants exclusion criteria included a history of neurological disorder, ADHD, schizophrenia or schizoaffective disorder, borderline personality disorder and substance use disorder within the past 12 months. All participants had normal or corrected-to-normal vision. The neuropsychological evaluation included the Trail Making Test (Tombaugh, 2004), the Hayling test (Burgess & Shallice, 1997), the Vocabulary Subtest of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) (Strauss, Sherman, & Spreen, 2006) and the French National Adult Reading Test (Mackinnon & Mulligan, 2005) (see Supplementary material S1 for details).

The project was approved by the regional ethics committee of the East of France (CPP EST IV). All subjects gave their informed written consent in accordance with the declaration of Helsinki.

### Racing thoughts groups

Participants were labelled as having 'No', 'Low' and 'High racing thoughts' based on their RCTQ scores. The groups were formed after visual inspection of the distribution of RCTQ scores and by balancing the number of subjects per group (see distribution in Supplementary material S2). Details about the cut-off score-values and demographic details are shown in Table 2.

| | Mania | Mixed mania | Depression | Mixed depression | Euthymia | Control |
|---|---|---|---|---|---|---|
| Number of subjects | 15 (4M/11F) | 9 (2M/7F) | 10 (5M/5F) | 15 (3M/12F) | 13 (8M/5F) | 21 (5M/16F) |
| YMRS cut-off scores | >5 | >5 | <3 | >2, ≤5 | ≤5 | / |
| QIDS-C16 cut-off scores | ≤5 | >5 | >5 | >5 | ≤5 | / |
| Lithium medication | 3 | 2 | 5 | 7 | 4 | / |
| Antiepileptic medication | 5 | 6 | 4 | 5 | 8 | / |
| Antipsychotic medication | 6 | 3 | 4 | 3 | 5 | / |
| Antidepressant medication | 2 | 4 | 5 | 5 | 4 | / |
| Benzodiazepine medication | 3 | 2 | 2 | 2 | 1 | / |

**Table 1.** Number of participants in the different mood states and cut-off scores used for the diagnosis.
YMRS = Young Mania Rating Scale; QIDS-C16 = Quick Inventory of Depression Symptomatology-Clinician-Rated Version.

| | No racing thoughts | Low racing thoughts | High racing thoughts | F | p |
|---|---|---|---|---|---|
| RCTQ scores | 0-7 | 8-53 | 54-132 | / | / |
| Total number of subjects | 25 | 30 | 28 | / | / |
| Number of healthy controls | 14 | 7 | 0 | / | / |
| Number of patients with mania | 1 | 7 | 7 | / | / |
| Number of patients with mixed mania | 0 | 1 | 8 | / | / |
| Number of patients with depression | 2 | 4 | 4 | / | / |
| Number of patients with mixed depression | 2 | 4 | 9 | / | / |
| Number of patients with euthymia | 6 | 7 | 0 | / | / |
| Mean age ± SD | 37.76 ± 12.35 | 42.27 ± 13.50 | 45.54 ± 11.51 | 2.56 | 0.08 |
| Mean year of education | 15.12 ± 2.11 | 14.10 ± 2.34 | 14.11 ± 2.38 | 1.73 | 0.18 |
| TMT B-A score | 32.20 | 37.71 | **57.30** | 4.61 | **0.013** |
| Hayling B-A score | 3.28 | 3.34 | 3.32 | 0.01 | 0.99 |
| WAIS | 101.59 | 99.50 | 92.76 | 3.03 | 0.054 |
| fNART | 111.68 | 111.50 | 108.07 | 2.47 | 0.091 |

**Table 2.** Demographic data of the three Racing thoughts groups.
RCTQ = Racing and Crowded Thoughts Questionnaire; TMT = Trail Making Test; WAIS = Wechsler Adult Intelligence Scale; fNART = French National Adult Reading Test. Significant differences are presented in bold.

### Experimental task and procedure

The procedure and analysis method were validated in a sub-group of the healthy controls and are detailed in Polgári et al. (2020). Throughout the experiment participants were asked to indicate perceptual reversals by pressing one of two buttons on a keyboard each time the perceived orientation of the Necker cube changed (left button for downward-left facing orientation, right button for upward-right facing orientation). Four experimental conditions were run in the experiment, each with a duration of one minute in order to minimize effects of fatigue in patients. First, in the 'Spontaneous' condition, participants were asked to report the perceptual reversals of the Necker cube that occurred spontaneously. Next, two attentional conditions followed whose order was randomized between subjects. In the 'Focus' condition participants were instructed to maintain for as long as possible their preferred orientation of the cube and come back to this orientation as quickly as possible in case of perceptual reversal. In the 'Switch' condition they had to switch between the two orientations as often as possible. Lastly, in a control condition two modified, non-ambiguous versions of the Necker cube were presented alternately on the screen with a mean duration of 3 seconds each, and subjects had to report, via button presses, each time they detected a physical alternation of the cube. This condition was used (i) to verify that participants were able to reliably report perceptual alternations, (ii) to verify the correspondence between ocular fixation coordinates when the Necker cube is ambiguous (and only perception changes) and when the figure changes physically. For details on the equipment see Supplementary material S3.

### Data processing

For each condition we extracted the number of button presses reflecting perceptual reversals. This number was used as an estimate of the number of "manual windows" i.e. the number of periods between subsequent button presses.

Ocular fixations (details on recording can be found in Supplementary material S3) were extracted for each subject and classified into one of two groups based on their x coordinates (left or right cluster) using the Expectation-Maximization (EM) algorithm (Witten et al., 2017). Each cluster was composed of at least one ocular fixation and its length depended on the number and duration of the successive ocular fixations belonging to the same cluster (Fig. 1). Ocular windows correspond to the alternating left and right clusters of ocular fixations and their number was extracted for each participant. More details can be found in Supplementary material S4 and Polgári et al., 2020).

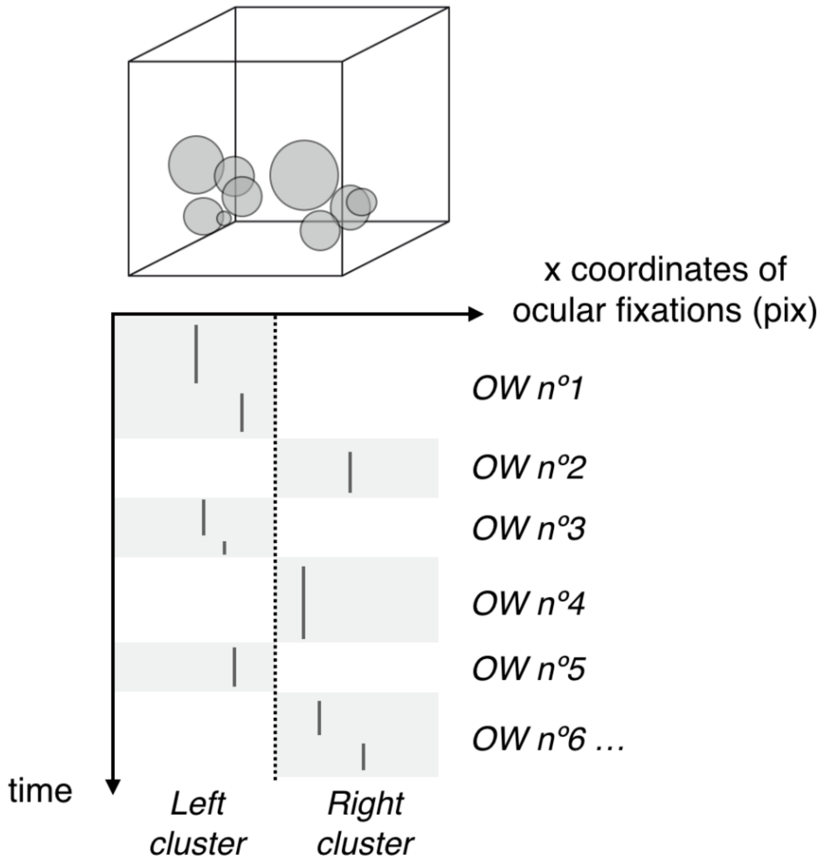


**Figure 1.** Schematic representation of the cluster analysis used for the computation of ocular windows

Ocular fixations are represented on the Necker cube by grey circles whose diameter is proportional to the duration of the fixation (upper part). The x coordinates of the fixations are reported on the graph (bottom part) by continuous lines whose length is proportional to the duration of the fixations. The threshold separating fixations on the left and the right side is computed by the EM cluster algorithm. Successive fixations belonging to the same side form an ocular cluster which corresponds to an ocular window (OW).

### Statistical analysis

Data analyses consisted of repeated measures ANOVAs and sub-analyses. For details see Supplementary material S3. Correlations were conducted by computing Pearson's correlation coefficients. The level of significance was set to $\alpha=0.05$ throughout the analyses. Since racing thoughts groups were close to differ in age and level of education, all analyses (when applicable) were verified with these two measures as covariates. The main results of our study were similar in the ANCOVAs (see Supplementary material S5).

## Results

### Number of manual windows

A one-way ANOVA conducted on the number of manual windows, with experimental condition (Spontaneous vs. Focus vs. Switch) as a within-group variable and the racing thoughts group as a between-group variable revealed an effect of experimental condition [$F(2,160)=21.00$, $p<0.00001$, partial $\eta^2=0.21$]. Sub-analyses showed that the number of manual windows was lower in the 'Focus' condition (12.81) compared to the 'Spontaneous' (15.02, [$F(1,82)=8.12$, $p<0.01$, partial $\eta^2=0.09$]) and 'Switch' conditions (20.58, [$F(1,82)=26.23$, $p<0.000005$, partial $\eta^2=0.24$]), and higher in the 'Switch' condition compared to the 'Spontaneous' ([$F(1,82)=19.16$, $p<0.00005$, partial $\eta^2=0.19$]) and the 'Focus' conditions (Fig. 2a). No effect of racing thoughts group or interaction between the variables was found.

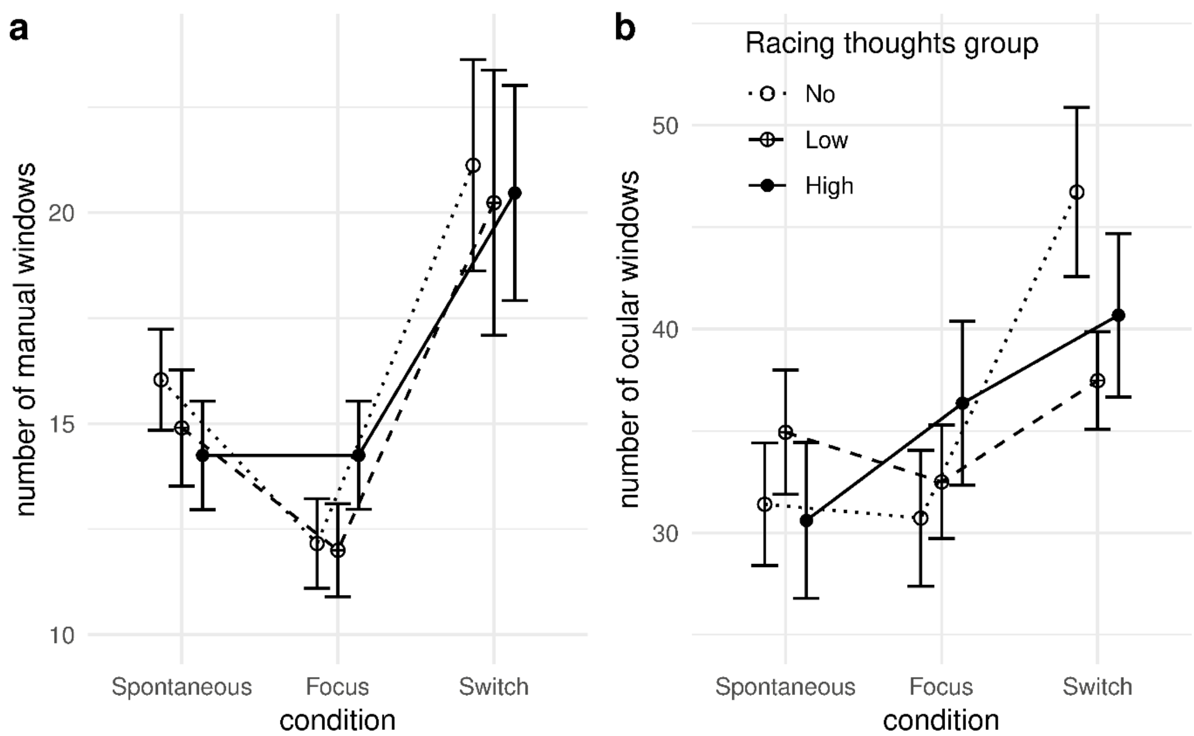


**Figure 2.** Mean number of manual (a) and ocular windows (b) in each experimental condition across the three racing thoughts groups.
Error bars represent ± SEM.

However, the graph suggested a lack of modulation of the manual window rate between the 'Spontaneous' and 'Focus' conditions in the "High racing thoughts" group, and, given there was a similar pattern for ocular windows, we verified to which extent the manual window rate was modulated in each group. This allowed us to verify whether abnormalities could be said to be restricted to ocular windows or not. Sub-analyses conducted in each group confirmed a decreased window rate in the 'Focus' compared to the 'Spontaneous' condition in the "No" and "Low racing thoughts" groups ([$F(1,24)=8.02$, $p<0.01$, partial $\eta^2=0.25$]; $F(1,29)=5.22$, $p<0.05$, partial $\eta^2=0.15$] respectively), but equal rates in the "High racing thoughts" group [$F(1,27)=0.00$, $p=1$, partial $\eta^2=0.00$]. All groups showed an increase of the manual window rate between the 'Spontaneous' and the 'Switch' conditions ([$F(1,24)=7.50$, $p<0.05$, partial $\eta^2=0.24$; $F(1,29)=4.86$, $p<0.05$, partial $\eta^2=0.14$; $F(1,27)=7.72$, $p<0.01$, partial $\eta^2=0.22$] "No", "Low", and "High racing thoughts" groups respectively).

## Number of ocular windows

We conducted an analysis on ocular windows similar to the one on manual windows. The analysis revealed an interaction between experimental condition and the racing thoughts group [$F(4,160)=2.64$, $p<0.05$, partial $\eta^2=0.06$] (Fig. 2b). The "No racing thoughts" group had a higher number of ocular windows in the 'Switch' condition (46.72) compared to the 'Spontaneous' (31.40, [$F(1,24)=19.43$, $p<0.0005$, partial $\eta^2=0.45$]) and 'Focus' conditions (30.72, [$F(1,24)=12.73$, $p<0.005$, partial $\eta^2=0.35$]). The "High racing thoughts" group had a higher number of ocular windows in the 'Switch' condition (40.68) compared only to the 'Spontaneous' condition (30.61, [$F(1,27)=5.15$, $p<0.05$, partial $\eta^2=0.16$]). The difference between conditions was not significant in the "Low racing thoughts" group. This reduced modulation of the window rate between the attentional conditions may suggest that oculomotor behavior is immune to instructions in the "Low" and "High racing thoughts" groups. This might have been due to a difficulty to adapt to new instructions when going from the 'Focus' to the 'Switch' condition, or the reverse. We verified this possibility by analyzing the effect of task order.

## Effect of task order

While the spontaneous condition was always performed first, the 'Focus' and 'Switch' conditions were run afterwards in random order. To verify how manual and ocular behavior are adapted to the history and order of the attentional instructions, we did additional ANOVAs on the number of manual and ocular windows. To explore the impact of instructions across time independent of the precise 'Focus' or 'Switch' instruction, we considered the rank of the test session ('Second session' vs. 'Third session'), which represented a within-group variable. Whether the second and third sessions were with 'Focus' or 'Switch' instructions depended on the order in which participants completed the two attentional conditions ('Focus then Switch' vs. 'Switch then Focus'), which was taken as a between-group variable. The groups that performed the attentional conditions in different orders ('Focus then Switch' vs. 'Switch then Focus') did not differ in age, level of education, score at the French National Adult Reading Test and at the digit-symbol subtest of the WAIS-III, and they produced similar numbers of manual [$F(1,81)=3.24$, $p>0.05$, partial $\eta^2=0.04$] and ocular windows [$F(1,81)=0.10$, $p>0.05$, partial $\eta^2=0.001$] in the 'Spontaneous' condition.

The analysis of the effect of order and rank on the number of manual windows did not reveal an interaction with racing thoughts group, meaning similar manual window modulation in all three racing thoughts groups.

In the analysis on the number of ocular windows a third degree interaction was found between order, rank and racing thoughts group [$F(2,77)=3.69$, $p<0.05$, partial $\eta^2=0.09$]. In the group that performed the conditions in the 'Focus then Switch' order an interaction was found between rank and racing thoughts group [$F(2,37)=5.92$, $p<0.01$, partial $\eta^2=0.24$]. Sub-analyses showed that only the "No racing thoughts" group increased the number of ocular windows from 'Focus' (30.93) to 'Switch' (47.67, [$F(1,14)=13.84$, $p<0.005$, partial $\eta^2=0.50$]). For the "Low" and "High racing thoughts" groups the difference was not significant ([$F(1,13)=2.71$, $p>0.05$, partial $\eta^2=0.17$], [$F(1,10)=1.20$, $p>0.05$, partial $\eta^2=0.11$] respectively) (Fig. 3 left panel).

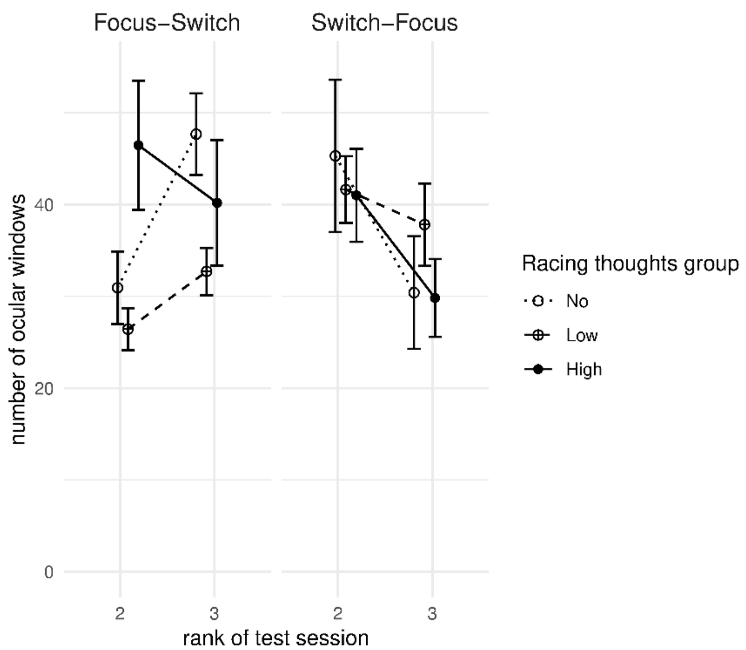


**Figure 3.** Mean number of ocular windows produced in the attentional conditions, considering the order in which they were performed.
Error bars represent ± SEM.

A further ANOVA with racing thoughts group as a between-group variable indicated that in the (first) 'Focus' condition the number of ocular windows differed between racing thoughts groups [$F(2,37)=5.04$, $p<0.05$, $\eta^2=0.21$]. Sub-analyses revealed that in this condition the "High racing thoughts" group had a higher number of ocular windows compared to the "Low racing thoughts" group (46.46 vs. 26.43 respectively, [$F(1,23)=8.84$, $p<0.01$, $\eta^2=0.28$]), and tended towards a higher number of ocular windows relative to the "No racing thoughts" group (46.46 vs. 30.93 respectively, [$F(1,24)=4.19$, $p=0.052$, $\eta^2=0.15$]). No between-group difference was found in the (second) 'Switch' condition [$F(2,37)=2.86$, $p>0.05$, $\eta^2=0.13$], indicating similar ocular window numbers in all three racing thoughts groups in this condition.

In the group that performed the conditions in the 'Switch then Focus' order no interaction between rank and racing thoughts group was found [$F(2,40)=1.09$, $p>0.05$, $\eta^2=0.05$]. A simple effect of rank revealed that all groups similarly decreased the number of ocular windows from the 'Switch' (42.23) to the 'Focus' condition (32.93, [$F(1,40)=10.25$, $p<0.005$, $\eta^2=0.20$]) (Fig. 3 right panel).

### Correlational analyses

To further verify the link between racing thoughts and an increased ocular window rate when subjects are required to perform the 'Focus' condition first, we performed correlational analyses between RCTQ scores and the number of manual and ocular windows in each attentional condition. In the group that performed the conditions in the 'Focus then Switch' order the number of ocular windows in the 'Focus' condition positively correlated with the RCTQ score ($r=0.45$, $p<0.005$, $N=40$), indicating that the higher the level of racing thoughts subjects reported, the more they made ocular alternations when they were first given the 'Focus' instruction. No other correlations with RCTQ scores were found.

We conducted correlational analyses between age, years of education and the number of manual and ocular windows in all three conditions. Age negatively correlated with the number of manual windows in the 'Spontaneous' [$r=-0{,}36$; $p<0.005$] and the 'Switch' conditions [$r=-0{,}32$; $p<0.005$], however no correlations were found with the number of ocular windows.

