Università degli Studi di Ferrara

ISTITUTO ITALIANO DI TECNOLOGIA

DOCTORAL COURSE IN
"Translational Neurosciences and Neurotechnologies "

CYCLE XXXIII

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TEMPORALITY and INTERSUBJECTIVITY IN SCHIZOPHRENIA, A DIALOGUE BETWEEN PSYCHOPATHOLOGICAL PHENOMENOLOGY AND COGNITIVE NEUROSCIENCE

Scientific/Disciplinary Sector (SDS) MED/25

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Year 2017/2020

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INTRODUCTION

Psychiatry, which has always been a border discipline, carries within itself different souls. Historically, some of the main contributions, particularly with regard to schizophrenia, have come from phenomenological psychopathology. This discipline, with its deep attention to the structures of experience, is being watched with increasing attention in order to limit the nosographic flattening of current diagnostic systems.

On the other hand, the development of cognitive neuroscience now makes it essential, for a discipline that wants to maintain its boundaries within the medical sciences, to undergo the empirical validation of neurobiological constructs.

Neuroscience has long been stigmatized of reductionism by scholars of classical psychopathology. In turn, the intuitions and reflections of phenomenologists have often been ignored because they are considered mere philosophical speculations, supported by the charisma of their proponents but not opened to the scientific debate.

Recently, however, a more intense dialogue has opened between these two disciplines, with the hope of translating phenomenological reflections into neurobiological hypotheses that can be tested.

As part of my doctorate in translational neuroscience, I had the opportunity to explore two themes in which the dialogue between phenomenology and neuroscience shows itself to be potentially prosperous: temporality and intersubjectivity.

I focused my thesis work on convergences and divergences of these disciplines, developing a review of the literature regarding the alterations of temporality in schizophrenia and an experimental work of action observation in psychotic onset patients on the subject of intersubjectivity.

The hope is that these first steps may indicate a method for finding useful tools to help those suffering from a disease that is still as obscure today as schizophrenia.

PART I: TEMPORALITY

The question of the consciousness of time is one of the main problems faced by philosophy, psychopathology and cognitive neuroscience. In this thesis I try to highlight how it is possible to find a continuity and a dialogue between these different disciplines.

It seemed possible to identify a "fil rouge" that starting from the thought of the founding fathers of phenomenology and passing through the intuitions of the main thinkers of phenomenological psychopathology reaches modern research centers, where the intuitions of the past are translated into testable theories, open to dialogue with “scientific” and quantitative research.

Alterations of consciousness and perception of time have been repeatedly highlighted in schizophrenia. This extremely complex and heterogeneous nosographic entity succeeds, by forcing us to thematize what is normally too evident to be recognized, to provide many suggestions for reflection on these areas. The hope is that schizophrenia itself could become clearer in its original enigmatic core by a better knowledge of the consciousness of the time.

The thesis work therefore starts from the exposition of the phenomenological conception of temporality according to Husserl, not the only one among phenomenologists to deal with the subject but the one whose ideas have found greater resonance in recent neurobiological hypotheses.

Phenomenology, as is well known, had a strong influence on both classical and contemporary European psychopathology. Several classical authors have described the alterations of consciousness of time present in schizophrenia, as well as in other pathologies. The second chapter illustrates the intuitions and reflections of the classical authors on this topic. The style of those years, however, led mainly to anecdotal descriptions and single clinical cases no longer in line with current research standards. The current generation of phenomenological psychopathologists is trying to verify the intuitions of past from a statistical point of view with tools which are more adequate for contemporary research; in the third chapter these current perspectives are described.

Up to this point the work shows an eminently phenomenological point of view and therefore, at least historically European, but the question of the perception of time in

schizophrenia seems to have opened a bridge between the two sides of the Atlantic ocean, bringing two culturally very distant worlds closer together.

In 1998 Nancy Andreasen in her article "Cognitive Dysmetria" as an integrative theory of schizophrenia: a dysfunction in cortical-subcortical-cerebellar circuitry? "[1] proposes a line of neurobiological research which, not focusing only on the acute aspects, tries to identify a common neuro-cognitive alteration, independent of possible symptomatologic profiles. According to Andreasen, this "trouble générateur" should concern the organization of information in the brain. Some authors have considered it possible that this alteration concerned the temporal organization of consciousness and have moved from there by carrying out neuro-cognitive and neurobiological research on this area. Chapter 4 aims to highlight the clues and theories that move in this direction.

I decided to develop a database that would allow to compare the studies carried out in the field of time perception in schizophrenia; Chapter 5 contains the methods for developing the database and some considerations that emerged from the analysis of the studies themselves. The database itself is attached in the form of descriptive cards of the individual studies.

After this first analysis of the studies, the necessity to relate the multifaceted aspects of temporality to specific behavioral and cognitive symptoms led me to a review analysis which concludes the first part of this work.

The goal of my thesis is to provide a guide which could be a sufficiently agile and complete tool on a fascinating and complex topic such as the consciousness of time in schizophrenia. The dialogue between different disciplines, even at the expense of a high level of specialization, was my guiding light in the development of the project and represents the strength and the main limitation of this thesis.

PHENOMENOLOGY

Founded by the mathematician turned philosopher, Edmund Husserl (1859-1938), phenomenology is the rigorous and methodical description of conscious experience. Phenomenology has often been used to study the mental structures that make up the human experience and how these can be modified in neuropsychiatric disorders. It is known that phenomenology studies consciousness, or rather what appears as an immediate datum to consciousness. However, Its research field is not limited to this, it also studies how unconscious automatic processing plays a decisive role in the organization of conscious experience[2]

Phenomenology is therefore in a privileged position to study the experimental data relating to the alterations of consciousness that characterize schizophrenia, which are disorders of the self or of the self-awareness. From a psychopathological point of view, the phenomenological approach proposes a "useful conceptual framework within which the explanation of pathological experiences could be tried"[3], to include the role of time in the genesis of schizophrenic symptoms. In what follows I will try to summarize some hypotheses within the framework of this particular conceptual framework. A first intuition has to do with the nature of the elaboration of time itself. In phenomenology, time is not necessarily studied and understood as a content of consciousness; rather it is a key component that structures the form of consciousness. Therefore, time seems to be a fundamental, "ontological" component of reality[3]. At the lower strata of the world's constituent processes, Husserl identifies the question of time and, more precisely, what he calls "the inner consciousness of time" (inneres Zeitbewusstsein).

Husserl's main thesis is that the perception of a temporally extended object, as well as the perception of succession and change, would be impossible if consciousness provided us with only a purely present or instantaneous portion of the object and if the stream of consciousness itself were a series of points of experience disconnected from each other, like a string of pearls. If our perception were restricted to the consciousness of what exists in the present moment, it would be impossible to

perceive something that is endowed with temporal extension and duration, since a succession of isolated and punctual conscious states does not make us as such capable of having consciousness of the succession and duration. Since we are obviously conscious of the latter, we must recognize that our consciousness, in one way or another, embraces much more than simply what is given in the present moment: it must be consciousness of what has already been and of what is about to happen. However, the crucial question remains: how are we aware of what is no longer and what is not yet? Some have proposed that imagination and memory play an essential role, and that it is these faculties that allow us to transcend the precise present. We perceive what is happening now, we remember what is no longer and imagine what has not yet happened; but according to Husserl we must distinguish between the direct experience of change and duration and merely imagining or remembering them. According to his perspective, we have an intuitive presentation of succession. So Husserl would insist that there is a phenomenological difference manifest between seeing a movement (which necessarily extends over time) or hearing a melody and remembering or imagining it. Furthermore, it would deny that the apprehension of a present representation of what has just passed can give us an intuitive awareness of something that has just passed.

In his analysis, Husserl emphasizes the "breadth" or "depth" of presence: when I have the experience of a melody, I do not simply experience a presentation of a note that is not a prelude to anything else; a note which is then completely blown away and replaced by the presentation of the next note. On the contrary, the conscience maintains the sense of the first note while I listen to the second, a listening that is also enriched by the anticipation of the next one (or at least by the anticipation of an upcoming acoustic event, if the melody is not known). To illustrate the situation, let's imagine we are listening to a sequence of notes composed of the tones Do, Si, Mi. If we focus on the last part of the sequence, the one that takes place when the Mi resounds, we do not find a consciousness that is exclusively aware of the Mi, but a consciousness that is still aware of the two previous notes, Si and Do. This does not mean that there is no difference between the consciousness of the present Mi and that of Si and Do. Si and Do are not simultaneous with Mi; on the contrary we experience a temporal succession. Si and Do have been, they are perceived as they

move away into the past, which is the reason why instead of experiencing isolated tones that suddenly replace each other, we actually experience the sequence in its temporal duration. In other words, according to Husserl, the reason we are able to perceive melodies is that consciousness is structured in such a way as to allow for this temporal presentation. When I experience something, every necessary instant of consciousness does not simply disappear in the next instant, but is held back by the intentional course, thus constituting a coherence that extends along an experienced temporal duration. In other terms terms, the basic unit of lived presence is not a present "without references", but a "block of duration", that is, a temporal field that includes the three temporal modalities of the present, the past and the future. Husserl uses these three technical terms to describe this temporal structure of consciousness. There is first (1) an "original impression", aimed exclusively at the portion of the object strictly limited to the present. The original impression never appears isolated and is an abstract component that in itself cannot provide us with the perception of a temporal object. It is accompanied by (2) a "retentio", or retention, which gives us the awareness of the portion of the object that has just disappeared and which thus gives the original impression a temporal context facing the past, and by (3) a " protentio ", or protention, which in a more or less indefinite way has as its intentional object the portion of the object that is about to enter and which provides the original impression with a temporal context facing the future.[4]

If we listen to a conversation, it is the retentional aspect that keeps the intentional attitude of the words of a sentence available even after the auditory signals are no longer present. Also, when I say a sentence, I have an anticipatory sense of how the sentence will end, or at least that the sentence will have some conclusion. This sense, which allows us to know where the sentence and the thought are heading, even if it is not completely defined, seems essential to the experience of speaking in a meaningful way. It is the protensive aspect of consciousness that gives us the temporal anticipation of something that is about to happen. As Husserl observed, it is protection that allows us to have the experience of surprise. If I am listening to my favorite melody and someone plays the wrong notes, I am surprised or disappointed. If someone cannot complete a sentence, I feel a sense of incompleteness, partly because conscience involves an anticipation of who will bring us the course imminent experience; and in these cases what actually happens does not correspond to my

anticipation. The content of the protention, however, is not always completely determined and may consist of a more general sense that could be expressed with a thought such as "something must happen".

According to Husserl's theories, retention is not a detail of the consciousness we perceive; on the contrary, we hear the tone that has just passed as if it has just passed precisely because we hold it back. The retentional aspect of consciousness which is present, and what is held back (and which has just passed) are not simultaneous. The tone just passed does not remain present in the consciousness as if it were reverberated in it, but the consciousness retains it as an intentional content: it retains the sense of what has just consciously passed. So the retention must be understood as a peculiar form of intentionality. Unlike the original impression, retention has the past as its intentional object. Unlike episodic memory, retention presents the past does not just represent it. In short, it allows us to intuitively grasp what has just passed and it is not the special apprehension of something present. As Husserl writes, "retention is not a modification in which the impression data are really preserved, only in modified form; on the contrary, it is an intentionality and precisely an intentionality with its own specific character. To emphasize this point once again, being retentionally aware of the portion of the object or event just passed does not imply having that portion simultaneously co-present to the senses in a strange distorted way.

Let's take a concrete example: if we look at a pedestrian crossing the street, our perception will not limit itself to capturing the present portion of its timeless movement. Perceptually, it is not as if the pedestrian suddenly appeared out of nowhere and, furthermore, we do not have to engage in any kind of explicit act of memory to establish the temporal context of its current position. Nor will it be the case, however, that all previous portions of its movement are perceptually present in the same way that its present position is. If this happened, the pedestrian would perceptually fill all the space it has just crossed. But we must also avoid the idea that the past portions of its movement remain visually present in some ghostly and vague way. The temporal "dissolution" in the past is not the same as the dissolution of an image that is dissolving, but that remains perceptually present. Retention holds back the sense of my experience just passed of seeing the pedestrian, but it does not achieve this by keeping a faded image in consciousness. On the contrary, by

retention we mean the fact that at any moment what we perceive is collected in a time horizon; its meaning is influenced by what happened before, which is still intentionally maintained. The fact that the tone just passed is intentionally retained means that its meaning or sense is retained as it has just passed.

Instead of having a memory that represents the object in question, retention provides us with an insight into the meaning of an object that has just passed. This is precisely what is required if something like the perception of succession is to be possible. Husserl would agree that the mere succession of conscious states does not guarantee the consciousness of the succession, but this does not imply the impossibility of a perception of duration and succession, unless one also accepts the idea that the perception it is reduced to the grasping of a mere present point; and this is precisely the idea that Husserl rejects. A perception cannot simply be a perception of what it is now; on the contrary, any perception of the present portion of an object includes the retention of the portion just passed and a protection of what is about to happen. The perceptive presence is therefore not punctual: it is a field in which the now, the no more and the not yet are given in a Gestalt horizon. This is what it takes to make it possible to perceive an object that lasts.

Given that retention constitutes the temporal horizon of the present, given that it constitutes what could be metaphorically considered to be the temporal equivalent of the periphery of the visual field, it should be considered part of perceptual consciousness rather than a form of memory, as of usually it is meant. As William James once said, "an object that is remembered, in the proper sense, is an object that has been completely absent from consciousness and is now reliving from scratch". It is brought back, remembered, fished out as it were, from a tank in which, along with countless other objects, it was buried and lost from sight ". We can only remember something that has been present and has now become past. Given this definition, it cannot be said that retention is a form of memory, because it is involved in the same process as making something present for the first time. It must be said, however, that this argument presupposes a rather narrow definition of what memory is. A more liberal reading allows us to say that memory is involved whenever information is retained over time and, according to this interpretation, retention constitutes a form of working memory.

According to Husserl's analysis, experiences of any kind (perception, memory, imagination etc.) have a common temporal structure such that each moment of the experience contains an intentional reference to past moments, an original impression of what is present and a protective anticipation of the moments of experience that are about to happen. Consciousness generates a field of lived presence. The concrete and full structure of this field is determined by the protective-original impression-retention structure of consciousness. Although the specific experiential contents of this structure change progressively, at each instant the tripartite structure is synchronously present as a unitary whole.[4]

Husserl then describes a tripartite structure of the consciousness of time, which is seen as an integration of the past, present and future. He gives the example of music. When we hear a tune, we are aware of this note, but we still have the previous note ("retention") in mind and we usually anticipate the note that will come ("protention")[5]. As Fuchs[6] points out "these synthetic functions, which operate at the most elementary layer of consciousness in an implicit, tacit or automatic way, are able to integrate the sequence of individual moments in an intentional arc," allowing the subject to connect closely with the world and , therefore, structuring the consciousness. It should be emphasized that the term "intentional" does not mean that the integration of past, present and future moments is deliberate and reflective. On the contrary, it is passive. According to phenomenologists, it is a fundamental mechanism by which we can consciously experience the world as a whole and as continuous over time. Furthermore, such mechanisms would shape all our experiences and influence our sense of self.[6] The passive ability to integrate past, present and future moments would allow us to think in meaningful units: protection would allow us to anticipate the next thought and words when we speak. This implicit or automatic temporal synthesis (or, in Husserlian terms, the "passive" temporal synthesis) contributes to the stability of the perception of the world. Husserl calls this "doxa", and exemplifies it as the certainty that the world will be invariant, allowing the subject to recognize himself in the world. This is one of the most basic processes that ensures that the world can be "taken for granted" [7]. "Consequently, the actions of normal people can presuppose a pre-established world, a spatial, temporal, causal and social order that their mental lives consist constantly "automatically"[7]

In his analyzes, Husserl also observed a fundamental paradox in the way we experience time. Time both "flows" (the experience of subjective flow) and "remains stable" (the now is still while time passes). Husserl was particularly troubled by this paradox and found it to be a central puzzle not only in how we experience time but also in how we perceive ourselves. How could the experience of subjective time be composed of two apparently contradictory elements: one being a flow and one being in the flow? Yet without these two elements there would be no experience of time. The German phenomenological philosopher Held[8] comments on Husserl's dilemma: "it is possible to bring the enigma of the lived present back to a fundamental problem: the experience of the full unity of being both flow and in the flow". Quoting Husserl: "The functioning of the ego leads continuously into its own horizons of the past and the future because it itself is what remains in the transition" (Das ich fungiere leitet in sich kontinuerlich in senna Vergangenheits- und Zukunftshoirzonte ueber, weil es selbst in stehen uebergaengig ist). Husserl identifies the position in the flow as that of the self: The permanent "I" (persistent, self-transcendent) continually emerges as an invariable structure of time: the flow itself. The ego is the temporal structure of flow (which is a totality that I cannot grasp in its entirety, but I can only live by "letting go" of the flow itself. This is the self that preserves itself by letting itself go into the flow in which it is obliged The original passive flow (that is, without the participation of the ego) is given as primal in a way that remains disconcerting [raetselhafte Vorgebenheit des urpassiven Stroemens]. But just as the passive and obligatory flow of time seems the first datum, in the in the same way the "self" that remains in the flow itself appears primal. Held[8] quotes a manuscript by Husserl: "The flow is always the first but the I is also the first" (Das Stroemen ist immerzu im Voraus; aber auch das Ich ist im Voraus). That is, the flow can only be experienced by an "I" which in some way remains preserved; vice versa, the ego is conserved only by letting itself go in a continuous process of self-displacement. At the center of the “nunc stans” there is a submission to one's transcendent.

CLASSICAL PSYCHOPATHOLOGY

One of the most fruitful interactions between philosophy and psychopathology concerns temporality. Authors such as Minkowski[9], Straus [10], Binswanger[11], Kimura[12] and Blankenburg[13] have described alterations in the experience of time, particularly in depression, obsessive-compulsive disorders, and schizophrenia.

The transition from philosophy to the psychopathology of lived time is a cornerstone of Eugene Minkowski's work[9]. With a Husserlian and Bergsonian background, Minkowski brings particular attention to the qualities of experience and the underlying structures in psychopathological research. The problem of lived time is explored with different facets in the famous “Le Temps vécu. Étude phénoménologique et psychopathologique " published in 1933. Minkowski correlates the concept of lived time to that of life itself, understood as " élan vital " towards the future and opposed to rational intelligence, which is instead represented by the spatialized time of clocks. Driven by the vital impulse, our life is oriented towards the future which makes it full of meaning, in an inseparable union from the becoming of the world.

Minkowski also defined the temporal dimension of schizophrenia as an essential element : the "loss of vital contact with reality". Following Bergson's distinction between objective and subjective or lived time, Minkowski argued that our experiences are constantly accompanied by a feeling of moving into the future, or of becoming (devenir). We share this sense of becoming with the surrounding world. Thus, the "vital contact with reality" refers to a relationship with the environment through a rhythm shared by the individual. "We don't just feel a generic sense of progression, in us as well as outside of us, but rather a unique rhythm common to us and to the surrounding world that makes me feel that I am advancing in my life simultaneously at the same time".

This idea derives indirectly from Kretschmer's distinction between "schizoid" and "cycloid" as fundamental personality dispositions, a distinction which was also based on temporal characteristics: in the schizoid there is a persistent tendency to loneliness and emotional detachment, while the cycloid is characterized by cycles of affective resonance, which culminates in the alternation between manic and

depressive states. Bleuler[14] redefined this distinction in "schizoidia" and "syntony", characterizing the vital principles of life in a non-pathological way. "Schizoidia" is the principle of withdrawal and return to oneself, while "syntony" means being open to the world and taking part in social life. The ideal would be to make contact with oneself while remaining in tune with the environment.) For Minkowski there is a profound asymmetry between these two principles: while attunement is a normal faculty that has no variations in degree (one cannot be too in attunement to something), schizoidia can become pathological when it escalates too much, causing a frank break with the environment and leading to autism and extremely rigid thinking and activity.[15]

Rhythm plays an important role in this: a person who shares most of his rhythm with his surroundings tends to be in tune, while a person who has a private rhythm tends to schizoidia. Sharing a rhythm involves a sense of contact or resonance with other people. In schizophrenia, Minkowski[15] stated, a desynchronization arises which implies that the patient no longer takes part in the collective or environmental becoming and no longer resonates with others.

In a chapter of his book "Lived Time" Minkowski directly addresses the problem of lived time in schizophrenia. Starting from his experience with a patient with whom he found himself living together for a long time as a personal doctor, a 66-year-old man afflicted by a delusion of guilt, Minkowski makes one of his most beautiful and accomplished analysis. Here are some extracts supplemented by Prof. Leoni's commentary:

“An atrocious punishment awaits him for his crimes. They will cut off his arms and legs of his family and they will then be exposed completely naked in an arid and abandoned ground. He will suffer the same fate; they will drive a nail in his head and pour all sorts of filth into his belly; mutilated in the most frightening way, he will be led in a great procession to a fair and condemned to live covered with insects in a cage with ferocious beasts or rats in the sewer, until his death ”. "Look, - the patient says one day, - I had not yet thought about tickets for the railway, trams, buses, subways ..." and "and this 'look, I hadn't thought about it' is repeated for every object you believe in that they have not yet taken into account ". It's about the politics of remnants, ”as he says. "All the remains, all the waste are put aside to be then

introduced into his belly, and this in the whole universe ... when you smoke, the ash, the used match and the cigarette butt remain; when eating he is worried about the crumbs, the fruit stones, the chicken bones, the wine and water that remain at the bottom of the glasses ... "

What is immediately striking, Minkowski observes, in this as in any other delusion, is "the content of the delusional idea or hallucination; it is here that the affective factors, the complexes and the symbolism that are so important in modern psychiatry intervene ". But, he continues, “here we are pursuing a completely different goal. How to get deeper into the nature of a morbid phenomenon, such as a delusional idea? " Thus Minkowski articulates the passage, he says, between the "facts of a psychological nature" and the "data of a phenomenological nature" concerning this same case, the explicit contents and meanings of a delusion, of any psychopathological form-of-life, must therefore be penetrated up to their constitutive moment: up to their most intimate motif, a sort of continuos bass which the variety of melodies we listen to always refers to, in a coherence that, between amazing and exhausting, snatches from Mikowski the irreversible Wesensschau stigmatized with the famous , disconsolate “I know everything about him”.

“From the first days of our life together, my attention was drawn to the following circumstance. Upon my arrival, the patient declares that the execution will certainly take place the following night; distressed, cannot sleep and keeps me awake; I console myself by telling myself that the next day he would see the groundlessness of his fears; but the same scene is repeated the next day, the following day and the following days. After three or four days, I had given up all hope”, Minkowski concludes. "What happened? Well, I had quickly drawn from the observed facts a conclusion for the future, on the contrary he had let them flow in front of him without drawing the slightest experience of them for the future. " And, again, shortly thereafter: "This propulsion towards the future is completely lacking in our patient ... time in him is divided into isolated elements, which in normal life we naturally integrate with each other". It is this fragmentation of time, this impossibility of the future and, more profoundly, of the temporal synthesis, of the unification of time in the plasticity and furniture and opening of a durée, Bergson would have said, to ensure that time does not assume and does not can take on another physiognomy than that of duty and repetition, that is, of guilt and punishment.

Time is experience, Minkowski essentially shows. And the forms of the past are ipso facto the contents and meanings - the transcendental contents and meanings, so to speak - of experience. They are its possibilities and impossibilities, its sense and nonsense, which, like foam on the waves, coming from quite another place, shines fleetingly on the light surface that enchants us with the name of psyche. In fact, it is not any past fault that assigns this existence to the exclusive dimension of being-past: proving it of a present, denying it a future.

The élan that moves it is found to be overturned, its intentionality overturned: the movement, transcendental or "structural", Minkowski says, is all one with which the past becomes the one and only habitable figure of time, guilt the only available form of life, punishment the only mask of presence in the world. It is the past itself that becomes - as such and whatever it is - the fault, when it detaches itself from the texture that weaves its unity with the present and the future, from the texture that draws its inextricable interweaving: a past which is for a future, a future which is for a past. The dissolution of this dialectical plot - of this Bergsonian durée pure: an “organization intime des éléments”, as we read in the Essai, which Husserl would have described in terms of stratifications of retentions and protections - translates into a sort of frozen suspension what, usually, it is a past on the way. A past not yet past: always still redeemable and renewable, always to come, so to speak, always already future.

The Japanese psychopathologist Kimura[16] distinguished between objective time and lived time. According to Kimura, lived time is characterized by its orientation towards the future. He distinguished 3 possible temporal orientations that each characterize a specific disorder, namely post-, intra- and ante-festum (literally "before", "during" and "after the party" - with "party" meaning some kind key event). The idea is that these 3 basic orientations are normally well balanced, but in cases of psychopathology, one or the other may dominate. Intra-festum orientation dominates in what we now call borderline personality disorder. These people are stuck in the now, without the ability to imagine horizons of possibility in the future, nor to conceive the past as a significant source for the constitution of a stable identity. The post-festum is an orientation that Kimura recognizes in melancholic depression, where feelings of guilt

arise and patients worry about the impossibility of overcoming the acts of the past. Thus, in post-festum orientation, suffering comes from the idea of being too late to change anything in the situation. Kimura states that schizophrenia involves a predominance of ante festum orientation. The schizophrenic patient appears to anticipate the future, often with some sort of constant sense of anxious impatience, and his acts, thoughts, and words may seem incomprehensible to the person who fails to recognize what, or perhaps how, the patient is anticipating. According to Kimura, the peculiar ante-festum orientation typical of the schizophrenic, including the characteristic forms of ontological anxiety and feelings of the uncanny, is the consequence of the patient's awareness of losing a stable self.

Showing affinity with Jaspers[17]'s "delusional mood" or Conrad's "trema" (described as stage fright[18]), the anticipatory attitude implies an attempt to defend the self against the threatening presence and influence of others. Karl Jaspers devoted a short section of his general psychopathology to the temporal alterations of schizophrenia. Drawing mainly from Fischer's clinical cases[19,20], he described how patients reported a sudden paralysis of time, a loss of continuity between past, present and future, or a déjà vu-like projection of the past into the present. One patient said: "There is no longer present, just a past orientation. The future is shrinking." Another patient described a "boring and prolonged time without end". Similarly, Ellenberger noted that individuals with schizophrenia can "feel time as if it were standing still in the present moment," which could be at the root of delusions of immortality. These descriptions seem to deviate from Kimura's ante festum orientation; however, they mainly refer to the transient states at the height of the psychotic revelation, also described as Conrad's "apophany".

Ludwing Binswanger (1881-1966), Swiss psychopathologist and leading exponent of existential analysis[21], applied the phenomenological approach to understand automatic processes in his analyzes of the self and schizophrenia. He proposed the idea that psychosis is in itself a "natural experiment" in which more hidden levels of the unconscious, otherwise inaccessible, are exposed. The phenomenological analysis of these automatic processes consists in a removal of the different constituent elements of experience, starting with the most immediately aware ones - as if the layers of an onion were removed - to see which layers remain underneath.

These layers or "genetic phases" can be abstractly separated by reflection, but they cannot be said to exist independently.

Another group of phenomenological psychiatrists belonging to the first Heidelberg school (Gruhle, MayerGross, Beringer) in the early twentieth century named and described self disorders (German: "Ichstörungen") and used mescaline intoxication in healthy individuals as a model of psychosis to explore the possible mechanisms of these alterations[22,23].

The Heidelberg group observed that when healthy individuals were under the influence of mescaline, they reported experiences very close to psychotic patients. Their relationship with past experiences was profoundly changed: the past did not seem to help shape present experience and future goals. One participant stated: "Everything I see is different, isolated, with no relation to what has happened in the past." Yet another: "I find it increasingly difficult to transform my impulses into goals and movement. That is, experience current is so new and compelling that there is a loss of relationship with the past and with the future. " Another subject stated: “During the experiment, I happened to receive a letter of great importance and which would have opened up opportunities for me. I read it with complete indifference without feeling or reaction. The whole thing seemed to me to make no sense, as if it belonged to a time past "[23].

Furthermore, the findings of the Heidelberg group have suggested a new mechanism underlying the disorders of the self in psychotic experience, where perceptions, movements, thoughts and emotions occur independently of the subject's will. Perceiving, moving, speaking, thinking, feeling and wanting are normally supported by unconscious, automatic processes, which therefore remain largely ignored. In disorders of the self, automatic processes are dissociated from the subject and therefore experienced as not under the control of the patient[22,23]. However, this does not mean that the automatic processing itself becomes aware.

In the alterations of the self present in schizophrenia, a dissociation occurs between conscious experience and the underlying processes, i.e. the automatic processes of a person appear to function independently of the will and disconnected from the self. This means that the automatic processes are experienced as independent agents causing extremely disturbing sensations for patients[24].

In other words, the psychotic experience associated with self disorders could derive from the alteration of the coordination of time between conscious and unconscious processes.

The disconnection of automatic processing from conscious experience can therefore be experienced as an intrusion, in the sense that phenomena become aware due to the lack of coordination over time between automatic and conscious processing

For example, in the insertion of thought, in the theft of thought, in influencing experiences, the various domains of experience (perceiving, moving, speaking, thinking, feeling and willing) appear as detached from the patient's conscious controlled processing. This experience of lack of control makes the patient's elaboration process seemingly foreign and influenced by external agents.

Mayer-Gross is the leading exponent of what later became known as the "basic symptoms" approach: the view that elementary perceptual abnormalities play a critical role in the development of positive symptoms of schizophrenia, including self. Phenomenological psychiatrists Matussek, Conrad and Binswanger also later developed this view[2425,26]

Blankenburg in his phenomenological analysis about the loss of “natural evidence” in schizophrenia, comes to similar conclusions. As Blankenburg[27] notes, our mental health is preserved through a certain "resistance to losing common sense." This resistance works precisely by ignoring the obvious, which requires no further exploration; it even "resists" further exploration. If this resistance is lost, his absence is painfully pregnant. A patient states: "What am I missing? It's something so small, but strange, it's something so important. It is impossible to live without. . . ". Blankenburg continues: "Not only has the patient suffered from the loss of something that appears to be very small, but he must also suffer that the rest of us barely appreciate this essential component of our experience and have the greatest difficulty in empathizing with. what it would be not to have it. " Again: "Common sense is based on habit. The natural self-evidence of daily existence draws its nourishment from its repetitiveness. "Blankenburg observes that common sense is based on judgments of the probable rather than on what we can directly ascertain as true. If certainty is required in the proper domain of the mere probable, then we try to construct what it is available to others as a matter of "subtlety" of feeling, that is, what

is intersubjectively acceptable but not accessible to direct rational analysis. This is consistent with the fact that automatic processing is impaired and must be compensated for. from conscious processing. He also points out how the disconnect between unconscious and conscious processing can lead to strange compensatory mechanisms in patients which further contribute to self disorders. The sense of self is partly defined by the temporal structure that it does not need to be conscious Furthermore, the role of the temporal structure in the experience of bodily presence (own and others) is shaped by unconscious processes, the alteration of which can therefore influence the feeling of being a unique individual.