Correlational analyses were conducted in each racing thoughts group between TMT B-A scores and the number of manual and ocular windows in order to verify a link between attentional switching deficits and increased window rates. In the "High racing thoughts" group (N=27) attention switching deficits as measured with the TMT positively correlated with the number of manual windows ($r=0.58$, $p<0.005$), the number of ocular windows in the 'Focus' condition ($r=0.41$, $p<0.05$) and the number of ocular windows in the 'Switch' condition ($r=0.47$, $p<0.05$). No other correlations were significant after correction for multiple testing.

## Discussion

The aim of the present study was to investigate whether temporal windows derived from manual and ocular behavior during viewing of the Necker cube could capture the phenomenon of racing thoughts in BP patients and healthy controls. In all groups temporal windows varied as a function of attentional conditions, showing that they followed instructions. Although our "High racing thoughts" group was exclusively composed of BP patients in an acute phase of their illness, the severity of their mood episode was mild-moderate. The mild severity of their state allowed them to perform the experiment and reliably report conscious perceptual alternations, at least in the 'Spontaneous' and 'Switch' conditions. However, in participants with racing thoughts, windows were less modulated by attentional instructions. Although the results on manual and ocular windows showed a similar pattern, a clear interaction between conditions was observed only for ocular windows. There is no evidence of a genuine increase of perceptual alternation in participants with racing thoughts, since all groups alternated perceptions at the same rate in the 'Spontaneous' condition. It is rather the cognitive control of alternations that is impaired in case of racing thoughts.

Taking into account the order in which attentional conditions were run showed an even more specific pattern of results. Specifically, in participants with racing thoughts, anomalies were observed in the ocular window rate in the 'Focus' condition when it preceded the 'Switch' condition. These anomalies are manifest in the abnormally high number of ocular windows in the 'Focus' condition when the instructions constrain participants to control their perceptual reversal rate for the first time, prior to the condition whereby an acceleration of reversals is expected. This shows that the inability to reduce the ocular window rate in participants with racing thoughts is not due to the necessity to go from the 'Switch' to the 'Focus' condition, but rather occurs when participants are instructed to restrict perceptual alternations after the 'Spontaneous' condition.

Participants who performed the attentional conditions in the 'Switch then Focus' order had equally increased ocular window rates in the 'Switch' condition relative to the 'Spontaneous' condition, independently of their self-reported level of racing thoughts. These results suggest that it is not following the attentional instructions in general that is difficult for the patients, but rather the 'Focus' condition specifically. The results suggest that in participants with racing thoughts conscious and non-conscious perceptual processes escape the cognitive control mechanisms, especially those elicited by the 'Focus' instructions. The correlation between the increase in alternation rates and flexibility deficits further supports this interpretation.

The "High racing thoughts" group displayed attention switching deficits on the TMT B-A, which correlated with the increase in the perceptual alternations in this group. This correlation further supports the interpretation that patients are not genuinely more flexible. Rather, the impaired control of conscious but also automatic perceptual processes underlies the cognitive flexibility deficits of the patients, and their inability to inhibit automatic perceptual alternations of the Necker cube. It is remarkable that there are similar reversal rates in the 'Focus' and in the 'Switch' conditions in the groups with racing thoughts. These results suggest that the 'Focus' condition paradoxically leads to increased reversals, as if ocular reversals were actually activated when cognitive control mechanisms are elicited.

The link between cognitive flexibility and deficient control of automatic perceptual processes in subjects with racing thoughts is consistent with findings in the semantic verbal fluency task in Weiner et al. (2019b). In this study, (hypo)manic patients used sound-based associations when instructed to produce semantically related words. Like in the present study, they circumvented constraining task instructions, i.e. cognitive control, and then displayed increased flexibility.

The clinical implications of our findings are noteworthy. Subjects with racing thoughts were impaired when the task involved cognitive control, and only then alternated perceptions excessively. These impairments are manifest to some extent at the level of conscious perception (ie. manual windows), but they are more apparent at the level of automatic and unconscious processing as reflected by ocular windows. Automatic perceptual processes measured via ocular windows appear to escape cognitive control. Instead of being rooted solely in mechanisms associated with consciousness, racing thoughts may also involve overactivation of more automatic processes. This may distinguish racing thoughts from other thinking abnormalities found in mood disorders, e.g. rumination, which have been mainly linked to cognitive control deficits (Whitmer & Banich, 2016). Akin to research on depressive rumination, studies on the mechanisms involved in racing thoughts are crucial, as they might foster new treatments targeting this understudied symptom (Piguet et al., 2010; Weiner et al., 2019b).

There are some limits to this study. The sample size in each sub-group of BP patients prevented us from distinguishing results as a function of the sub-groups. Several studies suggest slow perceptual switching in BP patients (Krug et al., 2008; Schmack et al., 2013; Ye et al., 2019), except in patients with mania (Hoffman et al., 2001). This difference with our study may be related to the types of BP sub-groups included in previous studies. For example, no euthymic patient was part of the group with the highest RCTQ scores. It would be of interest to distinguish temporal windows as a function of the BP sub-groups.

Moreover, the comparison of temporal windows between groups was based on patients' subjective responses on the RCTQ. This is a first methodological step when seeking an objective measure for a subjectively described phenomenon such as racing thoughts. Future works should follow an inverse logic and focus on testing the predictive power of ocular window rates to racing thoughts.

Nevertheless, our results show the interest of adding indirect measures of perception, like the analysis of ocular movements, that do not rely on the subjective decision of the patients. The recording of eye movements might be difficult to set up in clinical settings. However, any indirect measure would be useful, given the difficulty to evidence racing thoughts in laboratory settings (Weiner et al., 2019b).

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## Conflicts of interest

None.

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## 3.2. Supplementary material

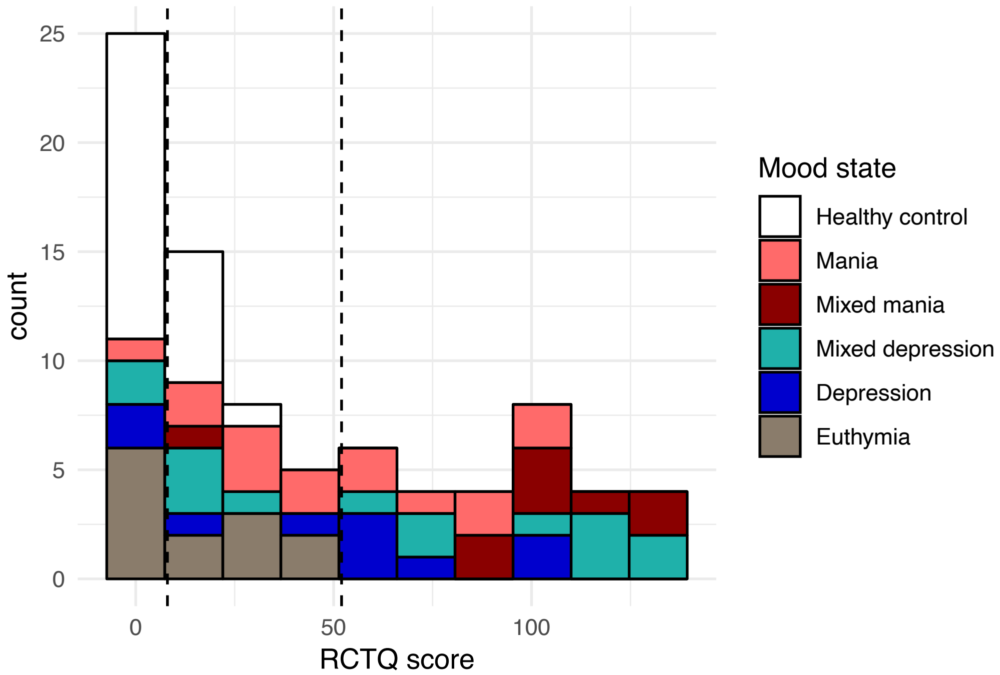
### S1: Neuropsychological evaluation

The Trail Making Task was used to assess processing speed (TMT-A, a condition where subjects had to connect a series of numbers in order, i.e. 1-2-3…) and attention switching (TMT-B, a condition where subjects had to connect targets by alternating between numbers and letters, i.e. 1-A-2-B…). The difference between the two scores ('time B' - 'time A') reflects attentional switching costs (TMT-B) by subtracting the general psychomotor slowing (TMT-A).

Further assessments included the Hayling test (Burgess & Shallice, 1997) assessing semantic inhibition, the Vocabulary Subtest of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) (Strauss, Sherman, & Spreen, 2006) assessing lexico-semantic abilities and vocabulary size and the French National Adult Reading Test (Mackinnon & Mulligan, 2005) measuring premorbid intelligence levels (see Table 2 in the main manuscript).

### S2: Figure S1. Distribution of the RCTQ scores and composition of the racing thoughts groups.

RCTQ score thresholds used to establish racing thoughts groups are indicated with dashed lines.



## S3: Equipment and stimuli

The study was conducted in a quiet and dimly lit room. Visual stimuli were generated by a Hewlett-Packard Compaq 8100 Elite 2 computer using programs written on MATLAB software (2007) by MathWorks and PsychToolbox (Brainard, 1997) and presented on a 21'' Sony Triton CRT screen.

Throughout the experimental conditions the Necker cube was presented on the screen for 60 seconds (Fig. 1). Each side had a length of 12° of visual angle, consisting of black lines (0.008 cd/m² and 0.18° thickness) on a white background (41.5 cd/m²).

An EyeLink CL 1000 (SR Research) infra-red video-based eye tracking system (sampling-frequency of 1000 Hz and a spatial resolution of 1024 x 768 pixels) was used to measure right eye movements throughout the experiment. Before each experimental condition the eye tracker was calibrated with a fixation dot that appeared repeatedly in different locations following a 9-point grid. Participants had to fixate the dot until stable eye coordinates could be measured. Head movements were minimized using a chinrest at a fixed distance of 70 cm from the computer screen. The number and duration of ocular fixations were registered and analyzed. Fixations were defined by stable eye position coordinates for a minimum of 90 ms and a maximum of 1000 ms. The processing of eye tracking data was carried out using programs written on MATLAB, and data was analyzed with Statistica® software 13.0. by Statsoft.

**Statistical analyses:** In the ANOVAs, within-group variables were the experimental condition (Spontaneous vs. Focus vs. Switch) and, for some analyses, the rank of the conditions ('Second session' vs. 'Third session'). Between-group variables were the Racing thoughts group ('No' vs. 'Low' vs. 'High racing thoughts group') and, for some analyses, the order group ('Focus then Switch' vs. 'Switch then Focus'). We added the partial eta-squared ($\eta^2$) as a measure of effect size.

## S4: Validation of the cluster analysis in the racing thoughts groups

The validity of our cluster analysis was verified by comparing the spatial coordinates of ocular fixation clusters in the control condition (where two non-ambiguous versions of the Necker cube were presented alternately on the screen) and in the other three conditions (where the ambiguous figure was presented continuously). In our preceding study, it was found that left and right cluster coordinates were similar when the figure is ambiguous and when it changes physically between two non-ambiguous versions, except when the instruction was to switch between perceptions. The similarity of coordinates between the ‘Spontaneous’, ‘Focus’ and ‘Control’ conditions means that the positions of left/right ocular fixations during viewing of the ambiguous Necker cube correspond to perceptual representations of the two interpretations (left/right orientations) of the figure.

Repeated measure ANOVAs were conducted in all three racing thoughts groups separately, with the abscissa of the ocular fixation clusters (left and right location) and condition (Spontaneous, Focus, Switch and Control) as within-group variables. A main effect of the abscissa in all three Racing thoughts groups indicated that the left and right fixation clusters had systematically different x coordinates in each condition (for details on statistics see Table S3).

| Racing thoughts group | Left coordinate (pixels) | Right coordinate (pixels) | F | P | $\eta^2$ |
|---|---|---|---|---|---|
| No | 608 | 683 | 129.83 | <0.00001 | 0.87 |
| Low | 635 | 710 | 167.03 | <0.00001 | 0.86 |
| High | 612 | 698 | 91.28 | <0.00001 | 0.80 |

**Table S3.**

An interaction between the abscissa of fixation clusters and condition was found only in the “No racing thoughts group” ([$F(3, 60)=6.06$, $p<0.005$, $\eta^2=0.23$]. A sub-analysis on the distance between left and right cluster coordinates (Right coordinate-Left coordinate) was conducted in this group in order to understand the origin of this interaction. Like in our preceding study, an effect of the condition indicated that the distance between left and right fixation clusters varied significantly throughout the conditions [$F(3, 60)=6.06$, $p<0.005$, $\eta^2=0.23$], and Tukey’s post hoc analysis showed that this distance was larger in the Switch condition (110 pix.) compared to the Spontaneous (51 pix., $p<0.005$) and the Focus conditions (63 pix., $p<0.05$). The distance between left and right fixation clusters in the Control condition (74 pix.) did not differ from the distance in the other conditions where the ambiguous version of the Necker cube was presented. In the other two racing thoughts groups no interaction was found indicating similar fixation cluster coordinates throughout the conditions. These results are consistent with the fact that the perception of the Necker cube is less influenced by attentional conditions in subjects with racing thoughts compared to the 'No racing thoughts' group.

We additionally compared the Racing thoughts groups on the number of temporal windows produced in the 'Control' condition with similar ANOVAs as described in the main text (Racing thoughts group as between-group variable). There was no effect of group in the 'Control' condition on the number of manual [$F(2, 80)=1.02$, $p=0.37$, partial $\eta^2=0.02$] or ocular windows [$F(2, 71)=1.34$, $p=0.27$, partial $\eta^2=0.04$].

## S5: Results of the statistical analyses with age and level of education as covariates (ANCOVAs)

### Number of manual windows

The conditions of application of an Analysis of Covariance were not met for the manual windows data (Age negatively correlated with the number of manual windows in the 'Spontaneous' [r=-0,36; $p<0.005$] and the 'Switch' conditions [r=-0,32; $p<0.005$]).

### Number of ocular windows

For ocular windows, which represented the main results of the study, we verified whether the statistics involving a comparison between groups changed or not when age and level of education were taken as covariates.

The interaction between the racing thoughts group and the condition remained significant for the number of ocular windows [$F(2, 156)=2.65$, **$p<0.05$**, partial $\eta^2=0.06$].

### Effect of task order

As for the analyses on the effect of task order, the 3rd level interaction between rank, order and racing thoughts group remained significant when age and level of education were taken as covariates [$F(1, 75)=3.33$, **$p<0.05$**, partial $\eta^2=0.08$].

The other interactions likewise remained unchanged when age and level of education were taken as covariates:

- In the group that performed the conditions in the 'Focus then Switch' order the interaction between rank and racing thoughts group was still significant [$F(2, 35)=4.28$, **$p<0.05$**, partial $\eta^2=0.20$].
- In the analysis in the (first) 'Focus' condition, the effect of racing thoughts group was significant like for the original analysis [$F(2, 35)=4.99$, **$p<0.05$**, partial $\eta^2=0.22$], with the "High racing thoughts" group presenting a higher number of ocular windows compared to the "Low racing thoughts" group [$F(1, 21)=9.02$, **$p<0.01$**, partial $\eta^2=0.22$].

Similar to the original result, no between-group difference was found in the (second) 'Switch' condition [$F(2, 35)=1.76$, $p=0.19$, partial $\eta^2=0.09$].

In the group that performed the conditions in the 'Switch then Focus' order, the interaction between rank and racing thoughts group remained non-significant [$F(2, 38)=1.06$, $p=0.36$, partial $\eta^2=0.05$].

### Control condition

For the analyses in the Control condition, the effect of group remained non-significant for both manual [$F(2, 78)=2.13$, $p=0.13$, partial $\eta^2=0.05$] and ocular data [$F(2, 69)=0.86$, $p=0.43$, partial $\eta^2=0.02$].

In Chapter 3 we saw that ocular windows can be considered a useful tool in clinical research, since they revealed a link between an alteration in the modulation of automatic perceptual processes and the symptom of racing thoughts in BP. We hypothesized that the timescale of alterations in temporal processing are different between BP and SZ (subjective present vs. functional moment, respectively). Thus, in the next chapter we use preliminary data to compare these two clinical groups on their reported level of racing thoughts and ocular window measurements in order to see to what extent alterations at the level of the subjective present are specific to BP.

Chapter 4

# Similar levels of racing thoughts, but different modulation of automatic perceptual processes in bipolar disorder and schizophrenia

In the following chapter we present preliminary data from an ongoing study. Hence, the results and conclusions described hereafter may evolve with the inclusion of additional participants to the study.

## Introduction

The clinical and conceptual description of racing thoughts, *i.e.* the subjective over-production and acceleration of thoughts, originates from the subjective reports of bipolar disorder (BP) patients (Piguet et al., 2010). These reports of anomalous experiences which centered around the flow of thought also served as the basis for the development of the Racing and Crowded Thoughts Questionnaire (RCTQ). In mood disorders, racing thoughts have initially been associated to the 'activation' symptom which is typical of mania and mixed states (*i.e.* manic symptoms mixed with depression, and non-pure depression) (Weiner et al., 2019). By 'activation' we mean behavioral excitation, agitation, increased alertness and energy, and rapid speech. Such 'activation' is not observed in pure depression. Despite their strong association with BP and mania, racing thoughts were proposed to be a trans-diagnostic feature found in healthy populations with sub-clinical mood variations (Weiner et al., 2018) and several other psychiatric conditions including anxiety disorders, borderline personality disorder, attention deficiency hyperactivity disorder (ADHD), sleep disorders (Bertschy et al., 2020). It can be noted that thoughts can be crowded or even racing without being associated to accelerated speech or agitation. It is possible for patients to report crowded thoughts independently of an 'activation' symptom. The presence of racing thoughts in other psychosis groups of the schizoaffective spectrum has not been verified, however.

Some symptoms affecting the flow of thoughts were described as qualitatively different in BP and SZ: Bleuler described the "loosening of associations" as a typical feature of SZ (Bleuler, 1950), while "flight of ideas" and rumination were more typically associated to mood disorders (Kraepelin, 1921; Nolen-Hoeksema et al., 2008). Despite these differences, several similarities in the coordination and quality of thought processes have been described in BP and SZ. Andreasen (1979) proposed that disorders in thought are different only in their level of severity, but not in quality, between SZ and mania. In a meta-analysis on formal thought disorder, Yalincetin et al. (2017) found no significant difference between acute SZ and BP patient samples, however in stabilized patient groups subgroups could be distinguished based on formal thought disorder. These findings show the clinical relevance of studies focusing on thought processes in psychotic populations and justify the present study investigating racing thoughts in both BP and SZ patients.

The first aim of the present study was to check whether racing thoughts, originally associated to BP, are also shared by other psychiatric conditions belonging to the schizo-affective spectrum. We compared BP and SZ groups on their reported level of racing thoughts using the RCTQ self-questionnaire. The second aim of the study was to compare the two groups on an objective behavioral correlate of racing thoughts. In Chapter 3 (Polgári et al., 2021), we described a link between elevated levels of racing thoughts and difficulties in the attentional modulation of ocular behavior during viewing of the bistable Necker cube. Ocular windows are proposed to reflect the alternation between the two possible conscious percepts of the Necker cube, but at a more automatic level than manual alternations (see Chapter 2; Polgári et al., 2020). Specifically, racing thoughts are suggested to be associated to disturbances in the control of automatic perceptual processes translated by the lack of modulation in ocular window rate.

Individuals with BP, individuals with SZ, and matched HC performed a two-minute version of the bistable Necker cube paradigm. As in our previous studies, participants reported manually reversals of the perceived orientation of the cube in different experimental conditions (spontaneous viewing condition vs. focus on one of the orientations). Ocular fixations were recorded throughout the experiment. Manual and ocular measurements allowed the computation of manual windows (reflecting reversals of the two percepts at a conscious level) and ocular windows (linked to alternations with a higher temporal frequency on a more automatic processing level) (Polgári et al. 2020).

If racing thoughts are reported by SZ patients similarly to BP patients, our measure based on ocular movements will inform whether the mechanisms supposedly underlying racing thoughts are shared by the two psychiatric groups or not. If ocular measurements lead to different outcomes in the two groups, it would suggest that racing thoughts, as auto-evaluated by patients via the RCTQ, may have several sources.

## Materials and methods

### Participants

Fourteen patients with SZ (mean age ± SD: 37.64 ± 9.33; 4 females), 18 patients with BP (mean age ± SD: 37.44 ± 11.13; 14 females) and 26 healthy controls (mean age ± SD: 35.08 ± 9.75; 14 females) participated in the study. Outpatients were recruited at the University Hospital of Strasbourg and fulfilled criteria for SZ or BP according to DSM-5 (REF). Healthy controls were recruited by advertisement and had no past or current diagnosis of mood disorder or psychosis. Exclusion criteria for all participants included a past or current diagnosis of neurological disorder, ADHD, borderline personality disorder, or substance abuse. All participants had normal or corrected-to-normal vision. In accordance with the declaration Helsinki, all participants gave their informed written consent. The project was accepted by the ethics committee CPP-Est IV (IDRCB 2016-A00106-45/n°HUS 6366).