The Ego, understood as what is preserved in the momentary transitions from moment to moment, is based on the original unity between being in the flow and the flowing itself. To the extent that one or the other of the mutually interdependent components of staying and flowing is interrupted, this will lead to an alteration of the sense of self. This fits very well with the first phenomenological studies of the Heidelberg group[28,29] on psychosis in the basic symptom model. For example, Heidelberg participants reported "The movements are experienced as abnormally slow or not perceived at all: the movement of my hand is experienced only in its start and end positions. In contrast, the movements can be exaggerated, perceived as too much. fast, stationary objects are perceived in motion. My movements seem artificial, foreign, like an automaton. "Regarding the distortions of time and space in the basic symptom model, subjects reported:" I could not imagine the future or the past. I have lived entirely in the present and also in a very narrow present. Time slows down, coming to a standstill with a sense of timelessness, or on the contrary, begins to accelerate. When time stops, you lose the sense of movement and space ".

A considerable number of psychopathological works also describe an breaking of the intentional arc in schizophrenia, which could lead to the first episodes of schizophrenic experiences or, otherwise, to alterations of the self or to a "weakened ego"[30] . If passive synthesis were to cease to occur in mental life, the existence of the world and its objects would cease[30], and the world could no longer be "taken for granted". Consequently, since the lower layers of mental life are compromised, the person feels threatened by a type of lack of self and absence of a world that leads him to experience "ontological anxiety".

The "absence of self" described here is not of a reflexive kind. Alterations of the self are hypothesized by phenomenologists who base their arguments on how the experience of the world should be based on a basic self. In particular, clinical observations lead to reinterpreting symptoms as conscious compensation for alterations in the self. Because the experience of patients in the world is distorted, they have to compensate for it. The world must be actively rebuilt (the person must engage in "rational reconstruction").

A wide range of symptoms can be understood as a consequence of this fundamental disorder of the self, such as hyperreflexivity or the loss of natural evidence. Thus, various altered aspects of the self could be understood or could manifest themselves as an attempt by the patient "to actively engage with to reconstruct the ontological foundations of reality". This is understandable as there is a balance between the pre-reflective and reflective self. If the pre-reflexive self is weakened, patients would compensate for this weakness by explicitly paying attention to aspects that we usually ignore. While it is an interesting idea, it has often been argued, and rightly so, that it is difficult to prove[31].

However, there is also more direct evidence of the distorted experience of the world of patients, who seem to move away from a lived and dynamic time. A thorough review of the literature suggests that direct experiences of an explicit feeling of time interruption may be more frequent than clinical experience suggests[32]. For example, patients describe feeling that time is standing still. One of Minkowski's patients gave the following explanation: "I am looking for stillness and I have a tendency to immobilize everything around me." Another patient reported: "Things are going too fast for my mind. [...] It is as if you see one photo in one instant and another in the next."[33] Similarly, in the words of another patient, "What is the future? It cannot be reached. [...] Time stands still [...]. It is a boring time, stretched without end"[19]. A schizophrenic patient of Bin Kimura quoted in Fuchs[34] says: "Even time flows strangely. It falls apart and no longer progresses. There are only countless if separated now, now, now. . It is the same with myself. From moment to moment, various "selves" arise and disappear completely at random. There is no connection between my present ego and the previous one. "

This brief excursion into the phenomenological approach suggests that time is a key component of experience and, rather than a content of consciousness, a dynamic component of consciousness.[343536] However, as pointed out at the outset, the evidence is based mainly on introspection and anecdotal references, and the conclusions are therefore necessarily limited. As we have seen, phenomenological theorizing interprets patient statements to explain non-verbal, pre-reflexive mechanisms. This could be considered a major flaw in the approach. It should also be emphasized that these hypotheses are not based on experimental work but on the understanding of the problems of the structure of lived time derived from the reflections of phenomenology and from anecdotal clinical observations.

CONTEMPORARY PSYCHOPATHOLOGY

Phenomenological psychopathology, in its most modern version, open to dialogue with cognitive neuroscience, brings both empirical and theoretical contributions to the problem of time. Leaning on the reflections of the psychopathologists of the past, however, it tries to overcome their methodological limitations.

The works of classical psychopathology, as we have seen, provide several examples of abnormal time experience (ATE) in schizophrenia. Minkoswski was the first to give an extensive description. He hypothesized that subjective time is altered in its flow, and is experienced as frozen, immobile, devoid of "vital momentum". He described the time of people suffering from schizophrenia as characterized by the loss of immediate attunement to the situation. He also highlighted the phenomenon of the spatialization of time: time is perceived as divided into juxtaposed elements that the schizophrenic is unable to put together. People with schizophrenia have also been described as living in an eternal "now" called by kimura bin ante festum in which something important is about to happen. Especially in the early stages of schizophrenia, time appears suspended: it is a paradoxical mixture of immobility and immanence.

The fragmentation of time has been regarded as a generating disorder of schizophrenia. Some of the most characteristic symptoms of schizophrenia (e.g. thought insertion, hallucinations or experience of passivity) have been interpreted as manifestations of a disorder of the constitutive synthesis of consciousness, so that every moment is experienced by the person as detached from the stream of consciousness and from the sense of self.

Starting from this perspective, in 2017 the interviews EASE[37] and EAWE[38]: examination of anomalous world experience were developed. From the authors' description: "Eawe: examination of anomalous world experience is a detailed semi-structured interview whose goal is to facilitate the description and discussion of a person's experience and their lived world. This tool is rooted in the tradition of psychopathological phenomenology and its goal is to explore, in a qualitatively rich way, six dimensions of subjectivity - that is, the experience a person has of: (1) space

and objects, (2) time and events, (3) other people, (4) language, (5) atmosphere, (6) existential orientation.

Eawe is based and primarily directed towards experiences believed to be common and sometimes distinctive of schizophrenic spectrum conditions, and the disintegration of consciousness of time obviously has important psychopathological consequences with regards to how a person perceives the world.

Regarding the dimension of time, the items described are:

ITEM	DESCRIPTION
2.1 Time or Movements Appear to Change Speed	Distortion of the in-the-moment experience of time or movements, with these either accelerated or slowed down
2.1.1 Time or Movements Seem Speeded Up	*"It seems to me that everything was going much faster than before. The nurses and the patients were moving … more quickly than is usual. When the doctor spoke it sounded fast, loud and at a higher pitch."*
2.1.2 Time or Movements Seem Slowed Down	"*Night seemed to be longer."* *"Longer slower time."* *"Time dilated.*
2.1.3 3 Time or Movements Seem "somehow" Both Speeded Up and Slowed Down	*"Time slower, faster, timeless."* *"Mouth movement and speech of other out of synchronizing: one faster and the other slower*

2.2 Discrepancy between Internal and External Time	The subject reports sensing that his own internal time clock is running at a different speed from the rest of the world
2.2. Internal Time Seems Slower than World Time	The subject experiences her own actions, thoughts, or emotions as immobile or very slow, while people and events move at a normal or faster pace. "*Outside things still go on, the fruits on the trees move this way and that. The others walk to and fro in the room, but time does not flow for me … What does the outside world have to do with me? I only bump up against tim*
2.2.1 Internal Time Seems Faster than World Time * The subject feels he is operating, or thinking, at a pace faster than that of the external world.	The subject feels he is operating, or thinking, at a pace faster than that of the external world. *"I felt I was moving normally and everyone was moving slowly."*
2.3 Disruption of Dynamic Organization of Time	The subject feels that the normal flow or passage of time cannot be taken for granted as a coherent but dynamic background for experience
2.3.1 Time Feels as though Completely Stopped, Static, Infinite, Disappeared	The subject may experience time as having halted or come to a standstill "*It feels as if it is always the same moment … like a timeless void."* *"Thought stood still, yes everything stood still, as*

	if time had ceased to exist." [*"I continue to live now in eternity, there are no more hours or days or nights."* *"I stopped to light a cigarette... I suddenly had the feeling as if I had been standing there for about two hours…checked my watch…. I had been standing there just for a couple of seconds."*
2.3.2 Time as Disjointed or Fragmented	A loss of normal, continuous temporal flow; instead, moments seem disconnected, disjointed, or out of sequence *"'While watching TV it becomes even stranger. Though I can see every scene, I don't understand the plot. Every scene jumps to the next, there is no connection."* *"The course of time is strange, too. Time splits up and doesn't run forward anymore. There arise uncountable disparate now, now, now, all crazy and without rule or order."*
2.3.3 Disorientation in Time	difficulty or confusion situating events within the passage of time , or regarding the notion of time itself *"I cannot remember time."* *"I looked at a clock and it didn't mean anything"*
2.3.4 Feeling Limited to or Isolated within the Present Moment	Difficulties representing, conceiving of, or feeling connected to one's own past or future , because one's experience feels restricted to the present

	"It's all collapsed into the present so I guess I don't see a future any more than I see a past. It just seems to be an omnipresent pure present presence, I guess."
2.3.5 Various Bizarre Experiences of Time	Including a general sense of strangeness, or more specific disturbances *"Time is somewhat changed. It isn't supposed to be the way it is. I don't know in what way "* *"'I thought I was controlling time. I thought I was here and in a different dimension at the same time."*
2.4 Disturbed Anticipation	The normal sense of imminence, of directedness toward an anticipated immediate future, is somehow altered or disturbed
2.4.1 Perpetual Anticipation (Conrad's Trema or Wahn-stimmung)	The feeling that something very important (though perhaps unidentifiable) is always about to happen, of "something imminent," of "living in an eternal and pregnant 'now'" or "a state of suspense" "*Then everything seemed to stop, to wait, to hold its breath, in a state of extreme tension….Something seemed about to occur, some extraordinary catastrophe."*
2.4.2 Constant Surprise due to the Inability to Anticipate Future Events	a pervasive sense of novelty, surprise, or anxiety regarding events that, normally, would not elicit such a response (since they would be expected

	"And everything was new for me, it was all new for me."
2.4.3 Feeling that "Anything Could Happen"	all possible unfolding events seem equally likely or unlikely, *"On the one hand there's this weird feeling that anything could be around the corner – monsters, the end of the world – and yet it's all still like 'so what.' There's no feelings of anxiety like one might expect. I notice this, and often wonder why these possibilities that would normally frighten people have no impact on me"*
2.4.4 Protention (Future Directedness) Collapses	a loss of immediate anticipation: a feeling that it is impossible to move naturally into the imminent future. "*Everything around me is motionless and congealed…I see the future as only a repetition of the past."*
2.5 Disturbed Awareness of the Expected Future	The imagined or conceived future (as distinct from the immediate/imminent future of protention) is experienced as irrelevant or nonexistent, as highly threatening, or as abnormally known or otherwise revealed in advance.
2.5.1 Future Seems Nonexistent	The subject is unable to think about, imagine, or otherwise conceive the possibility of a future time period *"'I cannot see the future, just as if there were*

	none. I think everything is going to stop now and tomorrow there will be nothing at all."
2.5.2 Future Seems Unimportant or Irrelevant	Future events seem to lack any significance or emotional charge
2.5.3 Future Seems Threatening	The subject describes experiencing the future as threatening or overwhelming The subject reports feeling the future is full of "*deadlines by which I would have to do things or everything would stop*."
2.5.4 Premonitions	The subject describes somehow knowing what was going to happen before it happened *"I felt something good was going happen to me*."
2.6 Disturbed Experience of Memories or of the Past	The remembered past is felt to be changed in some way, whether overly cut off, vague or obscure, disappeared, overly sped up or slowed down, disjointed, or intrusive9
2.6.1 Past Seems Cut Off	The subject feels dissociated from past memories , as if the past were utterly disconnected from, or unrelated to, the present moment (existing somehow like a "time before time"), or as if past events had never really happened to oneself (that they were merely imagined or dreamed, for example). *"'I was cut off from my own past, as if it had never been like that, so full of shadows…as if life had*

	started just now…"
2.6.2 Past Seems Vague or Obscure	it is difficult to remember. The subject may describe past as though "*lost in a fog."*
2.6.3 Past Disappears or Seems Nonexistent	The subject cannot remember past experiences at all and may feel the past never actually occurred *"Sometimes [the past] just doesn't seem to exist, so a memory, like my therapist can tell me something has happened, I'll think ok that exists because you're telling me about it right now, not because it actually happened….Sometimes I think that I never was a child, never had a childhood, never had a past."*
22.6.4 Past Seems Accelerated	In retrospect, past memories seem somehow condensed, Months and years fly by with excessive speed. One subject felt a past of twenty-nine years had lasted only four years at most and the smaller time-spans within this period were correspondingly shortened*"*
2.6.5 Past Seems Slower	The subject feels that past memories are drawn out , or that events occurred over a much longer period of time than was really the case *"'My own memory gives me the impression that this timespan, 3–4 months by ordinary reckoning, was an immensely long time for me, as if every*

	night had the length of centuries."
2.6.6 Intrusiveness of the Past	present, and even his future, feels somehow overwhelmed or overcome by his pas *"There is no more present, only a backward reference to the past; the future goes on shrinking – the past is so intrusive, it envelops me, it pulls me back*."
2.6.7 Erosion of Distinction between Past and Present	The subject is uncertain about whether she is remembering something from the past or actually living it in the present moment "*Time seemed like I was back in the past, not today's time."*
2.6.8 Past Seems Disjointed	Past events appear in retrospect as disconnected, disjointed, or out of sequence rather than a sensible series of events. *"'I feel as if I've lost the continuity linking the events in my past. Instead of a series of events linked by continuity, my past just seems like disconnected fragments*." *"When the visit is over, it could very well have happened yesterday. I can no longer arrange it, in order to know where it belongs*."

The items refer to a qualitative research concerning the world of schizophrenic patients. However, there are no pathognomonic items of the disorder or indicators of diagnostic accuracy. The tool was developed by some of the most eminent exponents of contemporary phenomenological psychopathology starting from what is present in the classical literature and from the collection of direct experience from patients.

The goal of this tool is to get out of the descriptive impoverishment that characterizes current nosography, centered on the striking and behavioral aspects to instead grasp the differences present on a subjective level even in the early stages of the disease and allow for an earlier and more adequate classification. In fact, the current poor diagnostic stability in psychiatry requires an effort in the development of more appropriate tools and phenomenological psychopathology, with its attention to the experiential and structural differences of the patient's world could prove to be an adequate tool.

A first qualitative research on the topic of temporality had already been carried out by Stanghellini et al. in the article "Abnormal time experiences in Major Depression: An empirical qualitative study"[39]. By analyzing 550 medical records compiled from 1979 to 1993 by John Cutting, an English psychiatrist with great expertise in phenomenological psychopathology, the authors were able to verify the incidence of abnormal temporal experiences (ATE) in a population of patients suffering from major depression. The results of the study made it possible to characterize what could be specific alterations that occur in depressive pathology, sometimes even described as pathognomonic by classical psychopathology but never subjected to empirical verification.

In a second work "Psychopathology of lived time: abnormal experience in persons with schizophrenia"[40], still working on the same clinical material, Stanghellini et al carry out a similar analysis, addressing however the alterations of temporality in schizophrenia and then comparing the conclusions reached in the two different diagnoses: major depression and schizophrenia.

The interviewer of the time, John Cutting, was not carrying out work directly oriented to the characterization of temporality but in-depth clinical interviews for a "second opinion program" in the South East of England. He had adopted a conversational

style oriented to the exploration of abnormal symptoms and perceptions, including more subtle experiences, usually ignored in routine practice. Some of the questions were aimed at exploring the time domain, some examples are as follows:

"Could you tell me about your experience of the time?"

"Think about an experience, a period of your life in which you were particularly aware of the time and tell me about it"

“Have you ever felt any oddities in the passage of time? For example in the continuity of time? Or in the way past, present and future are articulated? "

"Have you ever felt the speed of time speeding up or slowing down?"

"Do you think that the meaning you now attribute to time is somehow different from what you attributed to it before or to common sense?"

The clinical utility of this approach is developed on 3 levels: improve the characterization of the schizophrenic experiential structure, improve our understanding of the schizophrenic world and provide the basis for empirical research that is able to correlate the real experiences of temporality disorders with clinical symptoms and biological substrates. This approach therefore shows an important openness to dialogue with cognitive neuroscience and neurobiology that we will explore later.

Approximately 36% (109 out of 301) of the schizophrenia patients surveyed reported at least one ATE. ATEs were more frequent in acute disease (N = 109 of 198; 55%) than in chronic situations (N = 14 of 103; 13%). ATEs in people with schizophrenia were distributed across 3 domains with different subdomains

1) Disarticulation of the experience of time

2) Disturbed experience of the speed of time

3) Discrepancies in the experience of the time

1) Disarticulation of the experience of time: This domain is characterized by a breakdown of the joint and synthesis of the unitary process of primary impression-

retention-protection that underlies the individual experience of external objects and of themselves. This category includes 4 subdomains

a. Interruption of the passage of time. Patients experience time as fragmented. The original impression, retention and protection are disjointed. The intentional unity of consciousness is disturbed. The primary impression is no longer related to either the past or the future. The outside world appears as a series of snapshots. Typical phrase: "The world is like a succession of photographs".

b. Déjà vu / veçu. Patients feel places, people and situations as if they have already been seen and the news as they have already heard. This ATE involves a disarticulation of the temporal structure in which the retention is no longer distinguishable from the original impression. The feeling of already successful prevails. Typical phrase: "when I heard the news I felt I had heard it before."

c. Premonitions about himself. Patients feel that something is about to happen to them or that they are about to do something. This ATE involves a disruption of the temporal structure in which protention invades the present moment. Typical phrase "I felt something good was going to happen to me."

d. Premonitions about the outside world. Patients feel that something is about to happen to the outside world. Like the previous one, this ATE involves a disarticulation of the temporal structure in which protection invades the present moment. The is-about-to-happen prevails. Typical phrase: "Something is happening, as if a drama is about to unfold"

2) Altered experience of the speed of time.

a. Time experience as accelerated. Typical phrase: "Birds peck much faster than is possible"

b. Time experience as slowed down. Typical phrase: "Time stopped"

c. Experience of time as both slowed and accelerated. Typical phrase: "It was as if time was moving very slowly or quickly"

3) Discrepancy on the experience of time. Patients understand the meaning of time as discordant from the way they are used to or from how they consider the common experience of time to be.

a. Sense of time different from before. Typical sentence: "The feeling of time seemed different"

b. Loss of common references on time. Typical phrase: "I was looking at my watch and it meant nothing"

The results obtained, in the opinion of the authors, would confirm the pre-existing anecdotal findings and theoretical hypotheses on the phenomenological characteristics of ATE in schizophrenia on a larger scale. The main domain of ATE is the fragmentation of the experience of time, which means the breakdown of the pre-reflective synthesis of original impression-retention-protection on which a coherent sense of self and of the world develops. From the comparison between the results obtained in cases of major depression in those of schizophrenia the authors underline the definition of different alterations in the two disorders. In cases of major depression there would be no disarticulation of the retention-original impression-

protention synthesis. The main feature in major depression is the absence of time. Time would lack duration, not articulation. Although in major depression, ATEs include phenomena of slowing time as in schizophrenia. In major depression these are accompanied by feelings of despair and an atmosphere of decay and death that are very different from the feelings of amazement and perplexity that typically accompany similar phenomena in cases of schizophrenia. Minkowski and his commentators point out that in schizophrenia the experience of lived time stops. The loss of vital contact with reality, that is, the lack of attunement, the loss of natural evidence, the inability to immerse oneself in the world and solipsism are the main consequences. In major depression, the contact with reality is instead partially preserved but affected in terms of desynchronization: individual time and world time do not flow at the same speed and existence is totally dominated by the past.

An interesting reflection on the issue is the one brought by Fuchs[41] in his commentary article on the EAWE time domain. First of all, Fuchs provides a distinction between implicit and explicit temporality, or between temporality experienced in a pre-reflexive way and temporality experienced in a reflexive way.

Implicit temporality

Implicit temporality means "living in the time". It is the experience of the movement of life, which is implicit in our experience of being involved in the world and oriented towards our immediate goals. It permeates our bodily involvement in a specific situation. This implicit time is always present and underlying our experience, and it requires two conditions.

(1) The first condition is related to what Husserl called "internal consciousness of time", and corresponds to the basic form of pre-reflexive consciousness. Its continuity is based on the constitutive synthesis of experience: our experiences are unified thanks to the synthesis of components directed forward and backward. Husserl described how the internal consciousness of

time implies the synthesis of 3 moments: original impression, retention and protection. (see previous chapter). These 3 moments taken together can be referred to as a "duration block". Clearly, this synthesis is a passive or automatic process; the subject does not combine protention, original impression and retention in an active or reflective mode. This implicit synthesis is in fact the means through which the world is immediately perceived and through which an interaction is possible. The internal consciousness of time also includes a pre-reflective form of self-awareness. When I say a sentence, I maintain awareness of what I have just said and of what I am about to say, but also I am aware that it is I who have spoken and that I am continuing to speak. This is a pre-reflexive process: I don't need to reflect to become aware of myself. Indeed, this basic form of self-awareness is the basis for higher forms of personal identity such as the narrative self or the reflective self. The pre-reflective consciousness, also called "minimal self", must be considered inherent in the internal consciousness of time. The minimal self can only exist as a flow of time, however this flow also depends on the minimal self as it is the means through which it manifests itself.

(2) The second condition for implicit temporality is less linked to purely cognitive processes and more to the affective and dynamic dimension of lived time. It can be represented by concepts such as drive, impulse, affection. This second condition in fact concerns the affective-conative aspects of temporality. They are the roots of spontaneity, affective intentionality, attention and the pursuit of objectives. They are certainly key aspects of human life and correspond to what Bergson and Minkowski indicate with élan vital. Implicit temporality is therefore aligned with the intentional and teleological processes of life: "Time lived is connected with the experience of being embodied and being guided and directed towards the world in terms of bodily potential and possibilities." The passive synthesis and the conative-affective dimension of time are therefore closely linked and even inseparable even if they can be distinguished from a conceptual point of view. The possibility of identity over time of both the object and the subject of perception depends on the integrity of the consciousness of time and the intentional arc

Explicit temporality

However, we do not experience time only in a pre-reflexive way. Sometimes we are very explicitly aware of time, for example when we arrive late for a meeting, waiting for a long desired vacation, or when we remember past events. In these situations, in fact, a gap emerges between present and past, we experience a segment of time as “no more”, and we feel time go on without stopping, while it separates us from the things we lack. Both in anticipation of the future and in mourning for something that disappeared in the past, we perceive explicit temporality as segmented. When we are no longer immersed in our activities, and there is a feeling in which time seems to deny the implied or lived time. This explicit becoming of time can also lead to a confrontation with the finitude of life, and can include the conception of time as an inexorable and independent force that dominates us.

Explicit time is made up of the 3 components past, present and future. Like retention, original impression and protection, past, present and future require a certain degree of synthesis. In this case, however, it no longer concerns a passive or automatic process on the transcendental level, but an active synthesis carried out by the subject. It is the personal, extended or narrative self that binds the 3 parts together. The personal self is in fact capable of projecting itself into the future, and of recognizing its life story in a narrative form. This can also be said to mean a form of intersubjective temporality, as the narrative can become shared with other people. We even create objects like calendars and timetables to synchronize our explicit time with that of others.

Alterations of implicit temporality

In schizophrenia according to Fuchs it is possible to identify alterations of implicit and explicit temporality. Implicit temporality alterations are related to the underlying symptoms. Gallagher and Fuchs hypothesized that the protention function may have decreased in schizophrenia, leading to the failure of the ability to link experiences

that is constitutive of the intentional arc. In fact, the protective function can be considered responsible for extending through the intentional arch and directing it towards a goal.

Fuchs argued that protention would open a cone of possibilities. The cone originates in the present and continually moves forward. Within the cone are the more or less reliable events, while the edges of the cone correlate with increasingly unlikely associations and events. The cone becomes wider with increasing distance from the present moment, this corresponds to a decreased determination of the likely events to follow. These probabilities depend on my retentions, my current impressions and my intentions. To continue an intentional act, such as speaking, I have to focus my attention on the next appropriate component, while irrelevant ideas must be prevented or inhibited from entering the field of consciousness.

In schizophrenia, a decrease in protention function could be pictured as a modification of the cone, leading to a lack of focal attention and an intrusion into consciousness of inadequate (usually unlikely) ideas or impulses. The intentional arc therefore becomes perturbed, resulting in a temporal disintegration and a split in the continuity of experience. In speech, for example, the patient may no longer be able to extend the intentional arc of a sentence with meaning and must instead use isolated words to explicitly construct sentences. The individual elements of thought, perception or action then become disconnected fragments, which can even manifest themselves to the patient as alienated or opaque.

Therefore, the fragmentation of internal consciousness does not only imply a weakening of the intentional arc, but also a failure to inhibit inappropriate thoughts, which the patient experiences as intruders in his stream of consciousness as an insertion of thoughts, experiences of passivity or voices.

The transition from simple concentration disorders to thought blocking and interference cannot be explained as a simple disturbance of attention and understanding at the level of semantic connections. The disturbances must in fact be placed on a transcendental level where the temporal coherence of consciousness is constituted. It can be explained in this way: if the protective or anticipatory processes fail, the impending thoughts, movements or external events "overwhelm" the patient's protection. Appearing out of nowhere, they can only be experienced in the retentional

mode. This means that these experiences will appear to the patient as surprises or with a transcendental delay. He will feel a delay in his own consciousness as opposed to the rapidity of events, thoughts and feelings that overwhelm him and seem to intrude into his private sphere from the outside.

Another element is necessary to explain the fully overt passivity experiences: we have already seen how the internal consciousness of time is linked to the pre-reflexive self-awareness, if the temporal synthesis is disturbed, the patient also loses the continuity of his experience of himself. As a result, impending thoughts and impulses are no longer incorporated into a sense of belonging and intentional acting, causing transcendental depersonalization.

So what remains of this intentional interrupted arc that the patient experiences as his own experience can only be perceived as alien thoughts, auditory hallucinations, or passive movements. The breaking of the intentional arc and the fragmentation of the coherence of the self involve an externalization of the remaining parts that result in the first-rank symptoms of schizophrenia.

In summary, from a phenomenological point of view, the main schizophrenic symptoms can be described as disturbances of the transcendental constitution of the internal consciousness of time or lived time. These alterations manifest themselves in disorders of thought and attention, in the interruption of intentional acts, in the basic fragmentation of internal coherence and, in acute psychosis, in an externalization of consciousness in the form of first-rang symptoms.

Alterations of explicit temporality

The weakening of the retention-protention structure and the changes in self-consciousness concern the implicit or pre-reflexive temporal experience. However, explicit temporality can also be altered in schizophrenia, as Jaspers, Minkowski, and Kimura have suggested. The pre-psychotic phases can, for example, be characterized by an anticipatory feeling, often anxious for an imminent future, often with a subjective acceleration of time. This is what Kimura called the "ante-festum" orientation and may also be related to Conrad's trema. It can culminate in

experiences of an imminent end of the world - wahn-stimmung - and therefore lead to almost opposite sensations, namely the stopping of time, which we have already described above. In the post-psychotic phases, on the other hand, residual or negative symptoms can be understood as manifestations of a delay in the experience. The loss of thrust, the reduction of activity, and social withdrawal express a weakening of the affective-conative component of implicit time.

The patient can try to compensate for these disturbances on an explicit level, that is, by trying to execute every thought or movement with an effort of will, this attempt coincides with Minkowski's "morbid rationalism". Rather than living in time, the patient can therefore attempt to construct his own temporality in an explicit and intellectualized way. However, this results in a loss of spontaneity and fluidity of actions and thoughts, and in an attitude of hyper reflexivity. It particularly affects time synchronization with others, making social interactions difficult or impossible. The schizophrenic person loses the security of being in common time, in tune with others. Faced with these difficulties, many patients withdraw into isolation. The complexity and subtlety of common sense, that is, the implicit rules of social conduct, are often too difficult for these patients to manage. This can lead them to build "algorithms" - logical or mathematical rules of adequate behavior that arise from observing others. Autistic withdrawal can be understood as an attempt to reduce the burden of these complex social interactions. Another possibility is the minimization of change: when the stream of consciousness of time is fragmented, the repetition and even monotony of the surrounding world can help the patient create a substitute for the lack of inner continuity. Finally, delusions can also be related to the temporality disorder. The basic disintegration of the consciousness of time leads, as we have seen, to the fragmentation of thoughts and sensations or movements which are not immediately experienced as one's own. These fragments of the intentional arc can in a sense be recomposed on an explicit level, that is, by integrating them in a delusional way into the narrative. The patient now perceives that "others" are influencing him, moving his limbs, inserting thoughts into his head. Although these delusional explanations may reduce the burden of temporal disintegration, they cause greater disconnection from shared temporality with others. For the delusional patient, there is no longer an open intersubjectivity, because the delusion has always already determined what the other could mean or intend. The loss of the ability to move to different perspectives

excludes all other possibilities of interpreting what is frozen, the idiosyncratic reality of delusion thus stops the explicit or biographical time course to compensate for the fragmentation of lived time

It is clear, therefore, that implicit temporality disturbances can have an influence on the reflective aspects of consciousness, including explicit temporality. We synchronize with others, both implicitly and explicitly (eg through appointments, scheduling and "punctuality"). Synchronization does not mean complete congruence, but rhythmic or phasic harmonization. This becomes more evident in direct interpersonal contact. We wait before responding, but not too long. We alternate with each other and fit each other in conversation. We do this mostly implicitly, without the need to think about it. For schizophrenic patients the situation is different, and it is possible that empathy disorders, difficulties in understanding the intentions of others, or the so-called Theory of Mind, are at least partly related to synchronization problems with others. Explicit desynchronization and autistic withdrawal can be a reaction to these disorders.

COGNITIVE NEUROSCIENCE

Cognitive neuroscience has faced the question of the perception of time in schizophrenia. The reasons of this interest are many and the results they have reached are not yet complete, albeit full of interesting reflections.

First of all, the phenomena of altered subjective perception of time, recognized and studied from a phenomenological point of view, had been noted and had also attracted the interest of scholars of the cognitive aspects of schizophrenia[42,43]. They therefore wanted to qualify and quantify these alterations by collecting data which were however quite heterogeneous and led to different interpretations of the alterations of time in schizophrenia. For instance, patients have been found to overestimate the duration of an interval in a task in which they are asked to verbally report the duration of a presented stimulus[44–50] and in motor repetition tasks[51]. It has also been reported that patients underestimate the duration of the interval during production activities, which require the participant to respond when a target stimulus has been present for the appropriate amount of time[52]. Greater differences in time estimation of visual and auditory cues have also been reported in patients compared to controls[53]. When all data are considered together, however, the most reliable result is that patients show greater variability in perception of time intervals than controls[37,54–60].