Healthy controls were matched to patients on age, gender, and level of education. Since a one-on-one matching on all criteria over the three groups is difficult (only 3 HC matched to both a SZ and a BP patient), most HC were matched only to a SZ or a BP patient. However, given that the desired number of participants in each group has not been met yet, in the analyses all HC (those matched to SZ and those to BP) were pooled together, and statistical analyses were carried out on 3 groups (HC vs. SZ vs. BP). Groups did not differ in age [$F(2, 55)=0.42$, $p>0.05$, partial $\eta^2=0.02$], however a significant difference between groups was found on their level of education [$F(2, 55)=8.45$, $p<0.001$, partial $\eta^2=0.23$]. According to Tukey HSD post hoc the SZ group had a lower level of education (12.64 years) both compared to the HC group (14.62 years) and the BP group (15.89 years) who did not differ between each other.

### Evaluation of racing thoughts

Participants reported their subjective level of racing thoughts by filling out the Racing and Crowded Thoughts (RCTQ) questionnaire (Weiner et al., 2018).

### Experimental task and procedure

The task consisted of the Necker cube bistable perception paradigm. Participants indicated their perceptual reversals of the cube via button-presses (left button-press for downward-left facing orientation, right button-press for upward-right facing orientation). Contrary to the previous version of the experiment (see Chapter 2 and 3), in this study only three experimental conditions were run: Spontaneous, Focus, and Control. The first two conditions (Spontaneous and Focus) had both a duration of 2 minutes, and their order of presentation was randomized and counterbalanced between groups. In the Spontaneous condition, participants were instructed to indicate each time the perceived orientation of the cube changed spontaneously, without focusing on any of the two orientations in particular. In the Focus condition, participants were asked to maintain the percept of their preferred orientation of the cube and switch back to it as quickly as possible in case of a perceptual reversal. In the final Control condition, two non-ambiguous versions of the Necker cube were presented alternately with a mean duration of 3 seconds for a total duration of 1 minute. Participants were instructed to indicate each time the physical orientation of the cube changed. As in our previous studies, this condition was used to verify that participants were able to report changes in the cube's orientation (whether physical or only perceptual).

### Equipment and stimuli

The experimental conditions and apparatus were the same as described in Polgári et al., (2020, 2021) (see Supplementary Materials S3 in Chapter 3).

### Data processing

The same data processing method was applied as in our previous studies (Polgári et al., 2020, 2021) (see Methods section in Chapter 2 and 3). In each condition, the number of manual windows was extracted from manual responses reflecting perceptual reversals of the Necker cube. The number of ocular windows was extracted from ocular fixations, which were classified into two clusters using the Expectation-Maximization algorithm (Witten et al., 2017).

### Statistical analysis

We report ANOVAs, sub-analyses and Tukey HSD post hoc analyses carried out on the Statistica 13.0 software by Statsoft©. In the ANOVAs, Group (HC vs. SZ vs. BP) was taken as the between-group variable. The significance level was set to $\alpha = 0.05$ throughout the analyses. Since recruitment is still ongoing for this study and the desired number of participants per group has not been met yet, we also present descriptive analyses of data.

## Results

### RCTQ score

An ANOVA conducted on the RCTQ score with group (HC vs. SZ vs. BP) as a between-group variable revealed that the groups significantly differed in their reported level of racing thoughts [$F(2, 55)=6.28$, $p<0.005$, partial $\eta^2=0.19$] (Fig.1). Tukey HSD post hoc analysis showed that both BP and SZ patient groups had higher RCTQ scores (38.11 and 37.00, respectively) compared to the HC group (12.31). The two patient groups did not differ between each other.

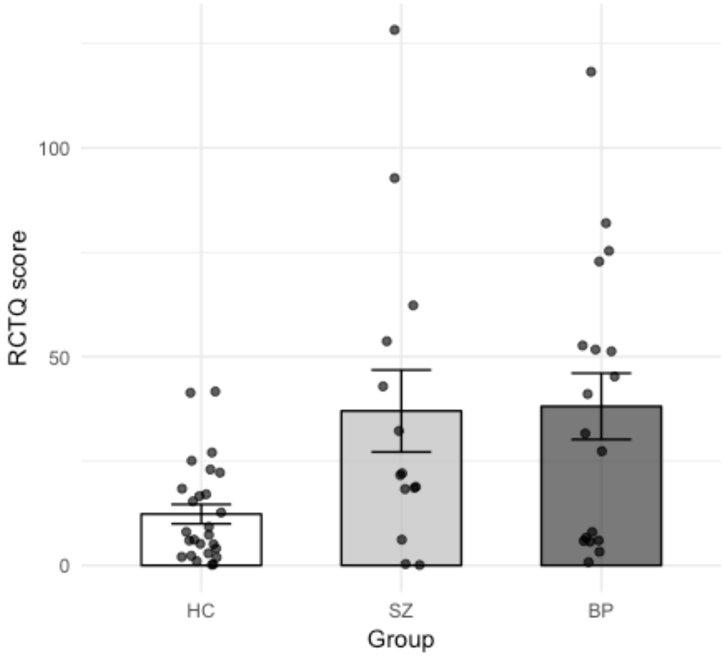



**Figure 1.** Average scores at the Racing and Crowded Thoughts Questionnaire (RCTQ) of the three experimental groups (HC=healthy controls, SZ=individuals with schizophrenia, BP=individuals with bipolar). Error bars represent ±SEM and gray dots represent individual data points.

### Manual windows

An ANOVA conducted on the number of manual windows with group (HC vs. SZ vs. BP) as a between-group variable and experimental condition (Spontaneous vs. Focus) as a within-group variable revealed a main effect of experimental condition [$F(1, 55)=17.69$, $p<0.0001$, partial $\eta^2=0.24$] with a lower number of manual windows in the Focus condition (19.86) compared to the Spontaneous condition (25.17) (Fig. 2a). No significant effect of group or interaction between variables was found. In all three groups a majority of participants presented a modulation of the number of manual windows between conditions, *i.e.* fewer windows in the Focus compared to the Spontaneous condition: 10 SZ patients out of 14 (71.43%), 13 BP patients out of 18 (72.22%), and 16 HC out of 26 (61.54%).

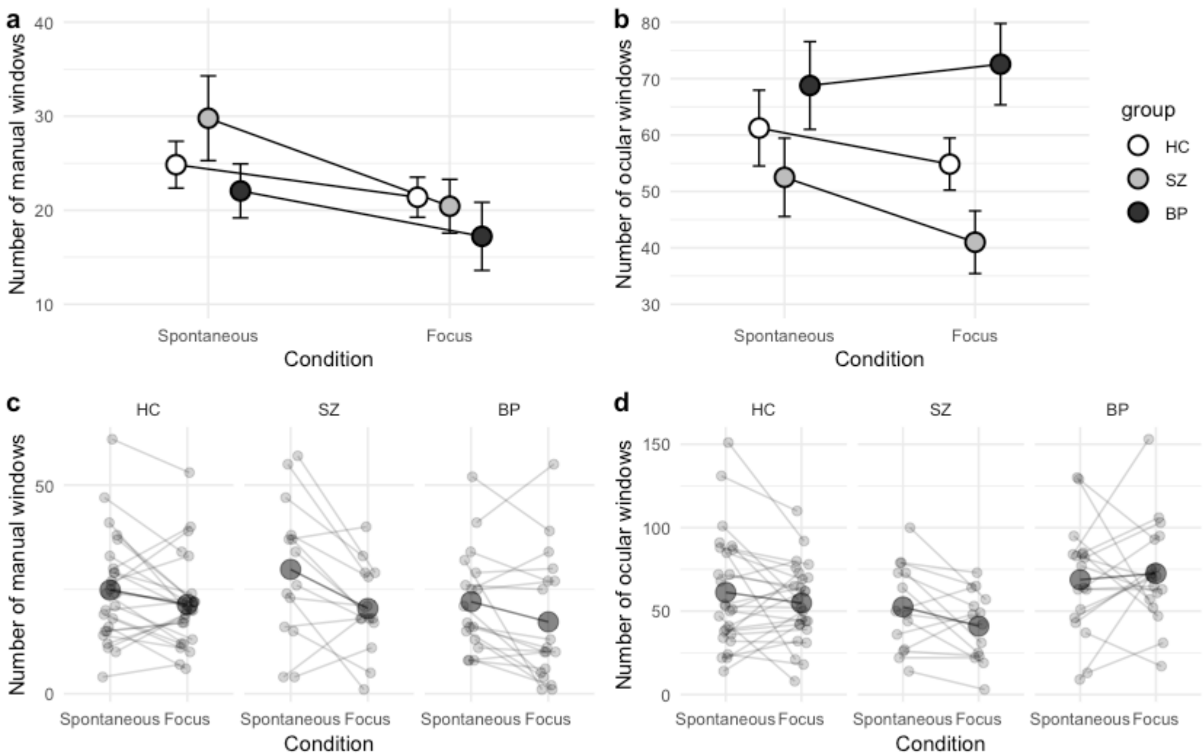



**Figure 2.** Average number of manual (a) and ocular windows (b) produced in the Spontaneous and Focus conditions by the three experimental groups (HC=healthy controls, SZ=schizophrenia patients, BP=bipolar patients). Error bars represent ±SEM.
Group averages and individual data points in each condition are depicted for manual windows (c) and ocular windows (d).

## Ocular windows

A similar ANOVA with the same variables conducted on the number of ocular windows revealed a significant effect of group [$F(2, 55)=3.70$, $p<0.05$, partial $\eta^2=0.12$] (Fig. 2b). According to Tukey HSD post hoc analysis the BP group had a higher number of ocular windows averaged over conditions (70.67) compared to the SZ group (46.75). The HC group presented an intermediate average number of ocular windows (58.04) and did not differ from the other groups. No significant effect of condition or interaction between variables was found. However, visual inspection of data points suggested a lack of modulation of the number of ocular windows between the Spontaneous and the Focus conditions in the BP group (Fig. 2b). This was also supported by the descriptive analysis of individual data points: in both the SZ and HC groups a majority of participants produced fewer ocular windows in the Focus compared to the Spontaneous condition (10 out of 14 and 15 out of 26, or 71.43% and 57.69%, in the SZ and HC groups respectively), however this tendency was inversed in the BP group with a minority of participants (7 out of 18, or 38.89%) decreasing the number of ocular windows from Spontaneous to Focus.

### Qualitative analysis of the effect of task order

When taking into account the order in which participants performed the two main experimental conditions, the sizes of the sub-groups become too small for statistical analyses with this additional 'order' variable. Hence, the effect of task order will be verified in future analyses once more participants will have been included in the study.

## Discussion

The first aim of the present study was to see whether racing thoughts, originally associated to BP, can also be found in SZ. Both SZ and BP patients reported similar scores at the RCTQ self-questionnaire. Both these scores were significantly higher than that reported by the HC group. This suggests that racing thoughts, as evaluated subjectively by participants, are present in different groups of the schizo-affective spectrum.

A second aim was to verify whether conscious and more automatic alternations of the Necker cube, as measured by manual and ocular windows respectively (Polgári et al., 2020), relate to racing thoughts similarly in the two groups. The three groups differed in the number of ocular windows they produced, with the BP group presenting an elevated number of ocular windows averaged over the two experimental conditions. Although results are still preliminary and it is too soon to draw solid detailed conclusions, the observation of individual data points suggests that BP patients present a deficit in the modulation of ocular behavior between experimental conditions, with an abnormally high number of ocular windows in the Focus condition. Most participants of both the HC and SZ patient groups decreased the number of ocular windows in the Focus condition, which is in line with previous results (Polgári et al., 2020) and extends them to a population with a diagnosis of SZ. Interestingly, SZ patients displayed seemingly normal ocular behavior comparable to that of the HC group. This is all the more intriguing that individuals with SZ reported high levels of racing thoughts, comparable to BP patients. This preliminary finding questions the meaning of the high RCTQ score in schizophrenia.

In our previous study (Polgári et al., 2021; Chapter 3) a deficient modulation of the ocular windows rate, especially in the Focus condition was related to high levels of racing thoughts in BP patients (note that in that study the group presenting the highest levels of racing thoughts was only composed of BP patients). In the present study this pattern is replicated in the BP group, however the similarly high levels of racing thoughts reported by SZ patients are not followed by altered ocular behavior. The results suggest that the level of information processing that is captured by ocular windows is altered in BP (with a heightened and non-controlled ocular windows rate), but preserved in SZ patients (with a modulation comparable to HC).

Several explanations to these findings are possible. It may be that in SZ an alteration is present at an intermediate processing level in the perceptual hierarchy comprising the lower level reflected by ocular windows and the higher level corresponding to conscious thought (*i.e.* the level at which racing thoughts are manifested). This way, anomalies at the level of conscious thought (*i.e.* racing thoughts) are present in both SZ and BP, however the deficient source mechanisms are at a different level of the hierarchy of information processing. It is possible that racing thoughts may have several different potential sources and the mechanisms that are investigated here with manual and ocular window measurements are only affected in BP. It is to be noted that racing thoughts are evaluated subjectively by patients, and are thus strongly dependent on individuals' decisional mechanisms, meta-cognitive capacities, and other high-level cognitive functions. We may wonder whether the RCTQ evaluates the same thing in SZ and BP. Considering that the RCTQ is a self-questionnaire, it is conceivable that thought processes that are different in SZ and BP are interpreted similarly by the patients while filling out the questionnaire. For instance, SZ patients may find disorganized thoughts to fit well with items of the RCTQ which describe "the mind jumping from one thought to another" or an "overflow of thoughts". The RCTQ undeniably reflects something from the patients' thought processes, both in BP and SZ. However, our results question the specificity of this self-rating scale and show the usefulness of additional objective measures.

One obvious limitation of the study is the small number of participants per group. Including more participants in the study will confirm or disconfirm our preliminary findings and interpretations. This will also allow the comparison of SZ and BP groups to their own matched control group, further improving the statistical power of our study. Although a confounding effect of level of education, which differed between groups, cannot be fully excluded, such an effect is unlikely considering our results. The level of education was comparable between the HC and BP groups and the SZ group had a lower level of education. If level of education played a role on ocular window rates, we would expect it to affect the modulation of this rate in the SZ group, however this was not the case. The SZ group had similar ocular behavior to that of the HC group, thus level of education seems unlikely to explain the elevated ocular window rate in BP.

All in all, our preliminary findings suggest that racing thoughts are reported to a similar degree in SZ and BP, however the sources of racing thoughts are suggested to be different in the two conditions. Our results show that seemingly similar thought processes, such as racing thoughts, present in both BP and SZ may have distinct underlying mechanisms. These findings highlight the usefulness of combining subjective measures of psychopathological phenomena with more objective measures in order to better understand the pathophysiological source(s) of these phenomena.

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In the previous chapter, we found a divergence between SZ and BP related to perceptual processing at the level of the subjective present. These findings are in line with our hypotheses concerning perturbations in information integration in time that would affect the two disorders at different time scales.

In the next chapter we again contrast the two clinical groups, but this time on temporal information processing concerning order. Deficits in order processing have already been described in SZ, however, no data have been published on temporal order processing and BP. The results of this study will inform about whether order deficits are specific to SZ or shared between the two conditions.

Chapter 5

# Impaired visual temporal order judgment in schizophrenia, but not in bipolar disorder

In the following chapter we present preliminary data from an ongoing study. Hence, the results and conclusions described hereafter may evolve with the inclusion of additional participants to the study.

## Introduction

In recent years, a growing body of literature consistently found evidence suggesting altered timing and time perception in schizophrenia (SZ). While most studies focused on temporal duration (*i.e.* time perception tasks) (for reviews see Ciullo et al., 2016; Thoenes & Oberfeld, 2017; Zhou et al., 2018), only few studies were conducted on succession (*i.e.* temporal processing), and this is especially true for temporal order processing. Although their number is small, the studies investigating temporal order in SZ converge to the conclusion that temporal order processing is impaired in SZ (Braus, 2002; Tenckhoff et al., 2002; Capa et al., 2014; de Boer-Schellekens et al., 2014; for reviews see Thoenes & Oberfeld, 2017; Zhou et al., 2018).

Disturbances in SZ were found in another facet of temporal processing, namely the detection of simultaneity and asynchrony. Performance on visual simultaneity judgment (SJ) tasks were found to be impaired in SZ: patients present an extended visual simultaneity threshold, meaning that they need a longer delay between two successive stimuli (or Stimulus Onset Asynchrony, -SOA-) than healthy controls to correctly judge them as asynchronous (Giersch et al., 2009; Lalanne, van Assche, et al., 2012a; Lalanne, Van Assche, et al., 2012b; Stevenson et al., 2017). A proper detection of asynchronies is a logical pre-requisite for the detection of temporal order, hence deficits in simultaneity and asynchrony detection could, in principle, explain SZ patients' impaired performance at temporal order judgment (TOJ) tasks. However, in a study comparing SZ patients' performance at SJ and TOJ tasks Capa et al. (2014) showed that patients' deficits at order detection are more severe than that predicted by their performance at SJ tasks. This suggests that ordering in particular is especially difficult for Sz patients.

Order deficits seem to extend beyond the limits of perception as investigated in the previously reviewed studies using psychophysics methods, since they have been found in studies on memory. In recency discrimination tasks where, after exposition to two words in two successive sessions, in a test phase participants had to judge which of the two words they had seen more recently. SZ patients performed more poorly than matched controls indicating that patients have impaired memories concerning temporal order (Schwartz et al., 1991; Elvevåg et al., 2000). Similar impairments were found for the recognition of spatio-temporal sequences and they were more severe than general memory capacities (*e.g.* retention and recall of items independently of sequence) (Dreher et al., 2001). Moreover, SZ patients were found to be impaired at ordering past and future events that they had previously dated in a pre-test phase (Ben Malek et al., 2019).

Thus, SZ patients seem to be generally impaired in tasks involving ordering events or items. The results imply that order processing in particular is altered in patients with SZ, however to what extent this deficit is specific to SZ is unknown. Could order deficits distinguish SZ from other psychopathologies with similar symptoms, such as bipolar disorder (BP), another psychotic disorder? To our knowledge, no data has been published on order processing (or processing of succession in general) in BP.

Comparisons between SZ and BP on other timing tasks had been done however, revealing common timing deficits to the two conditions. Bolbecker et al. (2014) found evidence suggesting that both SZ and BP patients are impaired similarly at sub-second duration estimations, with higher timing variability in both groups compared to controls. These findings indicate that SZ and BP patients share deficits in timing and time perception mechanisms concerning the content of time (*i.e.* duration). It is, however, unknown whether similarities between the two conditions extend to other aspects of time, namely succession. The aim of the present study was to investigate temporal processing in SZ and BP in a TOJ task. We sought to replicate the results of the literature concerning deficient ordering in SZ and to check to what extent these deficits are specific to SZ, or can be found in BP too. Temporal order processing in BP has not been investigated yet, thus our results will be informative about the extent to which the two psychotic disorders are comparable relative to temporal processing.

## Materials and methods

### Participants

Twenty-four patients with SZ (mean age ± SD: 38.96 ± 9.89; 4 females), 19 patients with BP (mean age ± SD: 37.21 ± 10.86; 15 females), and 30 healthy controls (HC) (mean age ± SD: 35.87 ± 10.17; 15 females) participated in the study. The studies presented in this chapter and Chapter 4 are part of the same ongoing study, thus for details concerning recruitment and exclusion criteria see the "Materials and methods" section of Chapter 4. The number of participants is lower in Chapter 4 compared to the present chapter, because eye tracking measurements are often difficult and data from more participants had to be excluded in that study. As described in Chapter 4, a one-on-one matching of participants over the three groups was not possible and HC matched to SZ or BP patients were pooled together. The three groups did not differ in age [$F(2, 70)=0.61$, $p>0.05$, partial $\eta^2=0.02$], however a significant difference was found on their level of education [$F(2, 70)=13.93$, $p>0.05$, partial $\eta^2=0.28$]. Tukey HSD post hoc analysis revealed that SZ patients had a lower level of education (12.42 years) compared to HC participants (14.57 years) and BP patients (15.79 years) who did not differ between each other.

### Equipment

The study was conducted in a quiet and dimly lit room. Visual stimuli were generated by a Hewlett-Packard Compaq 8100 Elite 2 computer using programs written on MATLAB software (2007) by MathWorks and PsychToolbox (Brainard, 1997) and presented on a 21" Sony Triton CRT screen.

### Stimuli

Stimuli used in the experiment are depicted in Fig. 1. The background was set to a black color throughout the experiment. The appearance of a central fixation dot (diameter 0.3 degrees of visual angle -deg. VA-) indicated the beginning of a trial. After a fixed period of 500 ms, two target squares (side length 2.5 deg. VA) filled in gray appeared on both sides of the fixation dot. The distance between the center of the squares was set to 12.2 deg. VA. The squares appeared successively following three Stimulus Onset Asynchronies (SOA) corresponding to the 3 experimental conditions: SOA=0 ms, SOA=17 ms, SOA=100 ms. The targets stayed on the screen for a maximum of 2 seconds, or until a button press occurred. We choose to use only three SOAs to determine the neural correlates of order processing with EEG and fMRI (data not shown).

### Experimental task and procedure

Each experimental condition comprised 150 trials yielding a total of $3 \times 150 = 450$ trials. In the conditions SOA=17 ms and SOA=100 ms (*i.e.* when targets appeared asynchronously) each order of appearance ('left-right' and 'right-left') was equally represented. Trials for each condition were mixed and displayed in a randomized order.

The task consisted of a TOJ task where the participants were asked to determine the order of the two target squares' appearance and respond to the side of the first target via a left or right button-press.