Role of dopamine

A second reason why cognitive neuroscience has been interested in the perception of time in schizophrenia is the finding of the key role played by dopamine, and in particular D2 receptors, both in the pathophysiology of symptoms of schizophrenia and in the perception of time.[61] The correlation between dopamine transmission and the production of symptoms of schizophrenia is now an established fact in the pathophysiology of the disease. At the same time, pharmacological studies indicate that performance related to the perception of time is highly sensitive to dopaminergic modulation. Dopamine agonists such as cocaine and methamphetamine cause a

perceived lengthening of time, while the dopamine antagonist haloperidol causes a subjective shortening of time[62]. There are also results showing how distinct drugs can selectively interfere with the perception of different time intervals. For example, Rammsayer[63] showed in human psychophysical experiments that the dopaminergic antagonist, haloperidol, significantly altered the discrimination thresholds of 100 ms and 1 s intervals while Remoxipride, another selective dopamine antagonist for D2 receptors, altered the processing of the time information on the one-second scale but not for 50 ms intervals[64]. It also emerges that the clinical efficacy potencies (in time modulation) of antipsychotic drugs are positively correlated with their ability to block specific subtypes of DA receptors (eg, D2 and D4)[65]. Finally, a binding correlation between affinity for the D2 receptor and the neuroleptic dose required to achieve a 10-15% reduction in the magnitude of perceived duration in a time interval recognition task was observed in rats, and was correlated to altered frontal striatal function also in humans[66–68]

The research therefore provides evidence indicating that schizophrenic patients exhibit a probable deficit in temporal processing related to abnormal dopaminergic activity in the striatal frontal circuits, which contribute to an altered perception of time[53,69].

Similar findings have been discussed in relation to patients with Parkinson's disease[70]. The importance of the normal DA function for the processing of time is in fact also suggested by the data of individuals with Parkinson's disease (PD).

For example, some patients on drug treatment with L-DOPA compared to controls have been shown to underestimate the length of a time interval in a tense task, have waited longer in a temporal reproduction task, and required a longer minimum time interval between paired stimuli to perceive two time-separated stimuli. Administration of L-DOPA significantly improved patient performance in all and between tasks[71,72]. Malapani and colleagues demonstrated deficits in temporal memory encoding in patients not being treated and recovered if treated with L-DOPA in a temporal reproduction task. They also found, by combining drug administration with different tests, that dopamine deficiency could cause distortions such that shorter intervals are perceived as increased and longer intervals as decreased[70,73].

Brain circuits

Of further interest are the overlaps between the neural circuits considered underlying temporal functions and those that have been implicated in the pathophysiology of schizophrenia[1,74,75]. For example, schizophrenia has been associated with impaired neural integration across the prefrontal cortex, thalamic and cerebellar regions[74]. The same regions are also involved in temporal estimation[76–78] and mediate temporal aspects of motor activities such as, for example, the rhythmically tapping with the finger[76,79,80] and eye-blink conditioning[81,82]. Schizophrenia has been further associated with disturbed neural communication within cortico-striatal networks[69], which are constitutive to the explicit encoding and representation of temporal information[83,84]. Fundamental for the functioning of the cortico-striatal timing network is the neurotransmitter dopamine[85–91] which, as we have already indicated, has also been linked to the clinical manifestations of schizophrenia[92].

Recent literature reviews on the neural basis of temporality[93–95] reveal a notable overlap in the brain circuits and structures that are affected by schizophrenia[96–98]. Although different brain regions have been implicated in both time perception and schizophrenia, the strongest link between the pathophysiological hypotheses of schizophrenia and the neural basis of time interval recognition is the role of the striatal dopaminergic system and the interconnectivity between the striatum and the prefrontal cortex (PFC).

Although the specific neural basis of schizophrenia are not yet precisely identified, one of the most general and replicable data is certainly represented by the hyperactivity of dopamine D2 receptors (DA) in the striatum of patients. All effective antipsychotic drugs antagonize D2 receptors, thus connecting them critically in the disease. Post-mortem studies have reported up-regulation of striatal D2 receptors in patients not undergoing pharmacotherapy[99]. These data were confirmed later in PET studies, demonstrating an approximately 12% increase in D2 receptor density in the striatum of drug-free and drug naïve patients, although not all patients show increased D2 receptor density. Patients also show increased occupation of the striatum D2 receptors.

Hypoactivity of the prefrontal cortex has also been reported[100,101] and PFC has long been the subject of schizophrenia research, given well-documented distortions in working memory, which requires functioning PFC[102,103]. An abnormal prefrontal cortex and impaired striatal functioning compromise the integrity of cortico-striatal circuits, leading to functional impairments[104].

In terms of the neural basis of temporal perception, there is a great deal of behavioral, pharmacological, genetic and nuero-imaging literature indicating a critical role of the basal ganglia in the processing of temporal information, especially the striatum and its connections with the prefrontal cortex[95]. Many studies indicate that the temporal processing of information can be distorted by manipulations targeting the DA system, particularly through the activity of the D2[95] receptor. For example, Meck[66] demonstrated that the dose of a neuroleptic needed to distort a rat's perception of a 10 to 15% time interval was negatively correlated with the drug affinity for DA D2 receptors. More recently, it has been suggested that spinous neurons of the striatal middle may serve as an indicator of neural activity in cortico-striatal circuits, and that synchronized activation of these neurons by input from the PFC regulates the level of activity in working memory. during interval recognition tasks[83].

According to this view, a DA pulse at the beginning of the interval to be timed signals the period during which the middle spiny neurons should monitor the fluctuations in the firing of PFC neurons to detect patterns of activity. When a second DA pulse marks the end of the interval to be timed (usually via the delivery of a reward), the firing pattern of the cortical neurons is memorized by strengthening the currently active synapses, thus providing a reminder of the time interval with respect to to which next the intervals can be compared. Although the validity of this theory has yet to be empirically demonstrated, there is evidence that an accurate time interval requires an intact prefrontal cortex, as lesions of the prefrontal cortex produce distortions in the perception of time[105–108]. Together, these results indicate that the perception of time requires the integrity of cortico-striatal circuits.

Research into the pathophysiology of schizophrenia and the neural basis of time perception indicates that in the brain the circuits involved in schizophrenia and those required for the precise temporal processing of information are strikingly similar.

Cognitive dysmetria and prefrontal theory

The main question raised by six decades of time research in schizophrenia currently concerns the nature of these disorders. Do these temporal disturbances result from perceptual dysfunction or from the well-known cognitive impairment associated with schizophrenia affecting a wide range of cognitive functions including attention, executive functions, memory (declarative and working memory) and processing speed[109]?

To better characterize time perception deficits in schizophrenia, it may be important to adopt a clear conceptual model.

The 'cognitive dysmetria' model proposed by Andreasen[1] suggests that schizophrenia is associated with a severe failure of a system of synchronization and prioritization of information that would be reflected in positive and cognitive symptoms.

The hypothesis that Andreasen supports is based on the observation of the diversity of symptoms with which schizophrenia can occur. These concern several domains: perception, language, thought, social interaction, motor activity and emotions. Not all patients have symptoms in every domain; for instance some patients do not have hallucinations while others do not have any language disturbance. However it is considered that there is a single underlying process that produces the different symptoms. The proposed model indicates as a possible underlying deficit an alteration in the system that coordinates the processing, prioritization and expression of information. To express the diversity of expressed disorders, the deficit is called "cognitive dysmetria".

In 2007 Vogeley[110] et al took up the concept of cognitive dysmetria introduced by Andreasen and related it to Husserlian theories on temporality. According to the authors, the tripartite conception of consciousness of a phenomenological matrix

based on retention, original impression and protection can correspond to the processes of working memory, interference control and preparatory sets of a neuroscientific matrix. As regards the latter, the authors take up the ideas of Fuster[111] which integrate the cognitive functions of the prefrontal cortex to develop a "prefrontal theories".

Essentially, Fuster proposes a tripartite concept, this includes working memory functions (linked to the past), inhibitory inference control (linked to the present), and preparatory sets (related to the future) as basic functions.

The working memory constitutes the "retentive function" of the pre-frontal cortex. The most important feature of the working memory is the changeability of the content and its "operational character", not intended as related to the type of information but to the process for which the content particular is kept "online". This is supported by cortical networks with reverberant activity within the networks themselves, in order to "organize" a prospective action. Working memory is essential for our subjective temporal experience by providing continuous access to real and contextual perceptions contained in the "memory of the present." The deficit of working memory is a known neuropsychological datum characteristic of schizophrenia. As regards a more detailed localization within the pre-frontal cortex, it is essentially the dorsolateral part of the PFC to be involved.

The preparatory set refers to "preparation for action." The preparatory set is thus prospective in contrast to the retrospective capacity of working memory. To illustrate this, Fuster refers to the "preparatory set" as a neural indicator of forthcoming actions. The PFC therefore would activate the motor apparatus in anticipation of the action.

Inference inhibitory control as the third integrative function of the PFC plays an important role in protecting the structure of thought or behavior management from the interference of influences that could conflict with it. Suppresses internal and external influences that could interfere with the sequence currently being approved.

For Fuster it is equivalent to a form of attention selection, that is, a form of selective attention to an internal representation.

It is well known from functional imaging studies that attention depends on the integrity of the PFC, predominantly from the anterior medial portion. Fuster's concept of "organization of behavior over time" is essentially based on temporal contingencies associated with bridging elements such as patterns, goals or intentions projecting further into time.

Working memory and preparatory set work together to "reconcile the past with the future. " These components therefore constitute a unitary element, holistic result of a given behavioral act that is generated on the basis of the different functions: The structure of the action is a temporal gestalt, like a melody. The prefrontal cortex would therefore be able to create a bridge between mutually contingent elements in behavior such as a sequence, a rational speech or the construct of a word.

Both Husserl's and Fuster's approaches therefore converge in 2 aspects.

First, they both develop a tripartite rather than a binary conception of time. While the binaristic conception leads to the idea of the clock which is characterized by before and after relationships (an event occurs at a given point-like moment in time and is before or after another moment), the tripartite conception corresponds to 3 different time domains : working memory (associated with the past), interference control (associated with the present) and the preparatory set (associated with the future). Husserl reconstructs these 3 components as intentional acts which include retention (as an intentional act directed to the past), original impression (as an intentional act directed to the present), and protection (as an intentional act directed to the future).

In particular, these 2 concepts converge in a common concept of the constitution of time from 2 completely different traditions, namely cognitive neuroscience and phenomenological philosophy.

Secondly, both approaches converge with respect to the extension of the experience of the present which is not considered a point-like element, but an integration of different cognitive sub-components that take place in a formally structured "temporal band" or "temporal field". Phenomenologically, the experience of the present is extensive. This experience corresponds to the neuroscientific observation that it takes certain lengths of time (which can vary) to activate a particular group of cells. Metaphorically speaking, 'Now' is not a 'position', but an 'extended space'. These are 2 essential aspects that demonstrate a close homology between cognitive

neuroscience and phenomenology in the consciousness domain of time. This close relationship allows us to propose neuroscientific hypotheses on the consciousness of time and its disorders that are based on phenomenological intuitions

Internal clock and scalar expectancy theory

Another hypothesis is that an "internal clock" may exist that allows the representation of real-time information used to process all temporal information[112]. The temporal processing deficits would then be attributed to a general deficit in the area of the brain responsible for the "internal clock". However, there is little consensus regarding the location associated with the internal clock. Several researchers have argued that the prefrontal cortex is not only involved in the general ability to process time, but may be responsible for our 'internal clocks'[71,78]. Others have argued that general temporal processing deficits are associated with the cerebellum[113]. Others believe that the basal ganglia are likely responsible for processing the internal clock and are involved in both short-lived, largely automatic, and longer time-interval processing[114–116]. The argument has also been made that both the cerebellum and the basal ganglia are involved in a coordinated timekeeping system with a convergence of central control of the cortex[117].

Finally, others have argued that temporal differences in performance processing during variable intervals may result from the use of different cognitive processes. Michon[118] points out that the variability depends on the activity performed, since the processing of temporal measures can vary in the degree of abstraction Nichelli et al.[78] suggest that the cerebellum could be involved in the estimation at short-term intervals, however, longer times at 2 or 3 s they can exceed the intervals that for which a basic activity is sufficient and can reflect the deficits of sustained attention or the use of particular mnemonic strategies.

A further development of the internal clock hypothesis is the Scalar Expectancy Theory (SET) by Gibbon and Church[119]. In this model, timing involves three levels of processing, namely a clock stage, a memory stage, and a decision stage, and the variability could result from any of these three stages[120]. First, the clock stage is

driven by a pacemaker, coupled to a counter (accumulator), which records the pulses emitted by the pacemaker. Note that the pacemaker rate can be modulated by physiological factors such as body temperature[121] and dopamine level[88], and that each person's pacemaker has its own default or natural rate. As for the counter, its access is controlled by a switch mechanism which is under attention control. More attention to time means that more pulses accumulate, which results in a longer perceived interval[122]. Secondly, timing variability can also arise at the memory level when comparing time intervals, depending on the memory load[123].

Finally, decision-making processes (response selection) can increase temporal variability[124]. Consequently, neurobiological dysfunctions in schizophrenia or cognitive impairment related to schizophrenia (e.g., deficits in memory and attention) can interfere with varying levels of time processing, especially in interval discrimination tasks. At present, however, no study allows us to distinguish the perceptual vs. cognitive impairment of temporal disorders in schizophrenia

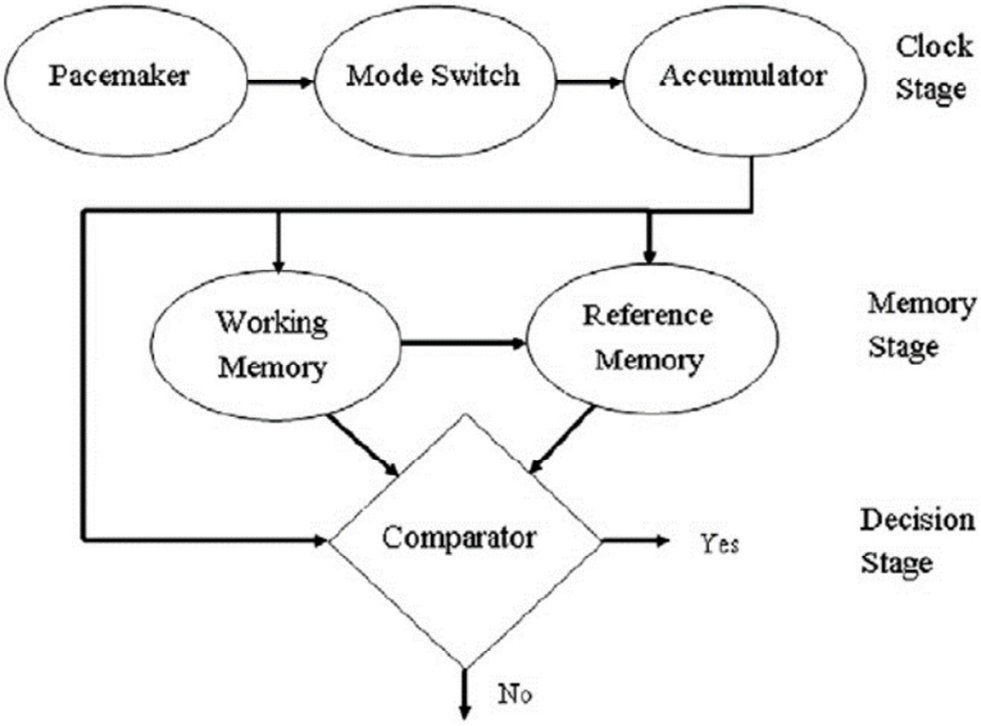


Fig. 1. Information-processing model of interval timing derived from the three stages (clock, memory, and decision) described by Gibbon (1977).