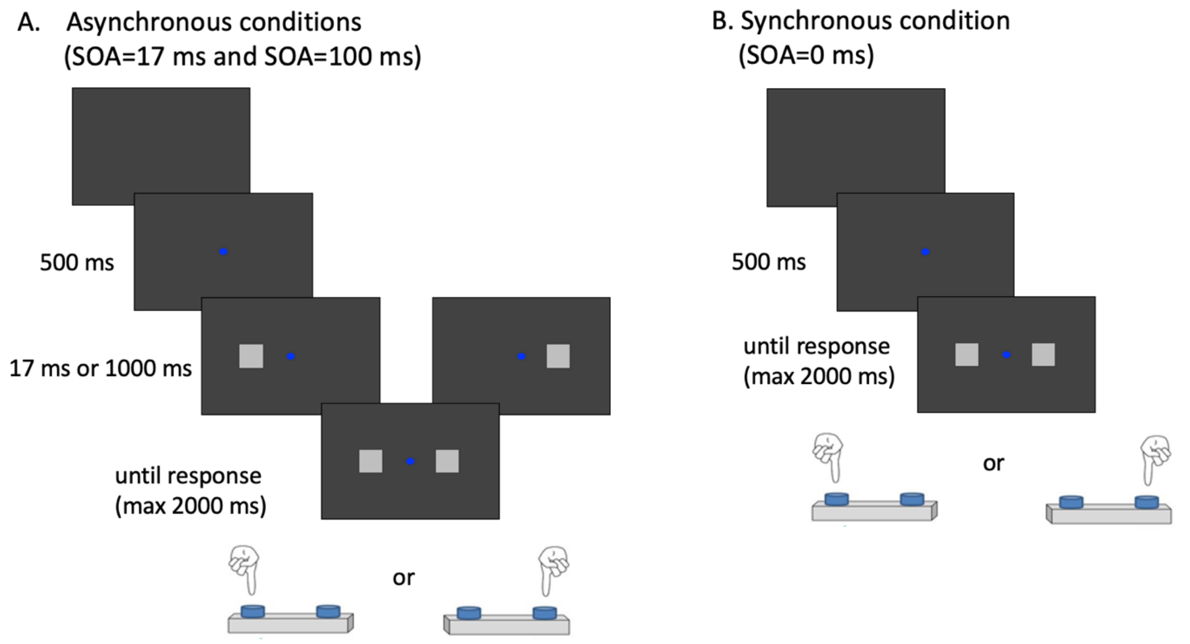


**Figure 1.** Schematic representation of the stimuli used in the conditions with an asynchronous target (*i.e.* SOA=100 ms or SOA=17 ms) (a) and in the condition with synchronous targets (*i.e.* SOA=0 ms).

## Data processing

Data processing was carried out in the R Studio environment (RStudio Team, 2016). Trials corresponding to omission errors (*i.e.* no response given by the participant) and anticipatory responses (*i.e.* response time < 150ms) were discarded from further analyses. Correct response rate (percent correct response) were calculated for each order ('left-right' and 'right-left') in each condition with an asynchrony (*i.e.* condition with a physical order), while for the synchronous condition "right first" response rate was calculated for each participant. Correct response rate or "right first" response rate were then averaged over participants in each group (SZ, BP and HC).

## Statistical analysis

We report ANOVAs and differences were localized using Tukey HSD post hoc analyses and sub-analyses. All analyses were carried out on the Statistica® software. The level of significance was set to $\alpha = 0.05$ throughout the analyses. The partial eta-squared ($\eta^2$) were added as a measure of effect size.

## Results

The choice of only three SOAs during the task impeded us from calculating thresholds in a typical way, and here we report results for each asynchrony, 100 and 17 ms.

### SOA=100 ms

In the condition with SOA=100ms, an ANOVA conducted on correct response rate with the order of target presentation ('left-right' vs. 'right-left') as a within-group variable and group (SZ vs. BP vs. HC) as a between-group variable revealed a significant main effect of group [$F(2,70)=4.09$, $p<0.05$, partial $\eta^2=0.10$] (Fig. 2a). Tukey HSD post hoc analysis showed that the SZ group had a lower performance (86.75 % correct responses) compared to the HC group (95.75 % correct responses). The BP group did not differ statistically from the other two groups, however their performance was very close to that of the HC group's (94.21 % correct responses). No effect of order of target presentation or interaction between the variables was found.

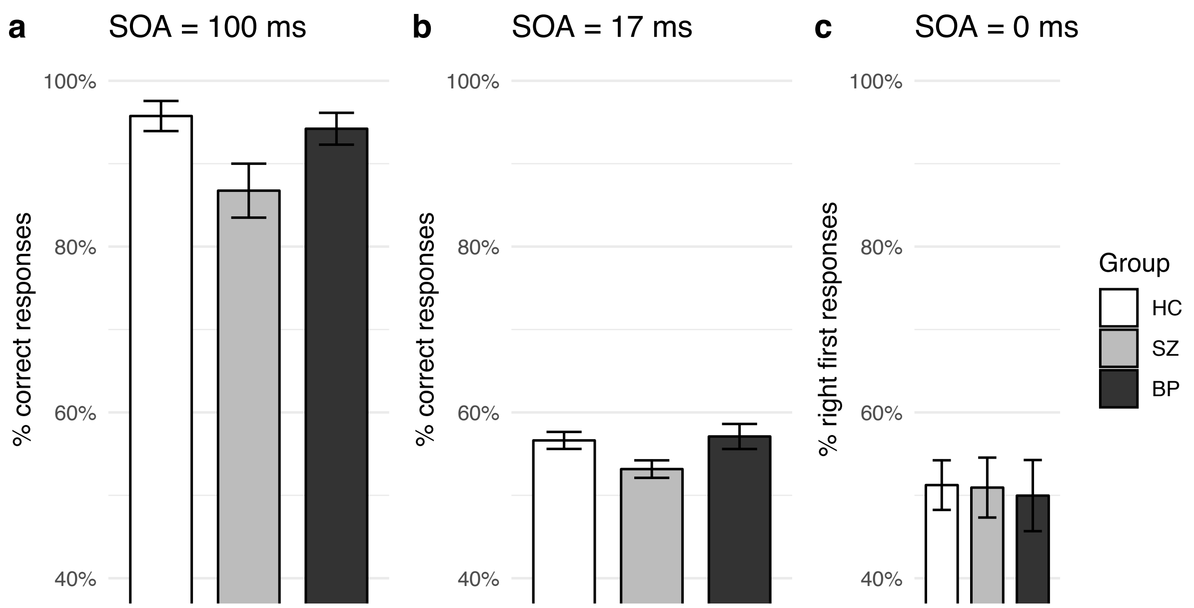


**Figure 2.** Performance of the three groups (HC=healthy controls, SZ=individuals with schizophrenia, BP=individuals with bipolar) in the condition with SOA=100 ms (a), with SOA=17 ms (b), and with SOA=0 ms (c). Error bars represent ±SEM and gray dots represent individual data points.

### SOA=17 ms

In the condition with SOA=17ms, an ANOVA on correct response rate with the same variables as described above revealed a significant main effect of group [$F(2,70)=3.27$, $p<0.05$, partial

$\eta^2=0.08$] (Fig. 2b). Tukey HSD post hoc analysis failed to reveal between-group differences. We conducted sub-analyses comparing groups one by one in order to localize the differences. They showed that the SZ group (53.17% correct responses) significantly differed from both the HC (56.62% correct responses, $F(1,52)=5.42$, $p<0.05$, partial $\eta^2=0.09$) and the BP groups (57.10% correct responses, $F(1,41)=4.81$, $p<0.05$, partial $\eta^2=0.11$) who did not differ between each other [$F(1,47)=0.07$, $p>0.05$, partial $\eta^2=0.002$]. Again, no effect of order of target presentation or interaction between the variables was found.

### SOA=0 ms

In the condition with SOA=0 ms, an ANOVA conducted on "right first" response rate with group (SZ vs. BP vs. HC) as a between-group variable revealed no effect of group [$F(2,70)=0.03$, $p>0.05$, partial $\eta^2=0.0009$] (Fig. 2c). The value of mean percent "right first" responses was close to chance in all three groups, as expected.

## Discussion

The aim of the present study was to investigate to what extent previously reported deficits at temporal order processing are specific to SZ or extend to BP, another psychotic disorder. First, we replicated the findings of the literature and brought further evidence that impaired performance on temporal order judgment tasks are robust findings in SZ. Second, temporal order processing seems preserved in BP. Performance for trials with supra- and subthreshold SOAs were comparable in the BP and HC groups. To our knowledge ours was the first study to investigate temporal order processing in BP.

Interestingly, HC and BP patients seem to have a better performance than SZ patients in trials with SOA=17 ms. This SOA is very close to the threshold for conscious detection of order (Capa et al., 2014; de Boer-Schellekens et al., 2014), and even asynchronies (Elliott et al., 2007; Giersch et al., 2009). In our task HC and BP patients may have detected the order of the stimuli in a small number of trials. Interestingly, this was not the case of SZ patients whose performance was below that of the two groups', close to chance. Moreover, SZ patients performed poorly both for suprathreshold and subthreshold SOAs. The fact that there is a suprathreshold impairment replicates earlier results (Capa et al, 2014). These results can be interpreted as further evidence that temporal order in general is a deficient process in SZ, independently of the temporal scale.

In sum, our results indicate that SZ patients are specifically impaired at temporal ordering. These deficits may be specific to SZ, since BP patients presented preserved performance at the TOJ task, comparable to HC. We cannot exclude however that other disorders belonging to the schizo-affective spectrum may present order deficits (*e.g.* schizo-affective disorder). It is possible that deficits at order processing are related to a specific symptom or dimension which can be found in different psychopathological conditions, such as disorganization symptom. In their study with SZ patients, Capa et al. (2014) found no correlation between patients' performance at the TOJ task and clinical symptoms. However, a direct investigation of the potential link between clinical symptomatology and order deficits in different clinical populations may improve our understanding about alterations in timing and temporal processing in psychopathological conditions.

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The results of the previous chapter support the idea that deficits in the processing of temporal order are specific to SZ. These temporal order judgement deficits rejoin another temporal disturbance in SZ which affects information integration at an automatic, non-conscious level, as evidenced by indirect measures in SJ tasks. It is unknown whether the deficits in order processing (at a conscious level) are related to disturbances at the level of automatic, non-conscious processing. Resolving this question requires to first determine in healthy individuals at which processing level temporal ordering starts.

In the next chapter we describe a study investigating whether temporal order processing is present already at an automatic, non-conscious level. The results of this study in healthy participants will help orient future research on temporal processing in SZ.

# Chapter 6

# The processing of subthreshold visual temporal order is transitory and motivation-dependent

The following chapter contains the original manuscript prepared for submission as: Patrik Polgári, Ljubica Jovanovic, Virginie van Wassenhove & Anne Giersch. (in prep.) "The processing of subthreshold visual temporal order is transitory and motivation-dependent".

*« Peut-on percevoir l'ordre là où l'on ne pourrait même pas distinguer la succession ? »*

*("Can one discriminate order when not even succession is being perceived?")*

*Fraisse (1957)*

## 1. Introduction

Order is an intrinsic property of our conscious experience. We experience time as flowing in a linear fashion (*i.e.* 'the arrow of time') and events, including our percepts, our actions and even our thoughts, take place either simultaneously or successively on the arrow of time. Thus, ordered sequences are ubiquitous in our environment and our everyday behavior (Lashley, 1951). However, an order of percepts does not necessarily imply a percept of order (James, 1890). Events that take place sequentially in our environment are processed sequentially by the brain, that is one after the other. Whether this also automatically entails the coding of temporal relationships of the different events relative to one another (*i.e.* processing the order of the events) is still an open question in psychology and cognitive sciences. Does the perception of order arise automatically from the sequential processing of events? Or is perceiving order derived only in constrained conditions when additional cognitive processes are mobilized? The aim of the present study was both to investigate the existence of automatic order processing, and the constraints limiting such mechanisms.

Subjectively, we feel immersed in our dynamic environment, which means that we feel that we are able to track the order of events as they take place. This phenomenological argument is in favor of an automatic processing of order. From an empirical standpoint, an automatic processing of order is plausible in light of several experimental results. Humans can extract and encode ordered sequences implicitly, *i.e.* when task instructions do not draw attention to the fixed temporal structure of the stimulus presentation, and participants are unable to report the previously viewed sequences in a post-test phase (Curran & Keele, 1993; Fiser & Aslin, 2002; Jun & Chong, 2016; Kidd et al., 2012). In those tasks, the order of the stimuli composing the sequences is clearly visible: for example, four consecutive stimuli appear sequentially in different locations, and the participants have to react after each stimulus. Participants' performance benefits from the repetition of a given sequence pattern, even when they are not informed and do not detect any pattern (Curran & Keele, 1993). Automatically encoded ordered sequences can be exploited implicitly to facilitate the detection of a subsequent target by guiding attention to its location (Olson & Chun, 2001; Ono et al., 2005). Studies in uni- and multi-sensory perception showed that the sequential order in which stimuli are presented is also encoded implicitly as a temporal sequence (Seitz et al., 2007). Additionally, implicit sequences can influence the perception on subsequent trials when the sequences are presented supraliminally (*i.e.* the asynchrony between elements of the sequence can be detected) or subliminally (*i.e.* asynchrony under the threshold of conscious perception) (Van der Burg et al., 2013; Harvey et al., 2014; Van der Burg et al., 2018; Marques-Carneiro et al., 2020). These results suggest that the brain can process temporally ordered sequences in an automatic manner.

Nevertheless, processing the sequence of stimuli is not equivalent to the processing of the relative position of the individual stimuli inside the sequence, that is, ordering them. Processing a sequence of stimuli, or benefitting from the repetition of a sequence, can be based on an automatic serial preparation to successive stimuli, *i.e.* an automatic replay of the sequence (Los et al., 2017). It does not require the coding of a higher-level representation of order between successive elements. The formation of such a representation might take unnecessary time which would be inconsistent with the high temporal resolution of automatic, unconscious mechanisms allowing us to follow information fluently over time (Marques-Carneiro et al., 2020). Moreover, automatically deriving the order of any set of events relative to one another may become an exponential burden when being in a busy street full of dynamic events that are not necessarily related to one another.

In a recent study, Chassignolle et al. (2021) found evidence suggesting that the order of stimuli that is not detected consciously can still be processed at an automatic level. In their cued reaction time task paradigm, the order of two colored cues ('red then green' or 'green then red') predicted the upcoming target shape ('+' or 'x') to which participants responded manually. Participants were informed about the contingency between cue-order and targets prior to taking part in the experiment. Participants improved their reaction times (RT) when the ordered cues were separated by suprathreshold, easily detectable 66 ms asynchronies, but also and, importantly, by subthreshold, undetected 17 ms asynchronies, compared to a control condition where the cues appeared synchronously (*i.e.* no physical order information). These results indicate that, even when under the threshold of conscious perception, order can be processed and used to prepare a response. However, the effect sizes were rather small, and given that participants were informed about the relationship between the order of the cues and the target, we wondered to which extent the effect was under top-down control.

In the present study we aimed to replicate the facilitation effect linked to an automatic order processing described by Chassignolle et al. (2021). We used a more difficult task than in

Chassignolle et al. (2021), to verify whether order could be used to orient participants' response choice in addition to speeding up their responses. Like in Chassignolle et al. (2021), the paradigm consisted in verifying whether subjects could use a short 17 ms asynchrony between two visual cues to predict the target luminance values. Participants discriminated the target luminance values, and those were contingent on the order of presentation of the two visual cues. Importantly, target values were chosen to be difficult to discriminate so that the baseline correct response rates were low enough to observe a potential facilitation effect. Additionally, in order to replicate the conditions of Chassignolle et al.'s (2021) study, participants were explicitly informed about the contingency between subthreshold temporal order cues and targets.

In our first experiment, the order of the cues predicted the target values in one group ('Predictive' group), while in another group no contingency was introduced so that the order of the cues did not predict the upcoming target ('Non-predictive' group). Similar to the analyses in Chassignolle et al. (2021), the performance obtained in the 'Asynchronous' condition (17 ms stimulus onset asynchrony, or SOA) was compared to that in a 'Synchronous' (control) condition (0 ms SOA). Our design aimed to verify whether the asynchrony had a non-specific arousing effect, independent of any order effect. Any non-specific effect of the asynchrony between the cues was expected to result in improved performance in both groups for asynchronous trials, whereas a replication of the results of Chassignolle et al. (2021) should lead to improved target detection thanks to the cues' order only in the 'Predictive' group. Furthermore, we had a long enough task to verify the evolution of performance over time. We reasoned that if participants' responses were based on the learning of the temporal sequence of cues and targets, similar to a temporal contextual cuing effect (*e.g.* "left cue" *then* "right cue" *then* "light gray target"), performance would stabilize and even improve over time asymptotically (Curran & Keele, 1993; Fiser & Aslin, 2002; Jun & Chong, 2016). In contrast, if the subthreshold order information could indeed be exploited, resulting from the formation of a representation of order and its use to predict the target (*e.g.* "left-right" *so* "light gray target"), performance may require cognitive resources and instead wear off with time. During the training phase, participants were trained to relate the order to the gray level associate one order with the target luminance (so that *e.g.* "left *then* right" cue signaled "light gray target" and "right *then* left" cue signaled "dark gray target"). If establishing a representation of order for sub-threshold asynchronies is usually avoided in order to discard spurious ordering in busy environments, the effect may disappear at a distance of the training phase (Poncelet & Giersch, 2015). This would be all the more the case that it is difficult to confirm the representation consciously in case of sub-threshold asynchronies.

We conducted a second experiment to explore more directly if the effects were under endogenous control, and more specifically modulated by participants' motivation. The same design was used as for the 'Predictive' group in Experiment 1, but this time participants' motivation was manipulated via a monetary incentive in two groups ('Incentivized' vs. 'Non-incentivized' groups). A stronger improvement in target discrimination that is linked to cue order in the Incentivized group compared to the Non-incentivized group would suggest that top-down factors, such as motivation, can play a role in the modulation of the use of subliminal order information.

## 2. Experiment 1

### 2.1. Methods

Participants

Twenty-five healthy participants (13 females/12 males, mean age ± SD = 21.16 ± 2.19) were recruited for Experiment 1. All participants had normal or corrected-to-normal vision and reported no neurological or psychiatric disorders. After analyzing performances in the Temporal Order Judgment (TOJ) tasks, one participant was excluded from further analyses because of above chance performance for 17 ms asynchronies, thus we considered that order with 17 ms SOA was not subliminal for this subject. Further analyses were conducted on the remaining 24 participants (12 females/12 males, mean age ± SD = 21.17 ± 2.24).

The project was approved by the local ethics committee of the University of Strasbourg (Unistra/CER/2018-02/3). All participants gave their informed written consent in accordance with the declaration of Helsinki (2018) and received a monetary compensation of 15 euros.

Equipment and apparatus

The experiment was conducted in a quiet, dimly lit room. The experimental paradigms were run using the MATLAB software (R2007a, MathWorks) with CRS VSG Toolbox for MATLAB. Stimuli were generated on a 20" 120 Hz CRT screen (resolution 800×600) using ViSaGe (Visual Stimulus Generator) by Cambridge Research Systems. Manual responses were recorded using two response-buttons. The distance between participants and the screen was maintained fixed at 110 cm using a chin rest.

### Stimuli

The background was set to a gray (21.0 cd/m$^2$) color throughout the experiment. All trials started with a central fixation dot surrounded by two black squares (0.76 cd/m$^2$, side length 0.7 deg. VA) on the left- and right-hand side. The distance between the centers of the two squares was set to 4.8 degrees of visual angle. Each square contained at its center a dot identical to the central fixation dot. After a fixed period, the dots inside the squares turned white (47.5 cd/m$^2$) representing the cues which followed three spatiotemporal patterns corresponding to the three conditions that were run in the Experiment (Asynchronous, Synchronous, No-Go, see below). Targets were two grey values that were designed to differ only slightly in luminance (light gray 18.3 cd/m$^2$, dark gray 16.7 cd/m$^2$) so that they would be difficult to distinguish.

The distance and the delay between the flash cues were chosen so that apparent motion is unlikely to take place (Strybel et al., 1990). We wanted to avoid a perception of apparent motion because it might have facilitated the detection of order (Cass and Van der Burg, 2014, 2019; Spence et al., 2003).

### Experimental tasks and procedure

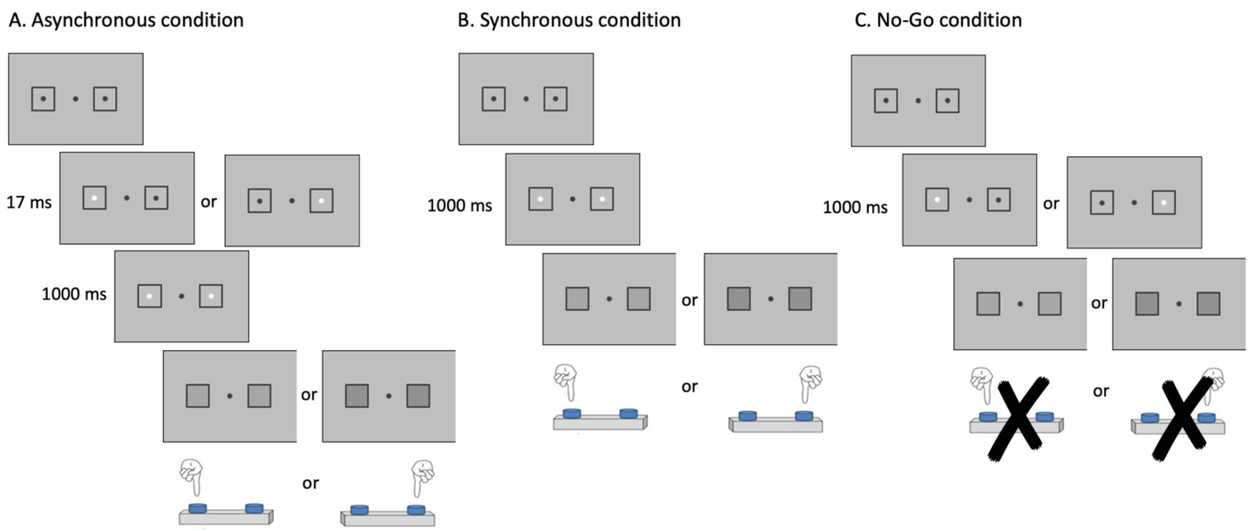


**Figure 1.** Schematic representation of the stimuli used in the Experiment 1 and 2.
All trials started with a central fixation dot surrounded by two squares, each containing a dot. Cues corresponded to the two lateral dots changing color from black to white either one after the other separated by a 17 ms delay (A), or synchronously (B). After a 1000 ms presentation period the cues were replaced by the target luminance values ('light gray' or 'dark gray') that participants had to identify via a button press on the corresponding side (left or right). In the No-Go condition the cue corresponded to only one of the dots turning white for 1000 ms, after

which the target appeared. In this No-Go condition participants were instructed to withhold their response. In the example shown in the figure a 'left then right' cue order is associated to the 'light gray' target and a leftward response, while a 'right then left' cue order is associated to the 'dark gray' target and a rightward response. The association between cue order, target luminance value and response side were all counterbalanced between participants. Stimuli and timeline are not drawn to scale. For illustration purposes the target luminance values were changed to be easier to discriminate than the ones used in the real tasks.

*-Subthreshold temporal order cued discrimination task*

In the Asynchronous condition (Fig. 1A), the cues (*i.e.* black dots inside the squares turning white) appeared one after the other, separated by a 17 ms asynchrony. Each cue order ('left-right' and 'right-left') was equally represented. The cues remained on the screen for 1000 ms, and were then replaced by a target (*i.e.* one of two gray values) filling the squares on both sides synchronously. The target remained on the screen until a response was given by the participant via a left or right button-press.

The Synchronous condition (Fig. 1B) was identical to the Asynchronous condition except for the white cues which appeared synchronously on the screen (SOA = 0 ms).

The No-Go control condition (Fig. 1C) was identical to the Asynchronous condition with the difference that only one of the two lateral dots turned white for a duration of 1000 ms before the presentation of the target gray value. In this condition, participants were instructed not to make a button-press in response to the gray value. This condition was introduced to motivate participants to attend to both the first and second cue before responding to the target in the other two experimental conditions. Theoretically, it would be possible to predict the upcoming target by attending only to the position of the first or the last element of the sequence of the cue stimuli, without taking into account the order relationship between them. A single stimulus would then lead to the response corresponding to either the first or second cue stimulus. A high commission error rate in the No-Go condition would indicate that the participant did not take into account both of the cues before giving a response in the other two conditions, thus it was used as an exclusion criterion.

Trials for each condition were mixed and displayed in a randomized order in each block.

The task consisted of two blocks of equal length separated by a short break. The number of trials in each block was 48 in the Asynchronous, 48 in the Synchronous, and 24 in the No-Go condition, yielding a total of $2 \times (48 + 48 + 24) = 240$ trials per participant. In this task, participants were divided into two groups.

The experimental design and procedure are depicted in Fig. 2A. In the 'Predictive' group (n=12, 11 females) the luminance of the target gray value (light or dark) was contingent on the order of the cues in the Asynchronous condition ('left-right' or 'right-left'), thus the subthreshold order predicted the upcoming target. The combinations of cue order ('left-right' or 'right-left'), target gray value (light or dark) and response side (left or right) were counterbalanced between participants in this group. In the 'Non-predictive' group (n=12, 8 females), a given cue order preceded a specific target gray value in only 50% of the trials and the other target in the remaining 50% of the trials, thus the subthreshold order did not predict the upcoming target. The combinations of target gray value and response side were counterbalanced between participants of this group. The Non-predictive group was introduced in the experimental design to make sure that any facilitation effect observed on participants' performance in the Asynchronous condition compared to the Synchronous condition specifically result from the processing of the order of the cues and not a non-specific effect of the asynchrony between the cues. The two groups did not differ in age [$F(1,22)=0.29$, $p=0.59$, partial $\eta^2=0.01$].

Prior to performing the subthreshold temporal order-cued discrimination task, all participants completed four training blocks. The first training block, used to familiarize participants to the target grey values, consisted of 24 randomly presented light and dark gray trials where participants received an oral feedback on the identity of each target gray value and were asked to press the response-buttons accordingly. In the second training block, all participants were told about the contingency between the subthreshold temporal order of the cues and the target gray values and performed two sub-blocks of 30 trials in a randomized order, containing either only light gray or dark gray trials (with the corresponding cue orders). The aim of this training block was to promote the association between each subthreshold order and the corresponding target gray value (similar to a classic conditioning paradigm). In the third training block participants performed 20 Asynchronous trials with the two types of asynchronies (cue order with its associated gray level) in randomized order and in the fourth training block a short, 40 trial-long version of the subthreshold temporal order-cued discrimination task (16 Asynchronous, 16 Synchronous and 8 No-Go trials). All participants received explicit instructions about the specific association between the subthreshold order of the cues and the target gray values present on the task and were trained the same way. For the Non-predictive group, the association remained true in only 50% of the Asynchronous trials in the main experiment (Fig. 2A).

*-Suprathreshold temporal order cued discrimination task*

This task was performed as a control after the subthreshold temporal order cued discrimination task in order to check that both groups were able to use an order cue to predict the upcoming target gray value when order is suprathreshold and when it predicts the target in 100% of the Asynchronous trials. Both groups performed the same suprathreshold task (*i.e.* 100% congruent Asynchronous trials), even the 'Non-predictive' group, in which previously gray levels were not contingent on the order of sub-threshold asynchronies (Fig. 2A).

This task was identical to the subthreshold temporal order cued discrimination task except for the asynchrony in the Asynchronous condition being 100 ms (and thus easily detectable) instead of 17 ms, and the shorter task length (24 Asynchronous, 24 Synchronous and 12 No-Go trials in a single block, yielding a total of 60 trials).

Similar facilitation effects in both the 'Predictive' and 'Non-predictive' groups when order is presented with 100 ms SOA and predicts the target in 100% of the trials would confirm that there is no difference between the groups in their ability to process suprathreshold order. This would also mean that the potential difference in performance between the two groups in the subthreshold version of the task would likely be due to the manipulation of the proportion of trials where the order cue correctly predicts the target. Furthermore, this task also allows to check that order can be detected by our participants and used to predict an upcoming target, at least when it is suprathreshold.

This task was preceded by two training blocks. The first one contained 30 Asynchronous trials and the second a 30 trial-long version of the task.

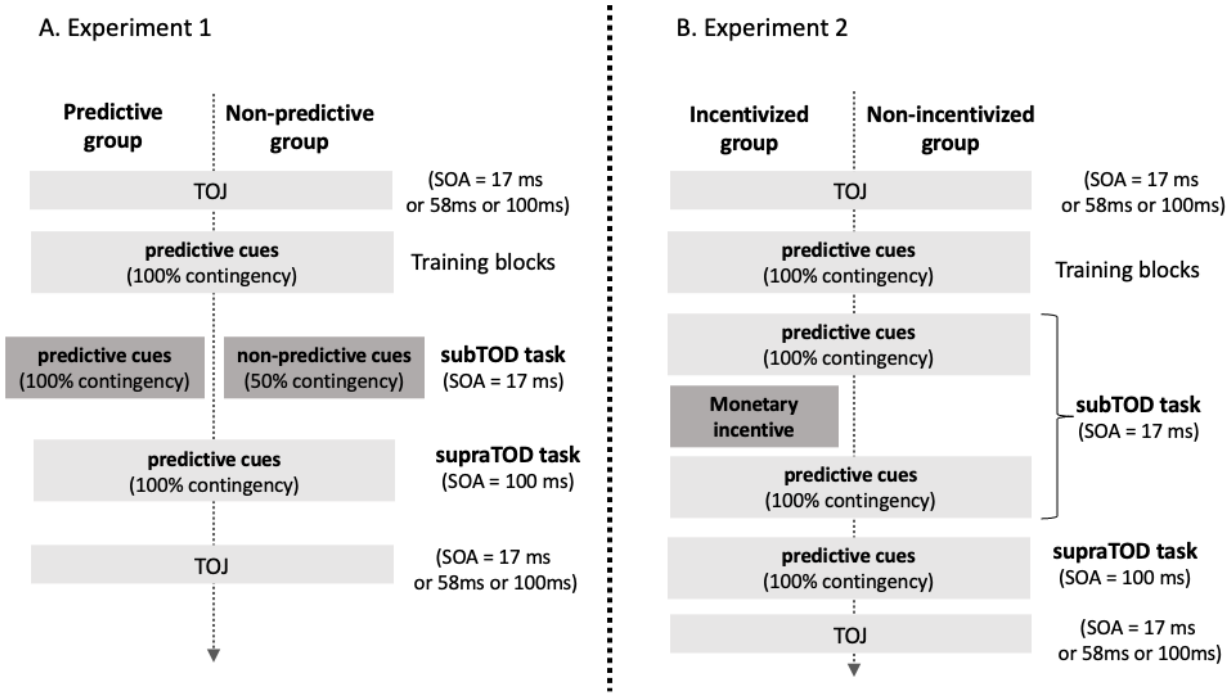


**Figure 2.** Procedures of the two experiments.
In Experiment 1 (A) the two groups differed only in the contingency rate between the order of the asynchronous cues in the subthreshold temporal order cued discrimination task ('subTOD task'), with the ordered cues always predicting the identity of the targets in the Predictive group and the cues bearing no predictive value for the Non-predictive group. Both groups began and ended the experiment with a temporal order judgment task ('TOJ') with three SOAs. Both groups performed the same suprathreshold version of the temporal order cued discrimination task (supraTOD) with the ordered cues predicting the identity of the targets in 100% of the Asynchronous trials.
In Experiment 2 (B) the two groups differed by the introduction of a monetary incentive at the middle of the subTOD task. The Incentivized group received instructions motivating them to attend to and exploit the order of the cues to improve their performance, while the Non-incentivized group received no incentive and carried on the second block of the task as before. Importantly, both groups performed the same tasks, with the ordered cues predicting the identity of the targets in 100% of the Asynchronous trials in both the subTOD and supraTOD tasks.

*-Temporal order judgment (TOJ) tasks*

At the beginning and at the end of the protocol, participants performed a classical TOJ task. Stimuli were identical to the cues in the previously described tasks but this time, the target gray values were not presented.

Three SOAs separating the onset of the white dots were used (17 ms, 58 ms and 100 ms), each presented over 40 trials in a randomized order, with equal numbers of 'left-right' and 'right-left' order presentations, yielding a total of 3×40=120 trials per TOJ task. Participants were instructed to make a button-press on the side of the first stimulus. This task was used to make sure that participants did not detect order with 17 ms SOA at the beginning or the end of the experiment, so that order remained subthreshold in the main task of the experiment.

#### Statistical analysis

We report repeated measures ANOVAs and differences were localized using sub-analyses. D-prime values, that index gray-level discrimination abilities, and beta (or criterion), reflecting a bias to respond "light gray" or "dark gray" (Macmillan & Creelman, 2004), were calculated using the psycho Package (Makowski, 2018) in the R Studio environment (RStudio Team, 2016). All analyses were carried out on the Statistica® software. The level of significance was set to $\alpha = 0.05$ throughout the analyses. The partial eta-squared ($\eta^2$) were added as a measure of effect size. In the TOJ tasks, individual performances for 17 ms SOA trials were compared to a hypothetical chance performance using a $\chi^2$ test.

### 2.2. Results of Experiment 1

The ability to discriminate the grey-levels was quantified by calculating d-prime for each participant in each block (four sub-blocks in the subthreshold, one main block in the suprathreshold version of the task) and each condition (Asynchronous vs. Synchronous). For this, we arbitrarily considered correct responses to light gray targets as hits and correct responses to dark gray targets as correct rejections. Thus, incorrect responses to light gray targets were considered misses and incorrect responses to dark gray targets were considered as false alarms.

#### Subthreshold temporal order cued discrimination task

We divided the trials into four sub-blocks to investigate the evolution of performance over time, and to test for a potential improvement or deterioration of performance. We compared sub-blocks with equal number of trials in each condition (first set of 24 Asynchronous and 24 Synchronous trials in the 1$^{st}$ sub-block, second set in the 2$^{nd}$ sub-block, etc.). A repeated measures ANOVA on d-prime with condition (Asynchronous vs. Synchronous) and sub-block (1$^{st}$ vs. 2$^{nd}$ vs. 3$^{rd}$ vs. 4$^{th}$) as within-group variables, and group (Predictive vs. Non-predictive) as a between-group variable revealed a significant three-way interaction [$F(3,66)=3.99$, $p<0.05$, partial $\eta^2=0.15$] (Fig. 3A).

We calculated for each participant the difference in performance between the Asynchronous and Synchronous conditions (*i.e.* $d'_{async} - d'_{sync}$) in each sub-block as a proxy for the facilitation effect linked to the use of subliminal temporal order information. We then conducted ANOVAs on this value in each sub-block with group as a between-group variable. A significant effect of group was found only in the 1st sub-block [$F(1,22)=14.10$, $p<0.005$, partial $\eta^2=0.39$] with a larger positive performance difference in the Predictive group (0.70) compared to the Non-predictive group (-0.54). In the other sub-blocks, no significant group effects were found (Fig. 3A).

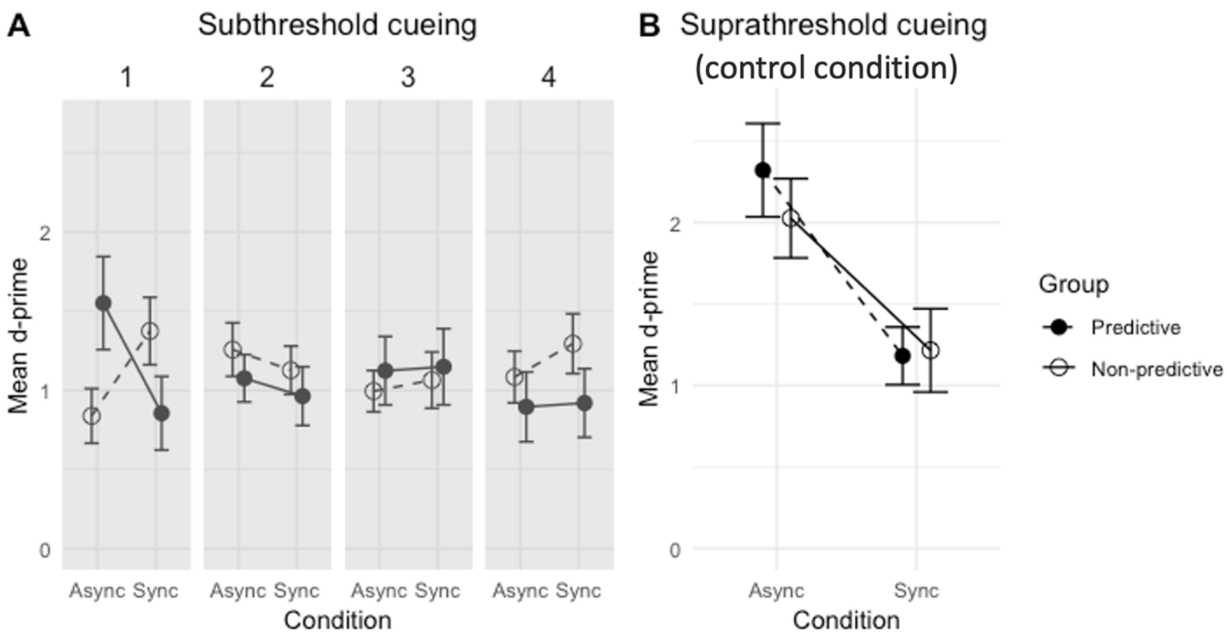


**Figure 3.** Mean d-prime values of the two experimental groups (Predictive vs. Non-predictive) in the Asynchronous ('Async') and Synchronous ('Sync') conditions in the 4 sub-blocks of the subthreshold temporal order cued discrimination task (A) and in the suprathreshold version of the task (B). In the subthreshold version of the task the congruency between order cues and targets was manipulated between the two groups (indicated with a gray background), however in the suprathreshold version of the task the cues' order predicted the targets in 100% of the cases. Error bars represent ±SEM.

We further compared d-prime between groups in each condition and each sub-block. In the Asynchronous condition of the 1st sub-block a significant effect of group was found [$F(1,22)=4.37$, $p<0.05$, partial $\eta^2=0.17$] with a higher d-prime in the Predictive group (1.55) compared to the Non-predictive group (0.84). No other group effects were found in the other sub-blocks.

In order to verify whether the effects on d-prime were linked to a difference between groups in their bias to give one response or the other, we conducted a repeated measures ANOVA on the beta decision criterion with condition (Asynchronous vs. Synchronous) and sub-block (1st vs. 2nd vs. 3rd vs. 4th) as within-group variables, and group (Predictive vs. Non-predictive) as a between-group variable. No significant main effects or interaction between factors was revealed.

### Suprathreshold temporal order cued discrimination task

An ANOVA conducted on d-prime with condition (Asynchronous vs. Synchronous) as a within-group variable and previous group distinction (Predictive vs. Non-predictive) as a between-group variable revealed a main effect of condition [$F(1,22)=20.98$, $p<0.0005$, partial $\eta^2=0.49$], with a higher d-prime value in the Asynchronous condition (2.17) compared to the Synchronous condition (1.20) (Fig. 3B). No interaction between factors were found, indicating similar d-prime values in both groups.

An ANOVA on the decision criterion with the same factors revealed no significant main effects or interactions between factors.

## 2.3. Discussion of Experiment 1

The results suggest that the subthreshold temporal order of the cues was processed and used to predict targets, thus improving discrimination performance, but only for a very short period at the beginning of the task. This initial pattern of results replicates the facilitation effect observed on RT by Chassignolle et al. (2021) in their study and extends it to participants' discrimination accuracy.

The facilitation effect observed in the suprathreshold version of the task in the two groups indicates that the groups did not differ in their general ability to detect and use order to predict an upcoming target. Hence, the results observed with the subthreshold cue order are unlikely due to a difference between the groups, and more likely to our experimental manipulation, namely the contingency between the subthreshold order of the cues and the target gray values introduced for the Predictive group.

Although present at the beginning of the task (1st sub-block), the facilitation effect linked to the cue order-target contingency is transitory and the effect disappears by the 2nd sub-block.

This result indicates that the effect of the exploitation of subthreshold order is rather small. The transiency and fragility of the facilitation effect suggests that the effects do not result from a purely automatic sequential learning process. The observed pattern is rather consistent with the formation and exploitation of an order representation to predict targets. At the least, the results show that the underlying process is fragile. Given the difficulty of the task, with very small differences between the target gray values, it might be possible that motivation plays a role. Participants can be expected to be more motivated at the beginning than at the end of a monotonous and difficult task (Esterman et al., 2014; Szalma & Matthews, 2015). Experiment 2 was designed to verify this hypothesis by manipulating participants' motivational level via a monetary incentive.

## 3. Experiment 2

### 3.1. Materials and methods

#### Participants

Thirty-five healthy participants (25 females/10 males, mean age ± SD = 23.34 ± 2.67 were recruited. All participants had normal or corrected-to-normal vision and reported no neurological or psychiatric disorders. After analyzing performances in the TOJ tasks, 4 participants were excluded from further analyses because of above chance performance for 17 ms asynchronies and thus we considered that order with 17 ms SOA was not subliminal for these subjects. After analyzing performances in the No-Go condition of the subthreshold temporal order cued discrimination task 1 participant with a high response rate in this condition was excluded because this result suggested he did not follow instructions. Further analyses were conducted on the remaining 30 participants (22 females/8 males, mean age ± SD = 23.47 ± 2.61).

The project was approved by the local ethics committee of the University of Strasbourg. All participants gave their informed written consent in accordance with the declaration of Helsinki. In this experiment participants' motivation was manipulated via a monetary incentive. Thus, at recruitment participants were promised 15 € and one group (Incentivized group) was proposed a doubling of their monetary compensation after the first part of the detection task, if they improved their performance in the second part. This group was composed of 15 participants (11 females) and the other group (Non-incentivized) was also composed of 15 participants (11 females). The two groups did not differ in age (Table 1). For ethical reasons, after completing the experiment, all participants received a monetary compensation of 30 euros regardless the group they belonged to or their performance at the task.