Changes in temporality and schizophrenic symptoms

Poor temporal information processing can contribute to a wide range of positive symptoms associated with schizophrenia. Deficient temporal information processing would lead to dysfunctions in timing or sequencing of mental activity and behavior, producing some classic symptoms of schizophrenia, such as delusions and disorganized behavior[1,54]. To illustrate how distortions in the perception of time could produce positive symptoms, consider delusional thinking. Distortions in the perception of time intervals could lead to the failure to correctly perceive the time sequence of contiguous events. This in turn could lead to a failure to attribute voluntary control to some of one's actions (lack of agency) or confusion about the relationship between one's actions and the outcome of those actions (for example, flipping a light switch turns on the light), giving the illusion of lack of control by the individual and control by some other entity, a common aspect of paranoid delusional thinking in schizophrenia[125–127]. Given the critical role of dopaminergic signaling in the perception of time, together with its documented dysfunction in schizophrenia, this interpretation may be consistent with current conceptualizations of the involvement of impaired dopaminergic signaling in producing positive symptoms via aberrant attribution of salience[128].

DATABASE AND REVIEW

If timing and symptoms are causally related in schizophrenia, one might expect a correlation between the severity of positive, negative, and cognitive symptoms and the severity of temporal changes. We have tried to address this question developing in first place a database detailing the studies about time perception in schizophrenia. This work naturally evolved in a review of the literature specifically about the relationship between psychopathological symptoms, cognitive symptoms and time alterations in schizophrenia.

Exploratory database: premises, development and first considerations

On the assumptions announced so far, I decided to analyze in more detail the studies that dealt with the perception of time in schizophrenia from a neurocognitive point of view and organize the results in a database that would make it possible to compare and interpret the data in a broad perspective and from different points of view. I chose to focus on the neurocognitive aspects for the greater number of studies in the sector and because the more strictly scientific matrix of the studies themselves allowed a more agile comparison.

To collect the studies, I carried out a systematic search of the literature on pubMed, with the collaboration of the staff of the company library of the S. Anna hospital in Ferrara using the following search criteria

Search: ((Schizophrenia OR "Schizophrenia"[Mesh])) AND ("time perception" OR "Time Perception"[Mesh] OR "temporal experience" OR "estimation of time" OR "time estimation" OR temporality OR "time consciousness" OR "experience of time" OR "time experience")

The research is updated to 20/02/2018.

At the first selection, 364 articles were identified that intercepted the indicated criteria, and I therefore proceeded to exclude those of no psychiatric competence

and that did not affect schizophrenia or the perception of time, thus reducing the number of articles concerned to 174.

I then divided these 174 articles according to the title and abstract into 4 groups by thematic relevance and cultural approach chosen. The identified categories were labeled as: 1) Cognition, 2) Phenomenology / Psychopathology 3) Neurobiology 4) Theories and Hypotheses.

Differentiation into different categories was necessary because, as has emerged in the discussion so far, the very nature of the investigation, that is, the perception of time in schizophrenia, has historically been and is still approached from radically different perspectives. Although I consider the dialogue between different disciplines an essential element of the progress of knowledge in the field of psychiatry, I felt that in a first phase it was necessary to direct the focus of research by recognizing the autonomy and dignity of each branch.

1) Cognition: this group includes those studies which, with the use of specific tasks and measurements that are as objective as possible, have tried to quantify the possible presence and nature of temporal alterations in schizophrenia. This category then became the main focus of the research leading to the development of a database that describes the studies in detail.

2) Phenomenology / Psychopathology: this category collects those articles that develop a descriptive analysis of the subjective experiences of time, focusing on elements not attributable to quantitative aspects

3) Neurobiology: this category includes those studies that examine the neuronal imaging, pharmacological and electrophysiological functioning of the structures underlying temporal processing in schizophrenia

4) Theories and Hypotheses: In this category were classified the studies that proposed theories or hypotheses concerning the connections between altered perception of time and schizophrenia, not yet supported by empirical results.

The in-depth work carried out during this research contributed to the development of the introductory part of this work.

The studies classified as aimed at cognitive aspects were subsequently analyzed in more detail to develop a database that would allow even very different works to be

compared with each other. The inclusion criteria were the publication in English, the presence of a temporal task that would allow a quantification of the temporal alteration, the presence of a sample of a patient suffering from schizophrenia and the presence of a control group.

40 studies carried out between 1956 and 2016 were then examined for a total of 1125 patients and 1148 healthy controls.

The characteristics examined were

- Year of publication

- Title of the article

-First investigator

-Journal

- Hypothesis / objective of the study

- Time range examined

- Diagnostic criteria

- Presence and type of controls

-Number of patients

-Presence or not of cognitive assessment

-Presence or not of psychopathological assessment

-Pharmacotherapy

-Tasks submitted

-Achieved results

- Presence or not of statistical analysis

- Authors' conclusions

-Bias

A limitation of the study is that database than PubMed have not been searched. For a more accurate review further searches should be extended to other databases (such as EMBASE, Scopus, Psycinfo or Google Scholar)

Years of publications, magazines and working groups

It is important to note right away how the focus on the theme has changed over time. At the beginning the issue was marginal and the articles were published in journals that mainly dealt with research on perception or cognition but not strictly on schizophrenia. In the decade 1983-1998 the topic did even completely disappear from the research agendas. It cannot go unnoticed that the resumption of publications on the topic followed the publication of Nancy Andreasen on "cognitive dysmetria", which, taking up Bleuer's conception of a fundamentally cognitive deficit in schizophrenia, preceded the increased interest in the topic, now also in journals more specific on schizophrenic pathology such as "Schizophrenia research" and "Schizophrenia Bulletin". The titles of the articles have also moved from more generic statements (ie "Time perception and schizophrenia" of 1977) to greater levels of detail (ie "Time perception disorders are related to working memory impairment in schizophrenia" of 2012). This reflects the greater degree of sophistication of the hypotheses under consideration. For instance, to compare these two studies again, the goal of the 1977 study was "To detect differences in time perception between Schizophrenic and controls" while in the 2012 study "to assess if in schizophrenic internal clock runs faster than that of healthy controls" showing the presence of precise underlying neurocognitive hypotheses, such as the possible dysregulation of an internal clock.

It was possible to recognize at least three working groups that have dealt with the topic more continuously, intercepting different aspects and bringing their data to support distinct pathophysiological hypotheses.

The first group which has been dealing with this topic since 2002 is the one headed by Davalos et al who currently continues to deal with time processing. In particular one of their current areas of interest is how the processing of time develops over the span of life and the relationship between a person's abilities to correctly process time

information and higher-order cognitive abilities such as planning, sequencing and executive functions.

In 2002, they investigated whether temporal deficits were linked to a specific sensory modality (auditory vs visual) or could be recognized as generalized alterations and whether the length of the time interval used in the task was a determining factor (even if the temporal examined, however, remains rather limited). The results obtained led them to conclude that the alterations in temporality were factors independent of the variables considered. Finally, they tried to correlate the time alterations in schizophrenia with the neurophysiological data of Mismatch negativity, but could not find any correlation.

It is very interesting that the another group, the one led by Carrol, which has been facing similar questions since 2008 found conflicting data. In regard of the comparison between different sensory modalities (auditory vs visual), differences between schizophrenic subjects and controls were found only for auditory aspects (in particular a decreased precision). They hypothesized a single mechanism at both millisecond and second level, and attributed longer temporal alterations to higher-order functions to explain the differences between temporal ranges in the perception of auditory stimuli. They also imputed alterations in different perceptual and motor mechanisms depending on the task used. A final important point highlighted by Carrol's group was that the correlations between temporal variability and psychopathological ratings suggested that the more stable alterations (therefore probably the cognitive ones) rather than the acute symptoms are probably those associated with the alterations of temporality.

The third group that is still dealing with the perception of time in schizophrenia is of the highest interest. It is the group that is led by Giersch and that more than the others moves in the wake of the tradition of phenomenological psychopathology, trying to translate the intuitions of classical psychopathologists into scientifically reproducible experiments. In their research project "Timing and Schizophrenia" which collects their studies on the topic, they specify as a goal "to understand how and why the flow of thoughts of patients with schizophrenia is fragmented over time. To achieve this we try to objectify which temporal prediction mechanisms are preserved and which are altered".

This approach represents today the highest level of integration between long-divided cultural currents such as phenomenology and cognitive neuroscience, and is therefore of particular value. The hypothesis that Giersch and his group follow is that in schizophrenic patients there is no alteration of the internal clock as claimed by other groups (and they have verified this hypothesis through a spontaneous drumming task) but a deficit of synchronization ability for which they have chosen to submit patients to a task with very short time intervals asking them to evaluate whether the stimuli presented were simultaneous or not. Martin relates these alterations to the descriptions of the implicit temporality alterations described by Fuchs also rejecting the hypothesis that the temporal alterations are linked to a direct alteration of working memory, argue that the cause of this difficulty in recognizing the order of events is to be linked to a deficit of information integration whose nature still remains to be defined.

Description of the subjects involved

The temporal span of the years in which the studies were conducted led to an heterogeneity of the diagnostic criteria used. From the first studies in which the diagnosis of schizophrenia was not even supported by a clear expression of the nosographic system considered to the use of the DSM-IV in the most recent studies. The distribution of the diagnostic systems used is : absence of criteria (17.5%); DSM-II (2.5%); DSM-III (5%); DSM-III-R (2.5%); DSM-IV (62.5%); ICD-10 (10%). In two studies, subjects not suffering from schizophrenia but considered at high risk (UHR) were also evaluated.

Sample sizes studied were often modest with 60% of the studies with less than 30 subjects and the two studies with the largest samples (one 80 and one 122 subjects) in which the diagnostic criteria are not clearly specified having been performed respectively in the 1966 and 1973. All studies carried out controls with neurotypical subjects.

In 47.5% of the studies some form of standardized cognitive assessment was performed and in 65% of the cases a psychopathological assessment was also performed with psychometric tools. These two parameters are extremely important

as, depending on the paradigms taken as a reference, they could influence or be influenced by the alterations of temporality. For example, if we consider the alteration of temporality as a fundamental cognitive deficit, we should be able to identify a correlation between cognitive resources and alteration of temporality. The same has to be considered when looking a possible causal link between alteration of temporality and productive symptoms. Looking at the development of time processing in correlation with these two parameters allows us to understand the possible links and bring elements in support of different theories. These open questions led us to do a review of the current literature to explore exactly these possible relationships, and which is detailed later in this work.

Another extremely important element in the analysis of the sample is whether or not subjects were on antipsychotic drug therapy. As we have seen, dopamine is an important direct regulator of temporal perception, so the use of anti-dopaminergic drugs represents an important bias in the interpretation of the data collected. In addition, we must also consider the indirect effect that these drugs can have on temporal processing through their action on the symptoms of schizophrenia or on the subject's cognitive abilities. In the studies examined, 22.5% did not specify whether patients were taking drug therapy or not, 5% indicated that they were not taking pharmacotherapy; 32.5% generically indicated their intake without providing the dosages and the remaining 40% indicated the average quantities taken made comparable by converting chlorpromazine into equivalents. It should be emphasized that even this last specification, obviously preferable to the absence of indications, is however poorly suited to making the extreme variability of the individual response to the drug and significantly assessing the impact on the performance performed.

Description of the tasks performed: Explicit timing tasks

The tasks used to study the perception of time in general and in the context of schizophrenia include the well-defined tasks of

a) verbal estimation of time,

b) time production

c) temporal reproduction

d) discrimination of duration

e) rhythm production tasks

a) In the verbal time estimation, a time interval is presented, defined for example as the inter-onset interval (IOI) between two short tones or flashes of light or with the start and end of a continuous listening or a visual signal, and the participant provides an estimate of this time interval in conventional chronometric units such as seconds or minutes. This task is most frequently used for prospective time estimation, where the participant is aware that time intervals need to be judged but can also be used retrospectively. For example, the participant may be asked to estimate how much time has passed since the start of the experiment, without being informed at the start of the experimental session that this time estimate will be required. In this case, the longer time intervals (from a few minutes to hours) are usually investigated, compared to the intervals of seconds or minutes that are typically used in the estimation of prospective time. It should be noted that in the retrospective the verbal estimation task consists of only one test since as soon as the activity includes test repetitions, it turns into a prospective time estimation task in which the participant is informed. The retrospective verbal estimation task therefore provides information on the accuracy of the temporal performance but not on its accuracy. The prospective verbal estimation task provides

information on both measures of temporal performance, accuracy and precision.

b) In time production tasks, a time interval is defined in terms of conventional chronometric units, for example "2.0 s", and the participant is asked to produce the interval, for example by giving two motor responses that mark the beginning and end. Sometimes, for a test, several productions are required rather than a single production. Note that in this case, however, the production of time is different from a rhythmic production task because the interval to be produced is defined in chronometric units (for example, "press the button once per second") and not in terms of a rhythm presented. The time production task also provides information on accuracy and precision, such as the tense estimation task. An important difference from the verbal estimation task is, however, that the production task requires timed motor actions. For this reason, behavioral outcomes will not only be affected by changes in the cognitive representation of time intervals or the "clock mechanism", but also by factors affecting the motor system.

c)In time reproduction tasks, a time interval is presented as in a) and the participant reproduces the interval as in b). Thus, the reproduction task combines the perception and (motor) production of a time interval, and again also provides information on both accuracy and precision. There are several variations of the temporal reproduction task. In addition to pressing a key to start and stop an interval, participants can be instructed to mark only the end of an interval, or to hold the key continuously during the interval. A recent study[129] shows that the different breeding methods are not equivalent to each other. The classic variant that includes the keys to start and stop playback produces the greatest accuracy while the method of continuous holding of the keys leads to the most accurate reproductions.

d) The duration discrimination task is a task in which two time intervals are presented successively and the participant has to decide which interval was longer and which interval shorter. Based on the association between a psychometric function and the detected data, the duration discrimination task provides an estimate of the limit between duration differences, which is the difference in duration between the two

stimuli at which the participant is able to identify the interval longer / shorter with, for example, 75% correct answers. The discrimination task between two intervals measures accuracy and provides a subjective point of equality estimate of the duration of the first and second time intervals. In single-interval discrimination tasks, a single time interval is presented for trial and must be compared with a so-called standard interval. The standard range is learned explicitly before the discrimination task or implicitly during the task. In the latter case, the participant develops an internal representation of a standard intermediate duration based on the elaboration of a comparison of several durations that are slightly longer or shorter than the intermediate ones. In a third variant, the standard interval is presented at each test before the judgment of the time interval, this is defined as a reminder task. A specific task of discrimination of duration of an interval that has been used frequently in the perception of time and in the literature in general in patients with schizophrenia is the temporal bisection task. In this case, the participant first learns a short and long anchor duration of, for example, 1.0 and 2.0s, Thereafter, intermediate durations ranging from 1.0s to 2.0s are presented and the participant is asked to categorize them as more like short or long learned duration.

e) Different variants of rhythm production tasks were used to study the potential effects of schizophrenia on the perception of time. In a continuation tapping activity, the process begins with the presentation of an isochronous rhythm sequence and the participants are asked to tap in sync with it. After a few seconds, the sequence stops and participants are required to continue drumming at exactly the same rhythm. The variability of the IOI produced provides information on the accuracy of the internal representation of the time to be produced IOI, but also on the motor variability.

The rhythm production task is closely related to the reproduction task, with the difference that in the reproduction task only a time interval is presented and played, while in this task it is necessary to reproduce these time intervals several times. In a rhythmic production task, participants provide motor responses (for example, by tapping with the index finger on an answer key) in synchrony to a continuously presented rhythmic sequence.

It has been suggested that the interception of synchronization involves automatically and unconsciously phase corrections that are different from the judgments on time

obtained in other paradigms. For these reasons, rhythmic production involves quite different processes than other time perception tasks.

Description of the tasks performed: Implicit timing tasks

There are also laboratory tasks used to study basic time processes that do not involve judgments about duration (i.e. that do not measure the perception of time) such as:

a) judgments of simultaneity

b) temporal order judgments

c) recognition of intervals

a) In the judgments of simultaneity, two stimuli are presented in succession or simultaneously and the participant must decide whether the two stimuli were synchronous or asynchronous. The participant's performance is determined based on the IOI between the two stimuli leading a percentage of "simultaneous" responses of, for example, 50%. This is called the simultaneity threshold or the point of perception of simultaneity. The smaller the simultaneity threshold, the greater the precision of the participant's judgments, indicating a higher temporal resolution of the sensory system.

b) In a temporal order assessment (TOJ) task, two different stimuli (e.g., two tones that differ in frequency) are presented successively, and the participant must indicate which stimulus was presented first. The IOI between the two stimuli at which a certain level of performance is achieved, eg. 75% correct answers, serves as a measure of temporal resolution (accuracy). The smaller the IOI that is sufficient to discriminate the temporal order of the two stimuli, the greater the temporal resolution of the sensory system.

c) An interval recognition task requires the detection of brief moments of silence in a continuous auditory signal, eg. white noise. The smallest gap that can be reliably detected (e.g., with 75% correct) serves as a measure of performance.

Meta-analysis

During the research activity, 2 meta-analysis articles emerged concerning the processing of temporal information in schizophrenia. Of extreme importance and value in developing the framework of the subject, they led me to wonder if the development of a database remained a useful process to further deepen knowledge on the subject. After reflection, I concluded that the development of the database and the analysis of the studies were still full of value, since, focusing on the individual studies and analyzing them in detail, it carried out work similar to the description of the "clinical case".

That is, by not dealing only with the common factors that can be recognized in a meta-analysis but by deepening the specific peculiarities of each study, I felt I could improve my knowledge on the subject and build support for the work of those wishing to further explore the subject. This idea of mine was reinforced by the fact that the results of the meta-analyzes were not homogenous, even if carried out after a short time (2016 and 2017), thus requiring a careful review of the data presented.

The results of the meta-analyzes are however obviously described in the present work for the great value they bring.

In the first meta-analysis: "Explicit Time Deficit in Schizophrenia: Systematic Review and Meta-Analysis Indicate It Is Primary and Not Domain Specific"[130] the authors carried out a quantitative and qualitative analysis of the explicit timing ability in comparative Schizophrenia patients with healthy controls. Since the time intervals used in schizophrenia studies range from milliseconds to hours, and require the use of additional cognitive processes, it is difficult to distinguish temporal perception deficits from more generalized alterations in attention and memory. To address this problem, the authors categorized each study according to the time interval (greater or less than 500ms) to try to isolate the deficits in different time processing mechanisms that can be "cognitively controlled" or "automatic". Automatic time measurement

systems without cognitive or attentional modulation are primarily involved in time ranges of milliseconds while systems based on higher level cognitive functions are used for longer periods of time.

The primary objective of this meta-analysis was therefore to investigate whether patients with a diagnosis of Schizophrenia show different alterations in the ability to produce an explicit estimate of the time spent through automatic and cognitively controlled processes. A further objective was to determine whether the temporal deficits in SZ derive from different cognitive alterations not attributable to isolated dysfunctions of temporal processing.

This meta-analysis included 24 studies of which 11 included temporal assessments in the range of milliseconds (automatic processes), 10 included measures of cognitively controlled time processing, and 3 evaluated both of these parameters. A total of 747 schizophrenic patients and 808 controls were examined.

The authors found that schizophrenic individuals are less accurate than healthy controls in estimating durations ranging from milliseconds to several minutes in a wide range of tasks traditionally employed to study explicit time. They also pointed out that subjects predisposed to hallucinations, with schizotypic characteristics or with a high genetic risk of developing schizophrenia also show alterations in the perception of time similar to those observed in schizophrenic subjects. This would suggest that time processing dysfunction can be considered an endophenotype of schizophrenia and the schizotypic personality.

In the second meta-analysis examined "Meta-analysis of time perception and temporal processing in schizophrenia: Differential effects on precision and accuracy"[131]analyzes time disturbances in schizophrenia considering three important distinctions:

a) perception of time (explicit time) vs time processing (implicit time),

b) accuracy vs precision

c) the specific task used in the study (for example, activities that involve or do not involve timed motor responses).

The work included 30 studies with a total of 957 schizophrenic patients and 1060 healthy controls.

Overall, the meta-analysis did not show any significant effect on the accuracy of the perception of time. On average, the bias did not differ significantly between patients and controls. However, the effect of schizophrenia on the accuracy of time perception depended on the task. Schizophrenic patients tended to overestimate the duration in the estimation of tense relative to controls and showed a significant underproduction of production time. Different results were observed in temporal bisection tasks. Here, compared to healthy controls, the schizophrenic patients underestimated the duration, meaning that they judged the comparison durations shorter than the controls (corresponding to a higher value of the bisection point in the patients).

In the different tasks, the estimated effect of schizophrenia on the accuracy of time perception did not differ significantly between the different intervals (ultra-short <1 s, short 1-10 s, medium 10 s - 10 min, large> 10 min) , although the overestimation in patients was more pronounced at medium intervals.

Unlike the ambiguous and rather small effects of schizophrenia on accuracy, the accuracy of the perception of time is clearly compromised. Patients' judgments were significantly more variable when compared to healthy controls. This result is evident in all tasks and in all time ranges. Since the effect of schizophrenia on accuracy did not differ significantly between discrimination tasks and reproductive tasks, it cannot be attributed to task-specific demands (e.g. fine motor skills)

CORRELATIONS BETWEEN TIME ALTERATIONS, COGNITIVE DOMAIN AND SYMPTOMS DOMAIN

Up to this point we have found quite strong evidences that in schizophrenia time perception may be altered[132,133,134]. What makes this topic problematic is the huge variety of way to measure time perception mechanisms which depend on a multitude of variables[135]. One of the main issues recently addressed by two meta-analysis is if what is altered in schizophrenia is implicit timing mechanism (pre-reflexive way of organising experience) or explicit timing mechanism (the ability to consciously express a judgment about the length of a time interval) with some evidences pointing at more basic layer of time experience involved[35,36]. Another main issue that has not been cleared up to now is the relationship of time perception alterations with the cognitive profile and the psychopathological profile, even if a recent meta-analysis on six studies has showed a possible connection between positive symptoms and altered time perception[136]. Cognitive features could be involved in time judgments in two way: on one hand temporal alterations could be part of a more general intellectual deficiency (i.e. working memory or attention) which would affect any task in an unspecific way and would arise in particular in explicit judgment tasks; on the other hand it has been theorized that implicit timing could be the basic unit organizing experience and its alterations could lead to many different cognitive disorders (which are indeed found in schizophrenia). This conceptualization is in line with the cognitive dysmetria[74,1] hypothesis which comes from a longstanding psychopathological tradition[49,6] and has been reframed considering as possible underlying brain dysfunction coordination of information in time[110].

However not only the cognitive profile has to be considered an important element to be investigated when studying time perception in schizophrenia but there are strong reasons to focus also on the psychopathological presentation[40,38]. There are indeed evidences that anxiety[137] as well as depression[39] and trauma[138] are able to affect time perception and as these dimensions are often involved in schizophrenia it is necessary to investigate if they could be mediators of this impairment. What is more there has been no systematic overview up to now trying to relate the timing disturbances to the actual symptom profiles. This would help to better understand if

there are clues which indicate if timing disturbances in schizophrenia are a stable dimension or they arise only when the illness is in an acute stage. Phenomenological psychopathology has suggested that the temporal feature of consciousness could be the basic layer from which the schizophrenic symptoms could arise but even if there are studies in this direction, there has not still been strong empirical evidences which can prove this idea.

Neurobiological data on time perception and on schizophrenia are another incredibly useful source of reflection on this topic: one of the most important findings in the field is the overlap of the dopamine role in both time perception and positive symptoms of schizophrenia.[62,63,64] These findings suggest the importance of a translational approach which could help to improve our knowledge on the physiopathology of schizophrenia. In this review we have wanted to focus our attention on how the different aspects of time perception in schizophrenia could interact within themselves, trying to compare the evidences from the literature which relate cognitive, symptomatic and neurobiological profiles with different timing disturbances.

Methods

We performed a systematic review adhering to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) recommendations[139]

At least two authors (EC, GS) independently searched PubMed using the following terms:

Search: ((Schizophrenia OR "Schizophrenia"[Mesh])) AND ("time perception" OR "Time Perception"[Mesh] OR "temporal experience" OR "estimation of time" OR "time estimation" OR temporality OR "time consciousness" OR "experience of time" OR "time experience")

Additionally, manual search from reviews and reference lists of included papers were performed. Literature was searched from database inception until 10/06/2020. The records were first screened at the title/abstract level. Full texts of articles surviving title/abstract screening were subsequently assessed, and the reason for exclusion (according to the criteria below) was noted.

A limitation of the study is that database than PubMed have not been searched. For a more accurate review further searches should be extended to other databases (such as EMBASE, Scopus, Psycinfo or Google Scholar)

Inclusion and exclusion criteria

Inclusion criteria were: i) diagnosis of schizophrenia, ii) timing assessment task as described in the manual "Timing and Time Perception: Procedures, Measures, and Applications"[135], iii) written in the English language, or any other language authors could translate.

Exclusion criteria were: i) absence of healthy controls ii) no diagnosis of schizophrenia iii) no task as assessed in "Timing and Time Perception: Procedures, Measures, and Applications"[135] iv) animal models v) reviews, meta-analyses, case reports or other non-original studies, vi) written in languages authors could not translate.

Data extraction

The following variables were extracted in pre-defined excel spreadsheets: first author, year of publication, title, PMID/doi, investigated time range, diagnosis, sample size, type of controls, number of controls, female percentages (sample), female percentage (controls), mean age (sample), mean age (controls), inpatients or outpatients, clinical phase, ongoing pharmacological treatment, implicit or explicit timing task, perceptive or motor timing task, modality of time assessment, index used for time assessment, cognitive assessment (if present) and its correlation with timing performance, symptom assessment (if present) and its correlation with timing performance, neurobiological investigation (if present) and its correlation with time performance, main findings of the studies.

Data extraction was performed independently by the same two authors who performed literature screening.

Items description

First author, year of publication, title, PMID/doi, investigated time range, diagnosis, sample size, type of controls, number of controls, female percentages (sample), female percentage (controls), mean age (sample), mean age (controls), inpatients or outpatients are self evident items which do not need any further description.

It is instead useful to dwell on the description of other factors whose nature is less intuitive

clinical phase: The clinical phase may be important in assessing whether alterations in the perception of time occur as a stable consequence of the schizophrenic syndrome or as an aspect of an acute psychotic episode.

ongoing pharmacological treatment: dopaminergic transmission influences the perception of time, as already demonstrated by psychopharmacological experiments[140] and the medical literature on Parkinson disease[141]. Antipsychotic drugs can therefore be expected to affect the perception of time. The receptor profile and the different levels of D2 affinity between first and second generation drugs could affect the performance of temporal tasks.

Implicit or explicit timing task: Explicit timing tasks require participants to attend to the duration of the stimulus, whereas in implicit timing tasks no explicit instruction to process time is received but time still affects performance.[142] Participants are unaware of processing time during implicit timing tasks. For example, when participants experience the temporal regularity of a sensory input, they can spontaneously adapt their behaviour to its temporal structure (e.g., clapping along to the beat). The temporal regularity allows them to build a temporal template of the repeated interval, which can be used to predict the time at which the next event will appear. Thus, there is an acquisition of temporal knowledge that is independent of awareness[143]

perceptive or motor timing task: perception tasks require an evaluation of elapsed time or other aspects related to temporality (eg judgment of simultaneity) without involving the motor system. On the other hand, motor tasks require the production of movement to reproduce a temporal range or a rhythm.

modality of time assessment: the perception of time can be evaluated through different tasks. To make the studies comparable despite some minor differences we have grouped the tasks according to the distinction proposed by Thoenes et al[132]. The main types of tasks encountered are:

-duration discrimination

-time production

-judgement of simultaneity

-temporal order judgement

-time reproduction

-verbal time estimation

-other

cognitive assessment (if present) and its correlation with timing performance: indicates the assessment tool used to perform the cognitive assessment. In the event that the study investigated the correlation between cognitive performance and performance in the timing tasks, we highlighted any correlations between these two items.

The main types of cognitive assessment encountered are WAIS, IQ, NART, TMT, WCST, HVLT-R

symptom assessment (if present) and its correlation with timing performance: indicates the assessment tool used to perform the symptom assessment. In the event that the study investigated the correlation between clinical state and performance in the timing tasks, we highlighted any correlations between these two items.

The main types of symptom assessment encountered are: CPE (Clopromazine equivalent), BPRS, SAPS, SANS, PANSS

RESULTS and DISCUSSION

Literature search and database

We identified 1490 possible records after removing duplicates, of which 1257 were excluded after title/abstract screening, and a further 166 publications were excluded after full-text review. These studies included data from 1949 schizophrenic patients and 2281 controls.

31 studies have performed at least 1 cognitive assessment, 44 studies have assessed symptoms in a following a manualized scoring and 10 studies have performed a neurobiological investigation. (see table 1).