## Equipment and apparatus

The same experimental setting was used as described in Experiment 1.

## Experimental task and procedure

The same experimental protocol and tasks were used as for the Predictive group in Experiment 1 with 3 differences. The experimental design and procedure are schematized in Fig. 2B.

(i) Like in Experiment 1, there were four sub-blocks of 24 trials in the Asynchronous, 24 trials in the Synchronous, and 12 trials in the No-Go condition, yielding a total of 4×(24+24+12)=240 trials displayed in a randomized order. The main structure of the experiment was the same as in Experiment 1 (*i.e.* two blocks separated by a break, each block containing two sub-blocks).

(ii) Participants were divided into two groups. The Incentivized group received a monetary incentive after the first block of the subthreshold temporal order cued discrimination task with the instructions specifying that if their performance in the discrimination of the target gray values improved in the second block of the task their monetary compensation would be doubled. After these instructions and before starting the second block of the task they performed again the Conditioning training block. The Non-incentivized group only performed the Conditioning training block between the two blocks of the subthreshold temporal order cued discrimination task and received no additional instructions. The re-training with the conditioning training block was designed to increase the chance that subjects would use the order to discriminate the gray levels. Since the motivational instructions were introduced in only one of the groups, the two blocks of the task had to be distinguished in the analyses (*i.e.* before vs. after motivational instructions).

(iii) Before starting the experimental tasks all participants completed the French versions of the Dundee Stress Scale Questionnaire (DSSQ) (Matthews et al., 2002) and the BIS/BAS scale (Caci et al., 2007). The DSSQ was used to evaluate participants' baseline motivational levels (*i.e.* before the experiment) with three sub-scores, 'success motivation' measuring their motivation to excel in their performance, 'intrinsic motivation' measuring their interest in the task, and their 'overall motivation'. With the BIS/BAS scale we were interested in the 'reward responsiveness' subscale because we hypothesized that, in combination with the monetary incentive, this trait may interact with participants' motivational levels and performance.

### Statistical analysis

In addition to the statistical analyses described in Experiment 1 we also performed ANCOVAs on data from the subthreshold temporal order cued discrimination task.

## 3.2. Results of Experiment 2

### Questionnaire scores

Separate ANOVAs with group as a between-group variable conducted on the DSSQ subscales indicated that the Incentivized and Non-incentivized participants had similar scores for all sub-scales of the questionnaire (Table 1).

A similar analysis was used to compare the groups on their score on the BIS/BAS 'reward responsiveness' sub-scale. The difference between groups was not significant, however a tendency was found with a slightly higher score in the Non-incentivized group (17.60) compared to the Incentivized group (15.80) (see Table 1). We hypothesized that the 'reward responsiveness' trait may potentially interact with participants' motivation and performance in the detection of subthreshold order following the monetary incentive. For this reason, we computed the improvement of detecting subthreshold order for each individual over the course of the experiment as the difference between an individual's performance in the second and first (SOA = 17 ms) TOJ task, henceforth noted *Δ*TOJ. *Δ*TOJ did not differ between the groups [$F(1,28)=0.27$, $p=0.61$, partial $\eta^2=0.01$].) The BIS/BAS 'reward responsiveness' score and the *Δ*TOJ were taken as covariates in the analyses on participants' performance at the subthreshold temporal order cued discrimination task.

| | Incentivized group average score | Non-incentivized group average score | F | p-value | partial $\eta^2$ |
|---|---|---|---|---|---|
| age (years) | 22.60 | 24.33 | F(1,28)=3.61 | 0.07 | 0.11 |
| DSSQ ‘success motivation’ | 17.23 | 19.87 | F(1,26)=2.39 | 0.13 | 0.08 |
| DSSQ ‘intrinsic motivation’ | 28.54 | 28.07 | F(1,26)=0.18 | 0.68 | 0.007 |
| DSSQ ‘overall motivation’ | 4.31 | 4.07 | F(1,26)=1.37 | 0.25 | 0.05 |
| BAS ‘reward responsiveness’ | 15.80 | 17.60 | F(1,28)=4.00 | 0.055 | 0.13 |
| BAS ‘drive’ | 8.73 | 8.33 | F(1,28)=0.36 | 0.56 | 0.01 |
| BAS ‘fun seeking’ | 10.67 | 11.20 | F(1,28)=0.55 | 0.46 | 0.02 |
| BIS | 20.00 | 21.73 | F(1,28)=1.82 | 0.19 | 0.06 |

**Table 1.** Age and average questionnaire sub-scale scores in the experimental groups.

## Subthreshold temporal order cued discrimination task

We conducted an ANCOVA on d-prime with condition (Asynchronous vs. Synchronous), block (‘before’ vs. ‘after motivational instructions’) and sub-block ($1^{st}$ vs. $2^{nd}$ in each block) as within-group variables, group (Incentivized vs. Non-incentivized) as a between-group variable, and $\Delta$TOJ and BIS/BAS ‘reward responsiveness’ score as covariates. A significant three-way interaction was found between group, condition and block [$F(1,26)=4,24$ $p<0.05$, partial $\eta^2=0.14$] (Fig. 4A).

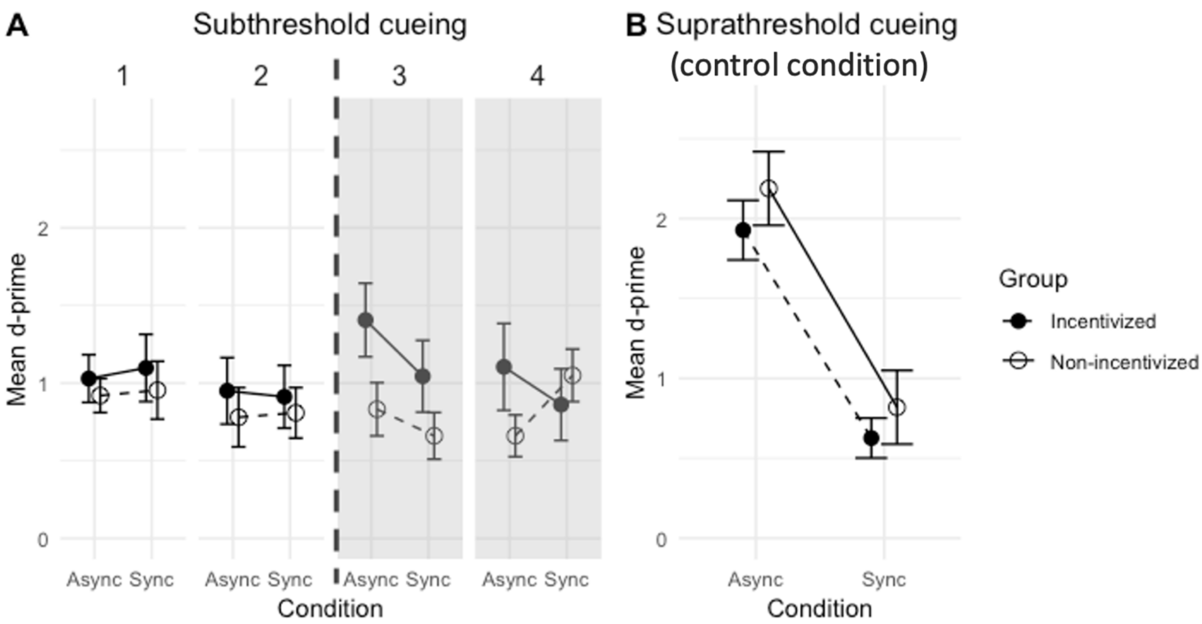


**Figure 4.** Mean d-prime values of the two experimental groups (Incentivized vs. Non-incentivized) in the Asynchronous ('Async') and Synchronous ('Sync') conditions in the 4 sub-blocks of the subthreshold temporal order cued discrimination task (A) and in the suprathreshold version of the task (control condition) (B). The Incentivized group received motivational instructions (*i.e.* monetary incentive) between the 2nd and 3rd sub-blocks of the subthreshold version of the task, represented by the dashed line. The two groups differed by the presence/absence of motivational instructions in the 3rd and 4th sub-blocks (indicated with a gray background). Error bars represent ±SEM.

As in Experiment 1, we calculated the difference in performance between the Asynchronous and Synchronous conditions (*i.e.* $d'_{async} - d'_{sync}$) for each participant and in each sub-block. We then conducted an ANCOVA on this value in each block with sub-block (1st vs. 2nd in each block) as within-group variable, group (Incentivized vs. Non-incentivized) as a between-group variable, and $\Delta$TOJ and BIS/BAS 'reward responsiveness' score as covariates. In the second block (i.e. 3rd and 4th sub-blocks) a main effect of group was found ([$F(1,26)=4.26$, $p<0.05$, partial $\eta^2=0.14$]) with a larger positive performance difference in the Incentivized group (0.30) compared to the Non-incentivized group (-0.11).

We further compared d-prime between groups in each condition and in each block with the same covariates as previously described. In the 2nd block (i.e. 3rd and 4th sub-blocks), the difference between groups tended toward significance in the Asynchronous condition [$F(1,26)=3.34$, $p=0.08$, partial $\eta^2=0.11$] with a slightly higher d-prime in the Incentivized (1.26) group compared to the Non-incentivized group (0.75).

As in experiment 1, we checked whether the effects on d-prime can be explained by a difference between groups in their response bias. We conducted an ANCOVA on the beta decision criterion with condition (Asynchronous vs. Synchronous), block ('before' vs. 'after motivational instructions') and sub-block (1st vs. 2nd in each block) as within-group variables, group (Incentivized vs. Non-incentivized) as a between-group variable, and $\Delta$TOJ and BIS/BAS 'reward responsiveness' score as covariates. No significant main effect of group or interaction with group was found.

### Suprathreshold temporal order cued discrimination task

An ANOVA conducted on d-prime with condition (Asynchronous vs. Synchronous) as a within-group variable and group (Incentivized vs. Non-incentivized) as a between-group variable revealed a main effect of factor condition [$F(1,28)=44.16$, $p<0.00001$, partial $\eta^2=0.61$], with a higher d-prime value in the Asynchronous (2.06) compared to the Synchronous condition (0.72) (Fig. 4B). No interaction between factors was found indicating similar d-prime values in both groups.

An ANOVA conducted on beta with condition (Asynchronous vs. Synchronous) as a within-group variable and group (Incentivized vs. Non-incentivized) as a between-group variable revealed no significant main effect of group or interaction with group.

## 3.3. Discussion of Experiment 2

Experiment 2 was designed to verify whether motivation played a role in the use of subthreshold order (SOA = 17 ms) to improve discrimination performance. When participants received a monetary incentive motivating them to improve their performance by using the subthreshold temporal order cues to predict the targets' luminance, performance improved. Results of the Non-incentivized group did not reveal any facilitation effect. The two groups did not differ in their baseline motivation levels as measured via self-questionnaires before the experiment, nor in their performance before the introduction of the incentive between blocks 1 and 2. The reward responsiveness trait tended to be higher in the Non-incentivized group, but between-group differences persisted in the ANCOVA taking this variable as covariate. Moreover, similar facilitation effects were observed in both groups when order was suprathreshold (100 ms SOA) and performance was similar in the subthreshold version of the task preceding motivational instructions. These results indicate that the two groups did not differ in their general ability to detect and use order to predict target. Thus, the observed facilitation effect linked to the use of subthreshold order is likely due to our experimental manipulation of participants' motivational levels via the monetary incentive.

## 4. General Discussion

The aim of the present study was to test the existence of automatic processing of temporal order, when the delay between sensory events is too short and under the threshold for conscious temporal order perception. Our results suggest a facilitation effect on participants' performance in the detection of target luminance values when targets are preceded by a subthreshold cue compared to a control condition where the cues are synchronous and bear no predictive information. This replicates the facilitation effect described by Chassignolle et al. (2021) on RT and extends it to discrimination sensitivity (d-prime) in an experimental setup where targets are more difficult to identify. The main result, however, is that the automatic processing of temporal order is very fragile, and sensitive to motivational effects.

Several aspects of our results showed the automatic processing of order to be fragile. In Experiment 1, the use of temporal order was transient at the beginning of the experiment and then its effect disappeared. In Experiment 2 it was present only in the Incentivized group, and only once participants had received motivational instructions. It should be noted that the facilitation effect observed at the beginning of the task (1st sub-block) in the Predictive group of Experiment 1 was not replicated in the Incentivized and Non-incentivized groups of Experiment 2, although the experimental conditions and instructions were identical at the beginning of the task in both experiments. We argue that this finding is consistent with the hypothesis that the facilitation effect linked to the processing and exploitation of subthreshold order is rather small and transitory. Analyses on the decision criterion in both experiments revealed that the results on target discrimination abilities cannot be explained by different response biases between groups.

Experiment 2 was designed to check whether the processing of subthreshold temporal order was linked to motivation. The facilitation effect was observed in Experiment 1 at the beginning of the task, but disappeared over the course of time. Such a transitory impact suggests that the effects resulted from the initial learning process. It is important to note that this learning is not purely automatic, since participants are explicitly told about the contingency between temporal order and luminance values. Discrimination performance is known to decrease with time during monotonous tasks (See et al., 1995), and a decrease of motivation or fatigue over time may explain the results. However, a more direct evidence of a role of motivation was required. By manipulating participants' motivational levels via a monetary incentive, the facilitation effect in participants' discrimination sensitivity was shown to depend on motivation. It has already been shown that top-down factors, like motivation, are necessary to establish predictive relations between stimuli even when the primers were presented subliminally (Custers & Aarts, 2011). Thus, the processing of subthreshold order may require such top-down factors to be initiated.

Since sufficient motivational levels are needed, it is unlikely that the processing of order, as investigated in our study, is an ongoing, online process in our day-to-day life. Even in the absence of motivation manipulation in Experiment 1, order processing occurred only after intensive training and wore off rapidly. This is logical, considering that if order processing were a continuously ongoing process, ordering events in time at a high temporal resolution would mean exponential costs. As emphasized in the introduction, the perception of order is different from an order of percepts (*i.e.* sequential processing of events). Processing the order means establishing a higher-order relationship between two events and encoding their relative position on the arrow of time. With more and more events unfolding and taking place as time passes, processing each event's position relative to the ones already processed would quickly become a resource consuming activity for the brain. It is thus most likely that motivation is an important factor that serves as a promoter of temporal order processing at the level of automatic and subthreshold visual information processing, when such process is needed or may bring a potential benefit in the task at hand.

One might wonder whether the fragile effects observed in the present study really concerned order processing. Several control conditions allow us to discard alternative possibilities. In Experiment 1, we manipulated the predictiveness of the cue order in two groups (Predictive vs. Non-predictive group). This experimental manipulation was introduced to rule out the possibility that the simple asynchrony between the cues (and not specifically their order) could have an effect on discrimination sensitivity. Since the facilitation effect was only observed in the Predictive group this alternative explanation can be ruled out.

Taken together, these results suggest that the processing of temporal order of sub-threshold asynchronies is possible, although it also likely depends on task constraints.

It is remarkable that the effect was fragile even though participants were explicitly informed about the contingency between order and target luminance levels. Whether it is possible to process subthreshold order when contingencies are not mentioned at all seems unlikely in light of our results, however it may be possible with other manipulations of top-down, possibly attentional factors (Custers & Aarts, 2011; Capa & Bouquet, 2018). Future studies investigating the automaticity of order processing may focus their design on similar experiments to ours, but where order is presented supraliminally, and no explicit instructions mention its contingency with target stimuli.

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Chapter 7

# General discussion

The main objective of the present thesis was to bring new insights into the temporal structure of consciousness with the perspective to better understand the altered temporal experiences reported by individuals with a diagnosis of SZ and BP.

Our hypotheses were formulated in the framework of Pöppel's (1997) temporal windows model in which incoming information is processed and integrated at different temporal scales. Based on phenomenological accounts, we hypothesized that BP patients' altered experiences of the present moment and increased mental activity translated by racing thoughts would be rooted in alterations in temporal processing at the level of the "subjective present" (second timescale). We contrasted these alterations with experiences of time fragmentation reported by SZ patients which could be related to temporal processing deficits at the level of the "functional moment" (millisecond timescale). We focused on this contrast because in SZ patients the ability to order events (at the conscious level) is particularly altered, and it was and still is unknown whether the impairments in information processing at an automatic, non-conscious level are related to these conscious ordering deficits.

## 7.1. BP, racing thoughts and the subjective present

Chapters 2-4 focused on the study of the temporal structure of conscious thought at the second scale. After validating a novel measure of periodic perceptual processes based on eye tracking measurements in the Necker cube paradigm (Chapter 2), we tested our measure as a potential neuropsychological equivalent of racing thoughts, a subjectively described symptom affecting thought, in a group of BP patients and healthy controls (Chapter 3). We found a link between altered thought processes (reflected by increased levels of racing thoughts) and perceptual information processing in individuals with racing thoughts at the level of seconds (as measured with ocular windows). The pattern of results on ocular windows in individuals with racing thoughts was replicated in the preliminary results of a study contrasting BP and SZ patients (Chapter 4). Interestingly, although SZ patients reported similar levels of racing thoughts to individuals with BP, SZ patients presented no alterations in ocular windows. Although these last results are preliminary, they suggest that alterations at the second scale of processing (*i.e.* "subjective present") are different between BP and SZ patients.

What are the implications of these results for our understanding of racing thoughts? And what does the use of the indirect measure of eye tracking reveal us about information processing in psychosis?

The computation of ocular windows from an oscillatory ocular behavior in the Necker cube paradigm gave access to lower-level perceptual mechanisms than manual windows (*i.e.* reports of conscious perceptual alternations). It was verified that there is a correspondence between ocular and manual windows, inasmuch as they both reflect perceptual alternations between representations of the Necker cube. The validation of our ocular measurement was achieved using the spatial coordinates of ocular fixations when the Necker cube was ambiguous vs. disambiguated. Thus, we measured perceptual alternations of the Necker cube at a conscious level (manual responses) and at a more automatic processing level with a slightly higher temporal resolution (ocular movements) in parallel.

In Chapter 3 we showed that in BP high levels of racing thoughts were associated to an impaired attentional modulation of manual and ocular windows' rate, although results were clearer in ocular measurements. Are ocular windows more sensitive to the alterations in perceptual processing in BP than manual windows? Or these bigger effects on ocular window measurements are simply due to the fact that ocular windows are more frequent, thus a bigger statistical effect can be seen even in a relatively short experiment? These interpretations cannot be totally excluded and (at least the latter) could be verified by a longer version of the experimental task. However, the pattern of results in healthy participants (Chapter 2) and participants with no racing thoughts (Chapter 3) are in line with a dissociation between manual and ocular windows' rate: the higher number of ocular windows compared to manual windows suggests that ocular alternations do not match conscious perceptual alternations, and the number of ocular windows did not decrease in the Focus condition compared to the Spontaneous condition even in participants with no racing thoughts. The latter shows that ocular windows are not sensitive to cognitive control to the same extent than manual windows, at least in the Focus condition. We argue that this dissociation indicates that ocular window measurements reflect non-conscious and more automatic mechanisms which escape top-down control. Whatever the exact explanation for the clearer results on ocular windows, it remains that ocular window measurements are useful, since this objective, implicit measure reveals alterations in perceptual processing linked to racing thoughts in BP. The deficient modulation of the window rates between attentional conditions points to a link between racing thoughts and altered cognitive control mechanisms. Although the manual responses suggested that all participants followed instructions (at least in the switch condition), it is likely that the more automatic mechanisms were more difficult to control consciously, which led to a larger effect on ocular than on manual windows. This attentional deficit manifests itself especially when patients are faced with constraining instructions (Focus condition), to which their perceptual system reacts by alternating between low-level representations of the Necker cube more quickly.

As discussed in Chapter 3, racing thoughts are not related to a general cognitive control deficit, since even participants with high levels of racing thoughts followed the instructions in the Switch condition. This suggests that cognitive control processes (linked to consciousness and necessary for the correct following of instructions) are relatively preserved in patients with racing thoughts and it is the control of lower-level, automatic perceptual processes that is impaired.

We may wonder whether the impairment in the control of automatic perceptual processes, as observed in the altered modulation of ocular window rate, is the origin or a consequence of altered thought processes? Our data cannot allow us to determine a causal direction between racing thoughts and automatic perceptual processes that evade control. However, it might be asked if the alteration of the modulation of window rates that we evidenced can also be found in other altered thought processes, namely rumination (Apazoglou et al., 2019). Racing thoughts have been proposed to be distinct from rumination (Bertschy et al., 2020) from a phenomenological perspective (note that both are assessed via self-questionnaires), but cognitive processes (involved in the control of ocular window rate) may be related to both symptoms. Investigating whether the altered attentional modulation in the ocular window rate also coincides with rumination would be an interesting follow up to our study, since it would give further insights about the extent to which automatic perceptual processes are linked to conscious thought processes and their alterations.

As discussed in Chapter 3, the question of whether our ocular windows measure would be specific enough to be used as an objective marker of a specific subgroup of patients needs further investigation in order to check the predictive potential of the measure and validate it as a diagnostic tool in more clinical populations than SZ and BP. For now, we can conclude that ocular windows are useful for informing about the neuropsychological mechanisms underlying racing thoughts in BP. Despite this, ocular windows cannot be considered as specific to racing thoughts (*i.e.* seen as a transdiagnostic symptom), since we saw in Chapter 4 that SZ patients also report racing thoughts similarly to BP, but ocular measures differed between the two groups. Both groups reported similarly elevated levels of racing thoughts, but ocular window measurements differed between groups (with a pattern in BP patients that is consistent with previous findings in BP patients in Chapter 3). Those results show that the implicit measure of ocular windows brings something new to our understanding of this symptom: similar subjective reports (*i.e.* self-questionnaire scores) seem to be underlaid by different or divergent processes. It is nonetheless possible that an altered attentional modulation of ocular windows is related to racing thoughts (or a more general alteration in thought and perceptual process) specifically in BP.

We argue that although phenomenology and the evaluation of patients' subjective experiences are valuable tools in clinical research, objective neuropsychological or neurophysiological measures are essential for the characterization of phenomenological accounts and the understanding of their underlying mechanisms which may have different origins. This approach could *in fine* lead to more reliable measures that are not affected by patients' decision and response biases, and thus be usable in clinical populations whose reports are less or non-reliable.

From a more fundamental research standpoint we may wonder about the nature of ocular windows and their role in the hierarchical model of temporal windows. Ocular windows are based on eye movements, thus they have a major motor component (despite the fact that they are intimately linked to perception). Do ocular windows belong to the subjective present (or the experienced moment), or do they belong to another integration window?

The duration of the subjective present (or the experienced moment) was proposed to be between 0.5 and 3 s. In this regard, ocular windows fit in the lower end of this timescale. However, they may reflect a temporal integration that is closer to the functional moment. Wittmann (2011) proposed that different kinds of functional moments may exist, other than the one described with a duration of a few ten of milliseconds by Pöppel (1997). This is consistent with the idea that windows of temporal integration would depend not on their duration, but the density of information they contain (White, 2017). According to this view, ocular windows could reflect the integration of non-conscious information with a higher temporal resolution, while the manual windows would reflect conscious information with a lower temporal resolution. Whether there is a direct link between these two levels, or whether they are separate but coordinated in parallel by a common mechanism (probably attentional, based on our results) is unknown. Future studies with longer task durations could bring answers to this question by directly investigating the temporal distribution of manual and ocular windows relative to each other.

## 7.2. Can deficits in order processing differentiate SZ and BP?

In Chapter 5 we looked at information processing at the sub-second scale for both suprathreshold, visible SOAs (100 ms) and subthreshold SOAs (17ms). This study focused specifically on the processing of temporal order, an aspect of temporal processing known to be altered in SZ. Our preliminary results are consistent with the literature in that we found impaired judgments of temporal order in patients with SZ (Capa et al., 2014; Stevenson et al., 2017). Our study also led to novel results concerning temporal order judgment in BP: to our knowledge no studies have yet investigated this form of temporal processing in BP. This study yielded new evidence confirming a divergence between SZ and BP. Deficits in temporal order detection seem to be specific to SZ, since order judgments were preserved in BP patients. These results support the idea that SZ and BP are separate conditions from a psychopathological standpoint.

Future studies should investigate in more detail the origin of altered order judgments in SZ. It is in fact still unknown whether SZ patients' poor performance comes from a genuine alteration in the detection of order, or it is rather related to alterations in decisional mechanisms playing a role in the response. Meta-cognitive deficits in perceptual tasks (*i.e.* the confidence concerning the reliability of one's own percept) may be only mildly altered in SZ (Rouy et al., 2021), however for the percepts to become conscious in the first place may be difficult in patients. It is conceivable that the formation of a conscious order percept is more difficult compared to that concerning a simple asynchrony. While in SJ tasks patients can detect the presence of an asynchrony if it is long enough, a conscious order percept may bear additional difficulties, since it is not just about the presence or absence of an asynchrony but about establishing a relationship between to elements. The upcoming analyses of our data (once a sufficient number of participants per group is included) should focus on implicit, indirect measures (*e.g.* sequential effects, Marques-Carneiro et al., 2020) to verify automatic processes, thus helping to disentangle the effects of a genuine deficit in order detection (which would be apparent in sequential effects) and that related to the information necessary for a response becoming conscious (which would only concern the current trial).

## 7.3. Why is temporal order important?

Keeping in mind our additional evidence of altered temporal order processing in SZ, one might wonder about the possible clinical implications of order deficits in psychosis. In fact, an altered temporal order processing may be linked to clinical symptoms such as delusion. Delusions are false beliefs that can put into play aberrant causal links between events. The temporal order between events can be used to derive the causal relationship between two successive events. Logically, temporal order is a prerequisite for causality, since the cause must always precede its effect: A cannot be the origin of B, unless A occurred before B. Thus, an erroneous percept of order can yield the perception of an aberrant causal relationship between two events, and ultimately play a role in the development of delusion.

It is known that SZ patients present alterations in automatic, non-conscious processing of succession (evidenced in SJ tasks) at the millisecond level. Whether these alterations in succession processing are linked with impairments in temporal order judgments even for suprathreshold SOAs is unknown. The first step in the verification of this possibility is to understand the level at which temporal order originates in healthy individuals. According to the results in Chapter 6, the automatic processing of order is probably not a permanently ongoing process. It is probably a difficult task for the sensory system and is highly sensitive to top-down effects. In light of these results, automatic and conscious order mechanisms for ordering events in time are likely not identical mechanisms. If the observed impairments in SZ for supra-threshold SOAs are related to disturbances in low-level, automatic processes, then the link is likely indirect.

If deficits in ordering events are related to clinical symptoms, such as delusions, this should be investigated at the level of conscious order processing. The link between perception of order and the perception of causality is known to not be unidirectional, since top-down effects (*e.g.* previous experience, expectations) can bias order judgments to conform with an expected and perceived causal link (Lagnado & Sloman, 2006). Future research should focus on the effect of causality perception on order processing, and how top-down factors like predictions and expectations based on the temporal context of the experiment influence order judgment. The addition of implicit, indirect measures will likely yield valuable information about automatic processing involved in the detection and perception of order and causal relationships.

If aberrant order processing plays a role in the development of delusions in SZ, how can we explain delusions in BP despite no empirical data on altered temporal order processing in BP?

First, similarly to what was observed in Chapter 4 on racing thoughts, similar symptoms may have different underlying mechanisms between the two conditions. Delusions in SZ and BP have been described as generally different from a qualitative standpoint, with persecutory delusions being more frequent in SZ, while BP patients being more prone to present delusions of grandiosity (Picardi et al., 2018). Delusions in the two conditions may have different origins.

Second, the heterogeneity of the BP group may provide answers. We cannot exclude the possibility that some BP patients in our study did in fact have worse performances at temporal ordering and certain symptoms (*e.g.* delusions) in these patients may be closer to those in SZ. Our small sample size however did not allow to investigate this question more closely. On a related note, the small sample size did not allow to distinguish BP patients with and without psychosis in different groups for the analyses unfortunately. Finer analyses taking into account these clinical characteristics in patients have to be done in order to verify these possibilities.

Moreover, a data driven approach could help confirm or disconfirm the idea that order processing could be more or less impaired in subgroups of patients. This methodology could play an important role in the delineation of diagnostic frontiers, determining subgroups of patients inside existing diagnostic categories or throughout categories of SZ, BP and others on the schizo-affective spectrum.

## 7.4. The usefulness of automatic non-conscious perceptual processes

Both results on ocular windows in the Necker cube paradigm (Chapters 2-4) and results on the automatic processing of temporal order (Chapter 6) are suggested to evidence a link between automatic perceptual processes and higher cognitive functions generally linked to consciousness (*i.e.* attention, motivation). These results show that perception and information processing are not only a conscious process, but non-conscious, automatic processes also play an important role in perception (Herzog et al., 2016; Giersch & Mishara, 2017). Also, the classically dissociated non-conscious and conscious processes (*i.e.* higher cognitive functions related to consciousness) might be more related than previously thought. As seen in Chapter 3, cognitive control mechanisms necessary in the execution of task instructions (*e.g.* 'Focus', 'Switch') interacted with low-level, automatic perceptual processes reflected by ocular windows.

Moreover, in Chapter 6, motivation was shown to affect the processing of sub-threshold order information. Investigating the link and interactions between conscious and non-conscious processes is an interesting and important line of research for the study of consciousness, but also for clinical research. Clinical research could benefit from this because automatic, non-conscious processes may be specifically altered in disorders of consciousness (*e.g.* SZ) (Frith, 1979; Giersch & Mishara, 2017) and may represent a source of valuable implicit measures with diagnostic potential at different stages of the disorders. Unraveling non-conscious processes using implicit measures may greatly improve our understanding of the pathophysiology of these disorders.

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# Summary in French / Résumé en français

## Temps, psychose et frontières diagnostiques

Tous les événements mentaux (perceptions, actes, pensées) s'inscrivent dans le temps. Par conséquent, notre système perceptif s'est adapté à traiter les informations qui proviennent de l'environnement dans leur contexte temporel. Ainsi nous pouvons dire, sans difficulté particulière, si deux événements ont eu lieu en même temps ou non, et entre ces deux événements successifs lequel est arrivé en premier, ou si un premier événement en a causé un second. Cette capacité à traiter et organiser les informations dans le temps est indispensable à notre survie et notre bon fonctionnement dans la vie de tous les jours.

Cependant, des altérations de la temporalité ont été décrites dans les troubles psychotiques, groupe de maladies psychiatriques qui se manifestent par une perte de contact avec la réalité et des symptômes tels que les hallucinations et le délire.

Dans les troubles bipolaires (*e.g.* manie, manie mixte, dépression mixte), les patients décrivent un rapport au temps altéré qu'ils caractérisent subjectivement par une production exacerbée et accélérée des pensées (Piguet et al., 2010 ; Bertschy et al., 2020). Ce symptôme d'accélération des pensées, ou « tachypsychie », est aujourd'hui diagnostiqué uniquement sur la base des rapports subjectifs des patients. Le développement de mesures objectives de la tachypsychie est nécessaire, d'une part, pour une meilleure compréhension des mécanismes sous-jacents de ce symptôme encore mal connu et d'autre part, pour améliorer le diagnostic des différents états dans lesquels les patients bipolaires peuvent se trouver et qui nécessitent des traitements médicamenteux spécifiques. Le phénomène de tachypsychie, tel qu'il est décrit aujourd'hui, suggère qu'il existe chez les patients une altération dans les mécanismes d'organisation des informations dans le temps à l'échelle de la seconde et de l'infra-seconde.

Dans un autre trouble psychotique, la schizophrénie, les patients peuvent décrire des expériences de fragmentation du temps, du flux de leur conscience et de leur sens de soi. Ces expériences aberrantes sont des manifestes des troubles du Soi, qui sont centraux dans la schizophrénie. En cela ces troubles pourraient être impliqués dans des symptômes « classiques » de la psychose (*e.g.* délire, quand les patients ne se reconnaissent pas comme l'auteur de leur acte ; hallucinations, dans la mesure où celles-ci reflètent une absence de reconnaissance de son discours intérieur) et leurs liens avec ceux-ci sont encore mal connus. Les résultats récents de notre laboratoire suggèrent que notre système perceptif est capable de traiter les informations à un niveau sub-conscient, avec une résolution temporelle supérieure à celle observée à un niveau conscient (Lalanne et al, 2012a, b ; Poncelet & Giersch, 2016). Il semblerait que ces mécanismes soient altérés chez les patients souffrant de schizophrénie (Lalanne et al, 2012a, b ; Martin et al, 2014) et qu'ils pourraient avoir un lien avec les expériences anormales de continuité du temps et/ou les symptômes cliniques classiques.

Le but de cette thèse est de mieux comprendre la structure temporelle de la conscience afin de mieux caractériser les altérations de la temporalité reportées dans les troubles bipolaires et schizophrénique. La thèse s'inspire du modèle des fenêtres temporelles Pöppel (1997; 2009 ; Wittmann, 2011). D'après ce dernier, les informations (percepts, pensées, actions) sont intégrées dans des fenêtres temporelles de taille différentes à différentes échelles temporelles. Ces différentes fenêtres s'organisent de façon hiérarchique. Ainsi des fenêtres temporelles élémentaires de quelques dizaines de millisecondes (ou « moments fonctionnels ») à l'intérieur desquelles toutes les informations sont traitées comme simultanées, sont imbriquées dans des fenêtres plus larges de quelques secondes qui correspondent à notre sentiment de moment présent (ou « présent subjectif »). Nous avons distingué des mécanismes à l'échelle de la seconde et à l'échelle de la milliseconde, en faisant l'hypothèse que les premiers concernaient plutôt les troubles bipolaires, et les seconds, plutôt la schizophrénie.

Dans les chapitres 1 à 3 de cette thèse nous nous sommes intéressés aux dynamiques du flux des pensées, et à l'étude du présent subjectif, une fenêtre temporelle d'une durée de quelques secondes, qui correspond à la réalisation d'un acte mental (Wittmann, 2011). L'étude du présent subjectif a été effectuée grâce à un paradigme de perception bistable. Pour cela nous avons utilisé une figure bistable, le cube de Necker (Fig. 1). C'est une image ambiguë qui a deux interprétations possibles équiprobables. En réponse à un tel stimulus notre système perceptuel essaye de résoudre l'ambiguïté en alternant notre perception consciente entre les deux interprétations possibles du cube. Pöppel (1997; 2009) a proposé une correspondance entre les durées de perception stable du cube de Necker (environ 2 secondes) et le présent subjectif. Ainsi la mesure de la fréquence d'alternances perceptives au cours de l'observation du cube de Necker permet d'opérationnaliser l'étude des dynamiques du flux de la pensée.

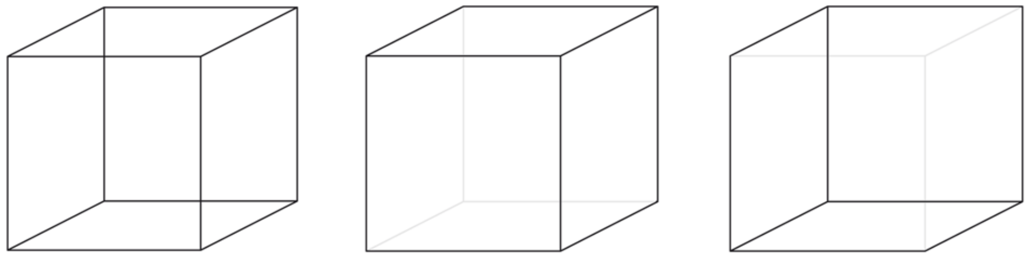

**Figure 1.** Le cube de Necker, un exemple d'image bistable (gauche) et ses deux versions non-ambiguës (milieu et droite).

Lorsque les participants observent le cube de Necker ils reportent manuellement (grâce à des appuis sur des boutons-réponse) les moments où leur perception consciente alterne entre les deux interprétations du cube. Ces réponses manuelles nous servent à calculer des « fenêtres manuelles », correspondant aux durées des perceptions stables des deux interprétations du cube. En parallèle nous avons aussi mesuré les mouvements oculaires des participants grâce à un dispositif d'oculométrie (ou d'eye tracking). A partir des fixations oculaires réalisées pendant l'observation continue du cube de Necker, nous avons déterminé des « fenêtres oculaires », basées sur des alternances entre deux parties fixées de l'image du cube (Fig. 2). Les fixations oculaires ont été classifiées dans deux groupes sur la base de leurs coordonnées spatiales (gauche vs. droite) grâce à un algorithme de clustérisation. Une fenêtre oculaire correspond à la somme des durées de fixations successives appartenant à un même cluster (Fig. 2).

Le chapitre 2 (article publié comme Polgári et al., 2020) nous a permis de valider la mesure des fenêtres oculaires au sein d'un groupe de volontaires sains. Les participants ont réalisé trois conditions expérimentales de la tâche dans lesquelles leur attention a été manipulée : observation passive et report des alternances perceptives spontanées, focus sur une des deux interprétations en la maintenant mentalement le plus longtemps possible, « switch » ou alternances perceptives forcées en alternant la perception le plus rapidement possible entre les deux interprétations. Les participants ont également effectué une condition contrôle où deux versions non-ambiguës de la figure ont été présentées de façon alternée (comme les deux formes géométriques au milieu et à droite de la Fig. 1).

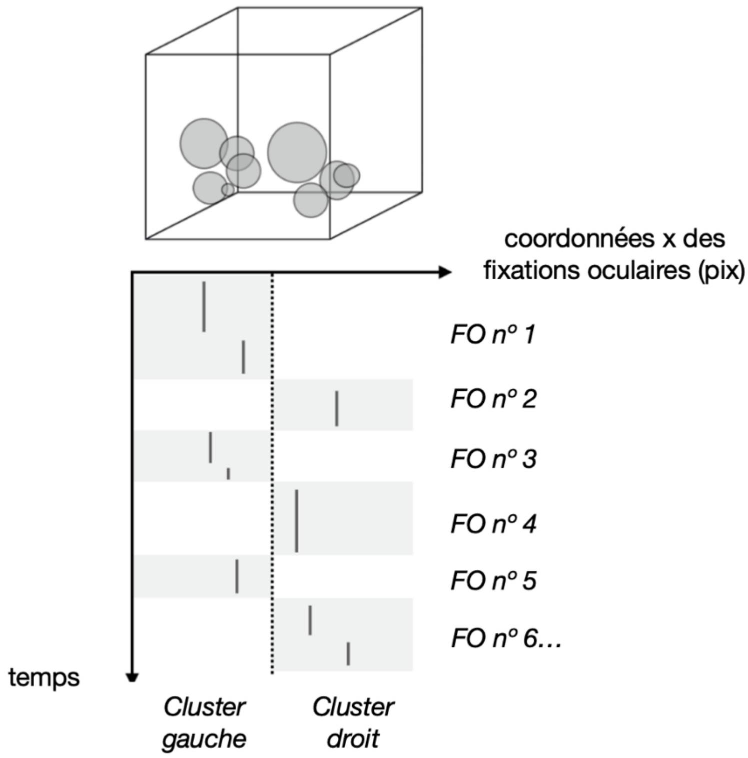


**Figure 2.** Représentation schématique de l'analyse de clustérisation utilisée dans la computation de fenêtres oculaires.
Les fixations oculaires sont représentées sur le cube de Necker par des cercles gris dont les diamètres sont proportionnels aux durées des fixations (partie du haut). Les coordonnées x des fixations sont reportées sur le graphe (partie du bas) par des lignes verticales continues dont les longueurs sont proportionnelles aux durées de fixation. La séparation entre les fixations de gauche et de droite est déterminée par l'algorithme de clustérisation. Les fixations successives qui appartiennent au même côté constituent un cluster ce qui correspond à une fenêtre oculaire (FO sur la figure pour « fenêtre oculaire »). Les bandes grises représentent chacune un cluster.

Grâce à la comparaison des fixations oculaires dans les conditions avec et sans ambiguïté dans l'information visuelle, nous avons montré une correspondance entre les coordonnées des fixations oculaires et les deux percepts du cube. Ce résultat valide l'utilisation des fenêtres oculaires dans l'étude des alternances perceptives. De plus, nous avons trouvé que les alternances oculaires s'effectuent plus rapidement que les alternances manuelles : le nombre de fenêtres oculaires est supérieur au nombre de fenêtres manuelles dans chacune des trois conditions expérimentales. Ce résultat suggère que les fenêtres oculaires correspondent à des alternances perceptives similaires à celles reportées manuellement, mais à un niveau d'intégration plus bas, plus automatique. Ceci rend les fenêtres oculaires particulièrement intéressantes car elles permettraient de mesurer des processus perceptifs plus automatiques que les réponses manuelles classiques, des processus moins affectés par des mécanismes décisionnels, ce qui rend leur application optimale chez des populations psychiatriques.

Dans le chapitre 3 (article publié comme Polgári et al., 2021) nous avons utilisé la technique des fenêtres temporelles manuelles et oculaires dans l'étude de la tachypsychie au sein d'un groupe composé de sujets bipolaires et sains. Les participants ont été classés en trois groupes sur la base de leur niveau de tachypsychie mesuré grâce à l'auto-questionnaire Racing and Crowded Thoughts Questionnaire (RCTQ) (Weiner et al., 2018) : « pas de tachypsychie », « bas niveau de tachypsychie » et « haut niveau de tachypsychie ». En effet la tachypsychie est un symptôme transdiagnostique, et peut même être présente dans des populations non-psychiatriques avec une instabilité de l'humeur sub-clinique. Chez les personnes ayant reporté un haut niveau de tachypsychie nous avons trouvé des altérations dans la modulation de la fréquence des fenêtres quand la tâche devenait contraignante (condition « Focus ») (Fig. 3), et ce particulièrement au niveau des fenêtres oculaires (Fig. 3b). Ces résultats suggèrent un lien entre la tachypsychie et les anomalies des processus perceptifs automatiques et leurs interactions avec des mécanismes attentionnels.

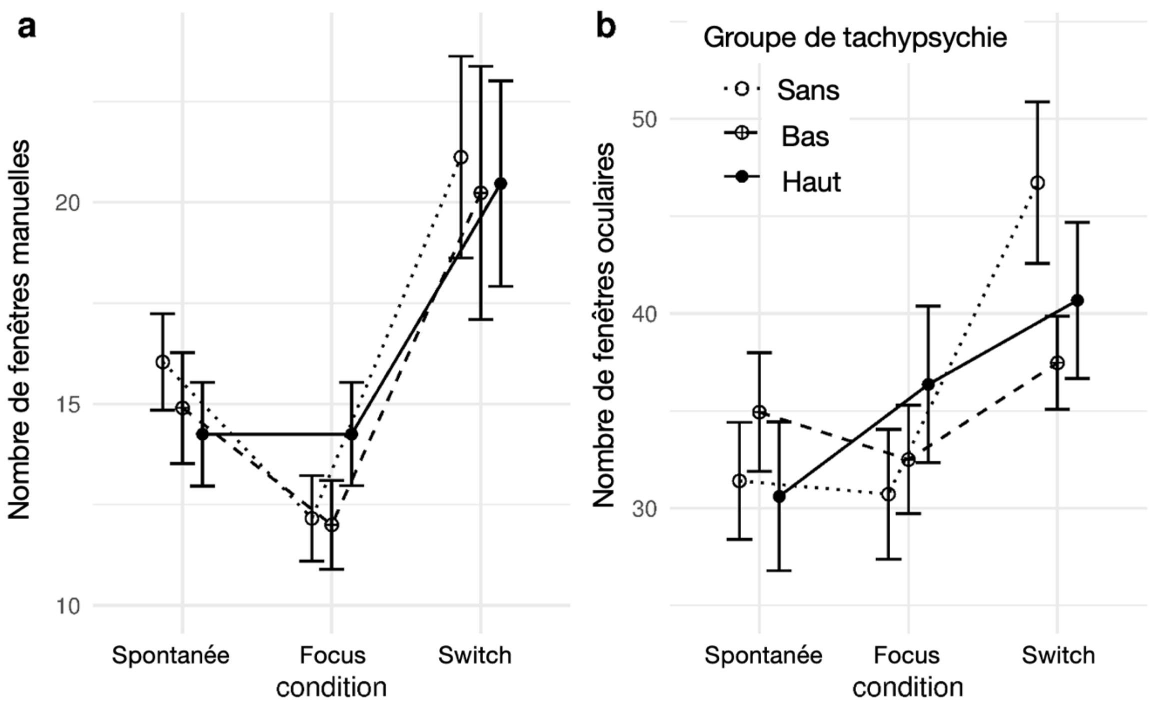


**Figure 3.** Nombre moyenne de fenêtres manuelles (a) et oculaires (b) produit par les trois groupes de tachypsychie (Sans=pas de tachypsychie ; Bas=bas niveau de tachypsychie ; Haut=haut niveau de tachypsychie) dans les trois conditions expérimentales (Spontanée, Focus, 'Switch'). Les barres d'erreurs représentent des ± erreur type. Le groupe présentant un haut niveau de tachypsychie a des difficultés à moduler le nombre de fenêtres manuelles et oculaires entre les conditions Spontanée et Focus (*i.e.* pas de diminution du nombre de fenêtres en Focus).

D'après nos hypothèses les perturbations de la temporalité retrouvées dans les troubles bipolaires et la schizophrénie concernent des niveaux d'intégration différents (présent subjectif vs. moment fonctionnel respectivement). Ainsi, dans le chapitre 4 (présentation de données préliminaires, étude en cours) nous avons comparé les mesures de fenêtres temporelles dans le paradigme du cube de Necker entre les deux groupes psychiatriques (et un groupe de sujets contrôles) afin de voir dans quelle mesure les altérations au niveau du présent subjectif sont spécifiques aux troubles bipolaires. Les deux groupes psychiatriques ont rapporté des niveaux de tachypsychie similaires, et leurs niveaux étaient supérieurs à celui du groupe de sujets contrôles. Cependant, un nombre de fenêtres oculaires augmenté et une altération dans la modulation de ces fenêtres oculaires étaient trouvés uniquement dans le groupe de patients bipolaires (Fig. 4b). Ces résultats suggèrent que des altérations dans la modulation des fenêtres oculaires sont spécifiques aux troubles bipolaires, et que les anomalies de la temporalité au niveau du présent subjectif sont dissociées entre les troubles bipolaires et la schizophrénie. Par conséquent, nous pouvons spéculer que la tachypsychie peut avoir des origines différentes, et les altérations de processus cognitifs qui contribuent à l'émergence de la tachypsychie sont probablement distinctes entre les troubles bipolaires et schizophrénique.

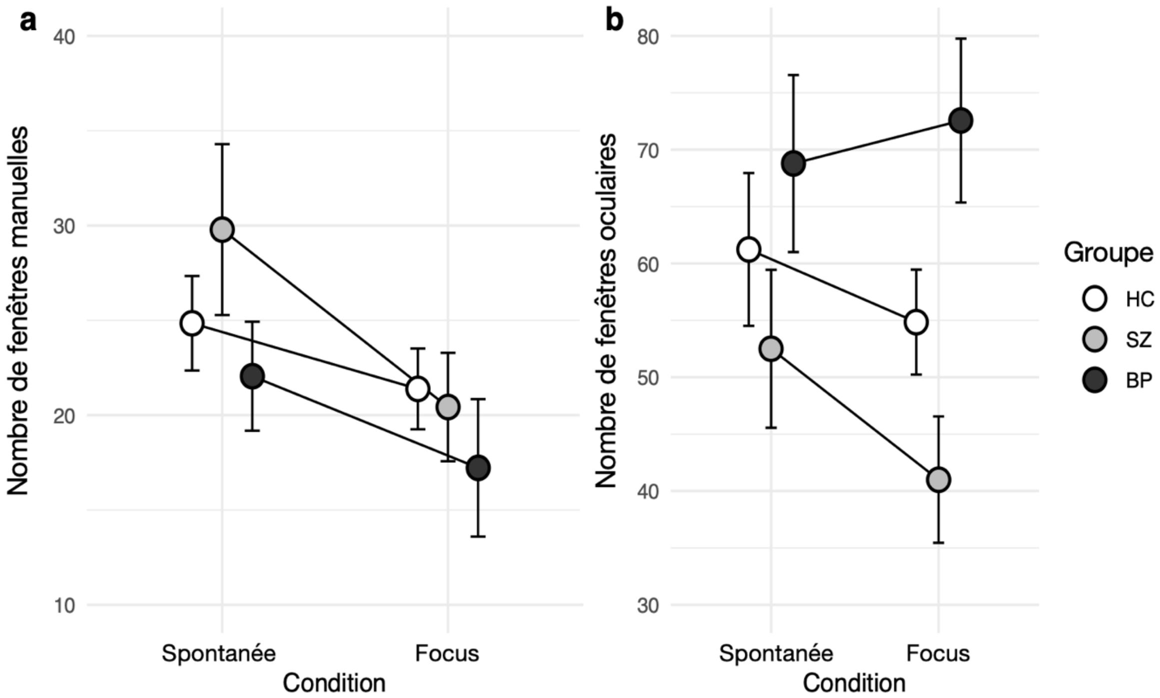


**Figure 4.** Nombre moyenne de fenêtres manuelles (a) et oculaires (b) produit par les trois groupes (HC= sujets contrôles sains, N=26 ; SZ=patients souffrant de schizophrénie, N=14 ; BP= patients souffrant de troubles bipolaires, N=18) dans les conditions expérimentales Spontanée et Focus. Les barres d'erreurs représentent des ± erreur type.

Dans le chapitre 5 (présentation de données préliminaires, étude en cours) nous nous sommes intéressés à la structure temporelle de la conscience du point de vue du traitement de l'ordre. Tout événement, physique ou mental, s'inscrit dans le temps et prend une position relative dans la séquence d'enchainement des événements. Ainsi le traitement de l'ordre temporel est indispensable pour avoir une représentation normale de notre environnement. Des anomalies dans le traitement de l'ordre temporel dans la schizophrénie ont été rapportés dans la littérature (Capa et al., 2014 ; de Boer-Schellekens et al., 2014) et ces déficits d'ordonnancement semblent être plus sévères que ceux prédits par les difficultés des patients à détecter des asynchronies simples sans en juger l'ordre (Capa et al., 2014). Il semble donc que l'ordonnancement des événements dans le temps soit un problème particulier pour les patients souffrant de schizophrénie. Cependant le traitement de l'ordre temporel n'a pas été étudié dans les troubles bipolaires. De façon similaire au chapitre 4, dans ce chapitre nous avons comparé la performance de trois groupes de participants (patients bipolaires, patients schizophrènes et sujets contrôles) dans une tâche de jugement d'ordre temporel afin d'investiguer dans quelle mesure les déficits d'ordonnancement temporel sont spécifiques à la schizophrénie. Deux carrés ont été présentés de façon successive sur un écran d'ordinateur et les participants devaient indiquer à chaque essai lequel des deux est apparu en premier. Différents délais séparant les carrés (ou SOAs, pour Stimulus Onset Asynchrony) ont été utilisés : soit une SOA supraliminale de 100 ms pour laquelle l'ordre est relativement facile à détecter, soit une SOA subliminale de 17 ms pour laquelle l'ordre n'est pas perçu de façon consciente, soit une SOA de 0 ms (synchronie parfaite). Nos résultats préliminaires répliquent les données de la littérature, d'après lesquelles le traitement de l'ordre temporel est altéré chez les patients schizophrènes (Capa et al., 2014) (Fig. 5). Ceci suggère que les troubles du traitement de l'ordre temporel sont spécifiques à la schizophrénie.

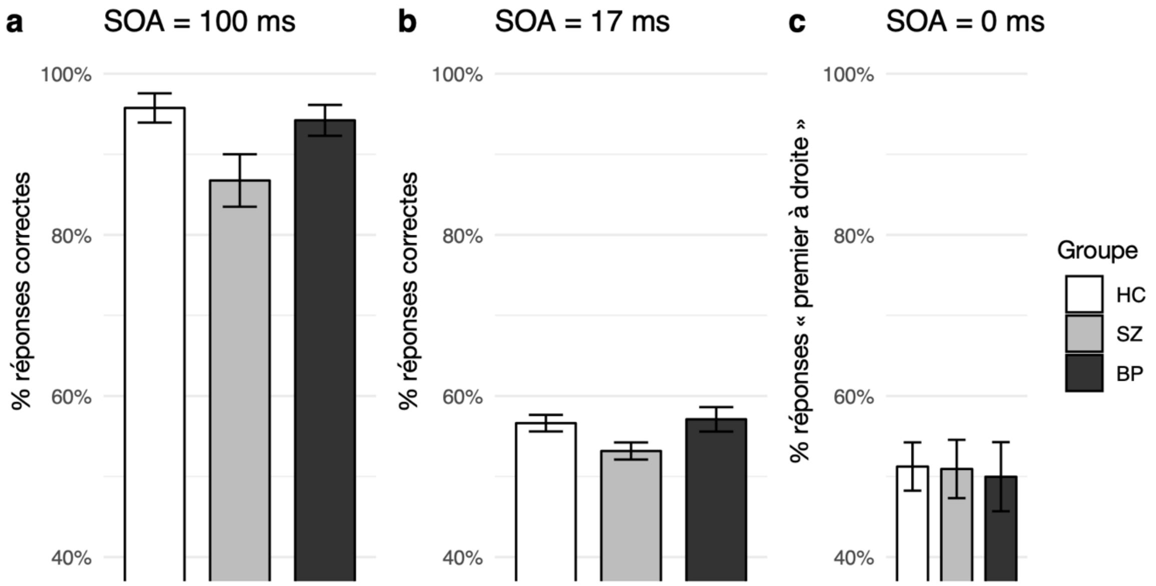


**Figure 5.** Performance des trois groupes (HC= sujets contrôles sains, N=30 ; SZ=patients souffrant de schizophrénie, N=24 ; BP= patients souffrant de troubles bipolaires, N=19 ) dans les conditions avec SOA=100 ms (a), SOA =17 ms (b), et SOA=0 ms (c). Les barres d'erreurs représentent des ± erreur type.

Afin de comprendre l'origine des troubles d'ordonnancement des événements dans la schizophrénie il est nécessaire de comprendre comment la perception de l'ordre émerge chez des sujets sans troubles psychiatriques. En effet, nous savons que le cerveau traite les informations à un niveau automatique et non-conscient avec une résolution temporelle supérieure à celle de la perception consciente (Lalanne et al., 2012a,b ; Poncelet & Giersch, 2016). Ce qui n'était pas clair au début de la thèse c'était si ce mécanisme automatique et non-conscient de traitement d'informations dans le temps comprend aussi le traitement de l'ordre qui relie les événements les uns par rapport aux autres. Il est important de répondre à cette question afin de pouvoir orienter les futures recherches sur l'origine des déficits d'ordonnancement dans la schizophrénie : les déficits d'ordre sont-ils en lien avec les anomalies d'intégrations temporelles connues à un niveau automatique et non-conscient dans la schizophrénie, ou les problèmes d'ordonnancement n'émergent-elles qu'au niveau de la perception consciente ? Le but du chapitre 6 (article en préparation) est de vérifier si l'ordre est un processus automatique qui a lieu à un niveau non-conscient ou s'il s'agit d'un processus qui dépend et dérive de la perception consciente.

Nous avons investigué le traitement automatique de l'ordre à travers une tâche inspirée de l'étude de Chassignolle et al. (2020). L'étude a été menée auprès de plusieurs groupes de volontaires sains. Les participants ont effectué une tâche de détection indicée où ils discriminaient à chaque essai la couleur de deux cibles. Les couleurs étaient grises et prenaient l'un parmi deux niveaux de luminances très proches et donc difficiles à distinguer. Les indices qui précédaient systématiquement les cibles contenaient une information d'ordre subliminale (SOA de 17 ms), et l'ordre (« gauche-droite » ou « droite-gauche ») prédisait l'identité de la cible (« gris clair » ou « gris foncé ») (Fig. 6). Si le traitement de l'ordre avait lieu automatiquement à un niveau non-conscient, les performances de détection des sujets devaient être supérieures dans la condition où les indices sont ordonnés (Fig. 6a), comparé à la condition contrôle où ils apparaissent de façon simultanée et n'apportent pas d'information prédictive sur l'identité des cibles (Fig. 6b). Une facilitation de la détection des niveaux de luminances liée à l'utilisation de l'information d'ordre a été trouvé, cependant cet effet était présent uniquement au début de l'expérience (1er sous-bloc de tache sur 4 sous-blocs) et disparaissait au cours de l'expérience. Ces résultats suggèrent que le traitement de l'ordre à un niveau automatique et non-conscient est possible, mais ne se fait pas systématiquement.

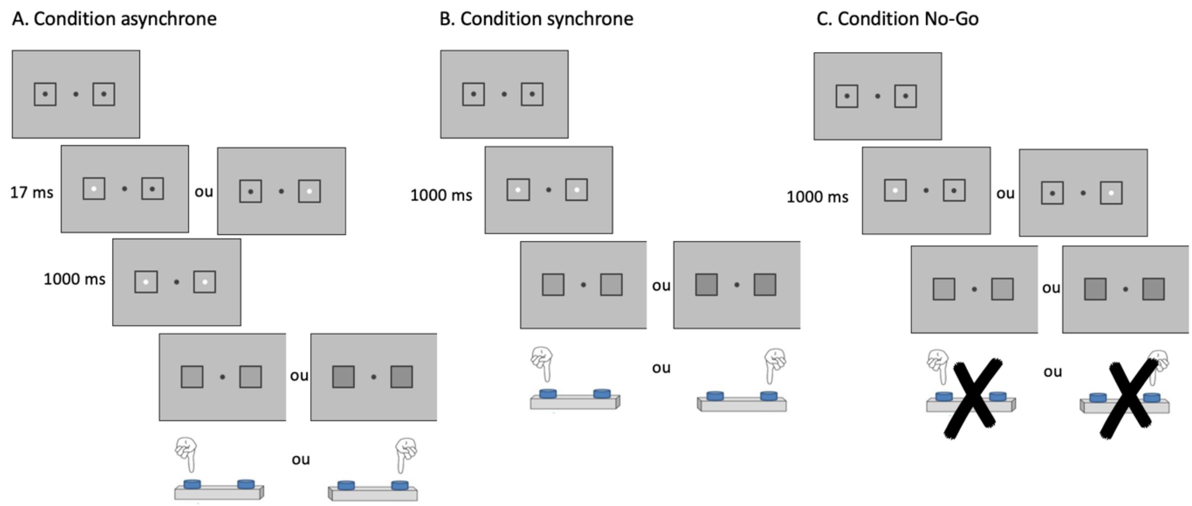


**Figure 6.** Représentation schématique des stimuli utilisés dans le chapitre 6.
Chaque essai commençait par la présentation d'un point de fixation central entouré de part et d'autre d'un carré contenant un point noir. Les indices correspondaient au changement de couleur de noir vers blanc des deux points latéraux soit avec un délai de 17 ms (condition asynchrone, A), soit de façon synchrone (condition synchrone, B). Après un délai de 1000 ms les indices ont été remplacés par une cible lumineuse remplissant chaque carré (luminance gris clair ou gris foncé). La tâche des participants consistait à identifier le niveau de gris (clair ou foncé) et répondre à la cible grâce à un appui sur un bouton-réponse (gauche ou droite).
Dans la condition 'No-Go' (C) la cible correspondait au changement de couleur d'uniquement un des deux points latéraux, suivi d'une cible. Dans cette condition 'No-Go' les participants devaient inhiber leur réponse à la cible. Le but de cette condition était d'inciter les participants à prendre en compte chacun des deux indices avant de répondre à la cible.

Dans l'exemple présenté ci-dessus l'ordre des indices « gauche puis droite » est associé au niveau de luminance gris clair et une réponse du côté gauche, tandis qu'un ordre « droite puis gauche » associé au niveau de gris foncé et une réponse du côté droite. L'association entre ordre des indices, niveau de luminance cible et coté de réponse était contrebalancé entre les participants. Les stimuli et la chronologie de la tâche ne sont pas représentés à l'échelle. Par soucis de clarté le contraste entre les niveaux de luminances cibles est exagéré pour les différencier plus facilement que dans la tâche réelle.

Dans une deuxième version de l'expérience dans laquelle nous avons manipulé la motivation des participants grâce à une motivation financière, nous avons montré que ce traitement de l'ordre automatique dépend de processus motivationnels. Ces données suggèrent que, bien que l'ordonnancement des événements soit indispensable pour avoir une représentation normale de notre environnement, le traitement de l'ordre des événements nécessite n'est pas systématique à un niveau automatique et non-conscient. Nous spéculons que ce mécanisme non-conscient pourrait alors avoir un coût trop élevé pour apporter un vrai avantage à notre fonctionnement cognitif. Traiter toutes les informations les unes par rapport aux autres dans le temps aurait un coût exponentiel dans un environnement saturé d'informations dynamiques. En conséquence, l'ordre serait traité automatiquement uniquement dans des conditions particulières de motivation et d'entraînement.

Les travaux de ma thèse ont permis de mettre en évidence des liens entre altérations des mécanismes cognitifs, des processus d'intégration d'information dans le temps, et de l'expérience temporelle subjective (la tachypsychie) dans deux pathologies psychiatriques appartenant aux troubles psychotiques. Ces travaux nous ont également permis de mieux comprendre la structure temporelle de la conscience grâce à de nouvelle caractérisations de processus de traitement d'informations dans le temps à des niveaux de processus automatiques et non-conscients.

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# Time, psychosis, and diagnostic frontiers

## Temps, psychose et frontières diagnostiques


## Summary

Psychosis, like schizophrenia (SZ) and bipolar disorder (BP), is defined as a loss of contact with reality, which has been related to difficulties synchronizing in time with the outer world. We explored the temporal structure of consciousness in SZ and BP. Racing thoughts are a frequent symptom in BP affecting conscious thought but are difficult to objectify. We developed a novel measure of perceptual processing at the level of seconds to show that elevated levels of racing thoughts in BP are linked to alterations in the control of automatic perceptual processes. When compared, we found a dissociation on our measure between BP and SZ patients. Besides, deficits in temporal order judgments were present only in SZ patients. It is unclear whether these deficits arise only at a conscious level, and we investigated order processing at an automatic non-conscious level. In all, we provide several conceptual and methodological tools to study the temporal structure of consciousness in SZ and BP.


Keywords: Schizophrenia, Bipolar disorder, Temporal order, Racing thoughts, Automatic perceptual processes


## Résumé

La psychose, comme la schizophrénie (SZ) ou les troubles bipolaires (BP), est une perte de contact avec la réalité qui a été associée à des difficultés de synchronisation au monde externe. Nous avons exploré la structure temporelle de la conscience dans la SZ et les BP. La tachypsychie est un symptôme fréquent des BP qui affecte la pensée consciente, mais qui est difficile à objectiver. Nous avons mis au point une nouvelle mesure reflétant un traitement perceptif au niveau de la seconde afin de montrer un lien entre niveaux élevés de tachypsychie et des altérations dans le contrôle de processus perceptifs automatiques. Lors de leur comparaison, une dissociation sur notre mesure a été trouvée entre la SZ et les BP. De plus, des déficits de jugements d'ordre temporel étaient présents uniquement dans la SZ. Nous ignorons si ces déficits émergent uniquement à un niveau conscient, nous avons donc étudié le traitement d'ordre à un niveau automatique et non-conscient. En somme, nous proposons plusieurs outils conceptuels et méthodologiques pour l'étude de la structure temporelle de la conscience dans la SZ et les BP.


Mots-clés : Schizophrénie, Troubles bipolaires, Ordre temporel, Tachypsychie, Processus perceptifs automatiques