PRISMA flow-chart

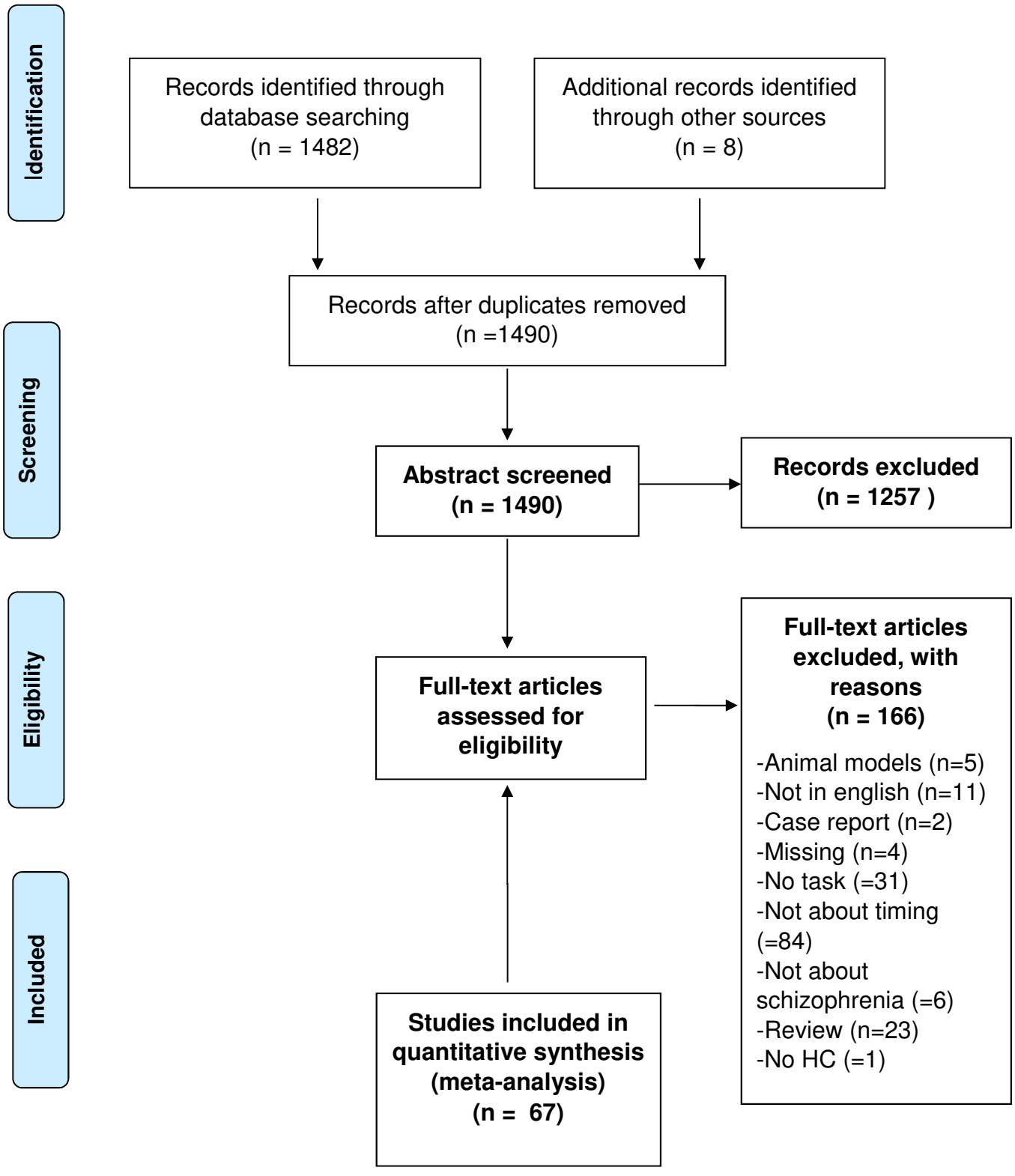


Table 1

First author	Cognitive	Symptoms	Neurobio		First author	Cognitive	Symptoms	Neurobio		First author	Cognitive	Symptoms	Neurobio
Moussa-	Y	Y	Y		Roy	Y	Y	N		Volz HP	N	N	Y
Ciullo V	Y	Y	N		Tschacher	Y	Y	N		Todd J	Y	Y	Y
Wilquin H	Y	Y	N		Schmidt	Y	Y	N		Tracy	Y	Y	N
Stevenson RA	N	Y	N		Davalos	N	N	Y		Rammsayer	N	N	N
Zvyagintsev	Y	Y	N		Herzog	Y	Y	N		Tysk L	N	Y	N
Losak J	Y	Y	Y		Carroll	Y	Y	N		Tysk	N	N	N
Graham-	Y	Y	N		Giersch A	N	Y	N		Tysk	N	Y	N
De	Y	Y	N		Lee	Y	Y	N		Wahl O	N	N	N
Zhang D	Y	Y	Y		Carroll	Y	Y	N		Densen ME	N	N	N
Su	Y	Y	N		Waters	Y	Y	N		Crain P	N	N	N
de Boer-	N	Y	N		Carroll	Y	Y	N		Accornero N	N	N	N
Oyanadel C	N	N	N		Foucher	N	Y	N		Lhamon WT	N	N	N
Chen	N	Y	N		Franck	N	Y	N		Rutschmann J	N	Y	N
Bolbecker	Y	Y	N		Davalos	N	N	Y		Johnson JE	N	N	N
Capa	Y	Y	N		Penney	N	N	N		Broadhurst A	Y	N	N
Martin B	N	Y	N		Ortuno FM	N	Y	Y		Carlson	N	N	N
Papageorgiou	N	Y	N		Yang YK	Y	Y	Y		Normington CJ	Y	N	N
Peterburs	Y	Y	N		Elvevag	Y	N	N		Dilling CA	N	N	N
Lalanne	Y	Y	N		Todd J	Y	Y	Y		Orme JE	N	Y	N
Lalanne	N	Y	N		Davalos	N	N	N		Rabin AI	Y	N	N
Turgeon	Y	Y	N		Elvevåg B	Y	N	N		Lhamon	N	N	N
Delevoye-	Y	Y	N		Bourdet	N	Y	N		TOT 67	31	44	10
Posada	N	Y	N		Davalos	Y	N	N					

Cognition and time perception results

As shown in table 2 in the group of studies where cognitive assessment were performed 6 of them (140 patients examined) found a significant correlation between the submitted timing task and the cognitive assessment as opposed to 13 (376 patients) which did not find any significant correlation; in 12 studies correlations were not searched.

In most of the studies, no matter if correlation was found or not there is more often a lower percentage of female than male, both on sample and in controls. The most represented age in both groups does not appear to be very different, with the 25-50 age range being the most represented.

In both group of studies (correlation found and correlation not found) the time ranges under examination were quite heterogeneous but when shortest time ranges were tested (less than 0,1 sec max), a significant correlation was never found.

In studies where correlation between timing and cognition was found clinical samples were composed most of times by chronic patients (4chronic, 2 ns) recruited in outward clinics (3 out, 1 in, 1out+in, 1 ns) and with no clear predominance for being treated with 1st or 2nd generation AP (1 first, 1 second, 1 both, 3ns).

On the other hand, patients where statistical correlation between timing performances and cognitive assessment was not found seemed to be more frequently inpatients (4 i, 1o, 3i+0, 5ns), without a clear definition of the clinical phase (3 chronic, 10 ns) and mostly treated with 2nd generation AP (0 first, 6 second, 2 f+s, 4 ns, 1 off).

Only explicit timing task were performed in studies where a correlation between timing task and cognitive assessment was found (6 E, 0 I), with 3 procedures looking for motor timing tasks and 5 for perceptive timing tasks.

In studies were correlations between timing and cognition were not found we can still find a majority of explicit timing but there are also a few studies considering implicit timing (10 E, 3 I) with a similar proportion of motor and perceptive tasks (10 M, P).

In both group of studies (correlation found vs correlation not found) the most frequent timing assessment used were WAIS and TMT.

		CORRELATION NOT FOUND	CORRELATION FOUND
Total number of patients		376	140
Number of studies		13	6
Control size		394	146
Out/inpatients (studies)	ns	5	1
	i	4	1
	o	1	3
	i+o	3	1
Clinical phase	Ns	10	2
	Acute	0	0
	chronic	3	4
treatment	Ns	4	3
	1st gen AP	0	1
	2nd gen AP	6	1
	1st + 2nd	2	1
	off	1	0
Explicit/implicit		10/3	6/0
Motor/perceptive		10/4 (9+1/3+1)	3/5 (1+2/3+2)
Time assessment	Dur.discr.	5	2
	T. prod.	2	2
	T.repr.	1	1
	Verb.est.	1	2
	JoS	1	0
	ToJ	1	0
	other	4	2
Cognitive assessment used	WAIS	8	4
	IQ	0	0
	NART	0	0
	TMT	3	2
	WCST	3	0
	HVLT-R	1	0
	other	2	1

Table 2 cognitive correlation found vs not found

<u>Legenda (tab.3-4-6-7)</u>

A= age

I/O= inpatients/outpatients

CP=clinical phase

T= treatment

E/I= explicit/implicit task

M/O= motor/perceptive task

TA= time assessment task

CA= cognitive assessment

SA=symptom assessment

Table 3: correlation found between cognitive performance and timing performance, studies description

Author	Year	Sample/ control size	Time range	% Female	A	I/O	CP	T	E/I	M/P	TA	CA	Findings
Graham-Schmidt	2016	39/43	200-600ms	26.5	43.1 ± 1.8	O	C	Ns	E	P	Verb. est.	TMT	The ANODEV revealed no significant main effect of backwards digit span score ($F(1, 37) = 0.18$, $p = 0.67$) but a significant main effect of interval ($F(1, 76) = 82.1$, $p < 0.0001$). The interval by backwards digit span interaction was also significant ($F(1, 76) = 10.4$, $p = 0.00$. As the interval increased to 400 and 600 ms, people with higher digit span scores reported a steady increase in the perceived interval. In contrast, people with lower digit span scores reported a more moderate increase in the perceived interva
Delevoye-Turrell	2012	24/22	500ms	41.7	39.4±8	O	C	Ns	E	M	Other (IRI+CV: spontaneous tapping Inter response Interval IRI + coefficent of variance)	WAIS	processing speed was negatively correlated with both mean IRI durations (r^2= 0.478), and mean CV (r^2= 0.348)
De Montalbert	2016	10/20	300-3000ms	30	21.6±6	O	C	2nd	E	P	Duration discrimination	WAIS + TMT	the scores for executive and attentional functions were significantly correlated with temporal estimation in the overlap condition (r =0.31,$p<0.05$ and=0.57,$p<0.05$, respectively). No correlation was found between working memory performance and time estimation (r =0.11,p >0.05).
Carroll	2008	23/22	300-600ms	34.8	M37.6 ±11.6 F43.6± 9.3	I+O	Ns	1st+ 2nd	E	P	Duration discrimination	WAIS	a statistically significant relationship was only observed between Picture Completion subscale scores and visual bisection point values in the schizophrenia group ($r(23) = .59$, $p = .003$)
Roy	2012	25/25	800-2400ms	4	Ns (18-35)	Ns	C	Ns	E	M+P	time reproduction + other (method of dynamic stimuli)	WAIS + other (WMS-III + CVLT-II + CPT II + stroop test)	Scores a t WMS and switching Stroop are significantly correlated with subjects' Fn (scores in MDS task). The coefficient of variation (reproduction task) is significantly correlated with the scores obtained with the following tests: Psycho motor speed, C GI_CB, WMS-III and spatial span .
Tracy	1998	19/14	7000-40000ms	52.6	47.3± 10.1	I	Ns	1st	E	M +P	verbal estimation + time production	Other	Older ages, more education, and poorer working-memory skills were associated with variance in time interval production

Table 4: no correlation between cognitive performance and timing performance, studies description

Author	Year	S/C	Time range	% F	Mean age	I/O	CP	T	E/I	M/P	TA	CA
Moussa-Tooks	2018	33/42	500ms	35.5	36.7±10.7	I	Ns	Ns	E	M	Time production	WAIS
Ciullo V	2018	30/30	200-1600ms	30	41.4±9.9	Ns	Ns	Ns	E	M+P	Duration discrimination + time production	TMT
Zvyagintsev M	2017	20/20	0-100ms	37.5	42.2 ± 7.3	I	Ns	2nd	I	P	Other	WAIS + TMT
Losak J	2016	28/27	50-175ms	21.4	32.0± 6.9	I	Ns	2nd	E	M	Other (interception task)	WAIS + WCST
Su	2015	24/24	0-1200ms	50	27.± 7.3	Ns	Ns	Ns	I	P	Other	WAIS
Bolbecker	2014	66/73	300-600ms	60.3	Ns	Ns	Ns	2nd	E	P	duration discrimination	WAIS
Capa	2014	20/20	0-96ms	30	37.2 ± 9.2	Ns	Ns	1st and 2nd	I	P	judgement of simultaneity + temporal order judgment	other
Peterburs	2013	22/22	3000-18000ms	31.8	32.7±7.6	O	Ns	Ns	E	P	Other	TMT + WCST
Lee	2009	38/38	400-800ms + 1000-2000ms	10.5	37.3±10.4	Ns	Ns	2nd	E	P	duration discrimination	WAIS + HVLT-R + WCST
Carroll	2009	32/31	500ms	71	M 37.3 ±11.4 F 43.2±8.3	I+O	Ns	1st and 2nd	E	M	time reproduction	WAIS
Elvevåg	2004	20/20	333-2333ms	Ns	37.4±8.4	I+O	C	2nd	E	P	duration discrimination	WAIS
Elvevåg	2003	19/23	125-875ms	21	32.8±8.39	I+O	C	2nd	E	P	duration discrimination	WAIS
Broadhurst	1969	24/24	5min	0	39.6±12.3	I	C	Off	E	P	Verbal estimation	other

Cognition and time perception discussion

One of the main questions raised about time research in schizophrenia concerns the nature of these disorders. Do these temporal disturbances arise of their own nature or do they emerge from the already known cognitive impairment associated with schizophrenia? cognitive deficits are recognized as a main feature of schizophrenia[144] and affect a wide range of cognitive functions including attention, executive functions, memory, processing speed[145] all potentially confounding factors when it comes to performing temporal tasks.

It is easy to understand how working memory or attention deficit can be misleading when performing any active task, so it would seem to be more appropriate to assess hypothetical “pure” time perception alteration using perceptive, implicit tasks.

But the relationship could also be understood in a reverse way with a basic time perception alteration leading to more unspecific cognitive task.: in 1998 Andreasen proposed the 'cognitive dysmetria'[1] model which suggests that schizophrenia is associated with a severe failure of a system of synchronization and prioritization of information that would be reflected in positive and cognitive symptoms. The proposed model indicates as a possible underlying deficit an alteration in the system that coordinates the processing, prioritization and expression of information.

In 2007 Vogeley[110] et al took up the concept of cognitive dysmetria introduced by Andreasen and related it to Husserlian theories on temporality. According to the authors, the tripartite conception of consciousness of a phenomenological matrix based on retention, original impression and protection can correspond to the processes of working memory, interference control and preparatory set of a neuroscientific matrix

Despite the theories proposed it is however, it is still uncertain whether the temporal deficit is concomitant with other cognitive deficits, consequent or to the cause.

The results from our review allow us to outline some considerations: (see table 2-3-4)

1)Both the number of studies and the absolute number of patients is greater in the group of articles that does not find a correlation between cognitive alterations and

alterations in the perception of time. A possible interpretation of these results is that the perception of time should be considered as a cognitive alteration in its own right, which may or may not be concomitant with other known cognitive alterations. It seems difficult to imagine that the alterations in the perception of time are therefore the basic layer from which further cognitive alterations derive, as it was possible to hypothesize following Andreasen's cognitive dysmetria theory.

2)These considerations become even more evident if we consider the shorter time ranges, where the pre-reflexive capacity is at stake. In these studies, especially where implicit tasks were used, it was never possible to find a correlation between cognitive performance and temporal analysis.

3) Even in the studies where there is a correlation, there is a fair heterogeneity of the results that put into consideration different cognitive abilities or show alterations only in specific subscales of the tests submitted (see table 3).

4) To complete the discussion, it should be emphasized that it seems to be more difficult to find a correlation between cognitive symptoms and the perception of time when subjects use second generation antipsychotics. These data can be interpreted as a possible indicator of a mediating role of dopamine deficiency which alters both the perception of time and cognitive performance causing an apparent correlation when first generation antipsychotics are used. On the other hand, it was not possible to draw clear indications from our review on the impact of the clinical phase (acute-chronic / inpatient-outpatient), data that could partially modify the conclusions reached.

At present, in contrast to the application of cognitive dysmetria hypothesis to a temporal layer of experience it appears that the cognitive deficits of schizophrenia and the alteration of temporality in schizophrenia belong to two disjoint domains.

Symptoms and time assessment results

We identified 44 articles where a symptom assessment was performed. As shown in table 5 in the group of studies where cognitive assessments were performed 15 of them (472 patients examined) found a significant correlation between the submitted timing task and the symptom assessment as opposed to 20 (551 patients) which did not find any significant correlation; in 9 studies correlation were not searched.

As we could find in the studies where a cognitive assessment was performed, also in these studies there is more often a lower percentage of female than male, both in sample and control groups. The most represented age range in both groups does not appear to be very different (slightly higher in the no correlation group), with the 25-45 age range being the most represented.

In both group of studies, the time ranges under examination were quite heterogeneous, with more often an absence of correlations when time ranges under examination were shorter. However, no cut-off time range was found in these studies

In studies where correlation between timing and symptoms was found, clinical samples were composed most of times patients recruited in inward clinics (5 in, 3 out, 2 out+in, 5 ns) and mostly treated with 2nd generation AP (1 first, 4 second, 5 both, 5 ns). There is no clear indication about the clinical phase as most of the time it was not specified (2 chronic, 1 acute, 12 ns)

On the other hand, patients where a statistical correlation between timing performances and symptoms assessment was not found seemed to be more frequently outpatients (2 in, 6 out, 6 out+in, 6 ns), mostly clinically labelled as chronic when clinical phase was searched (9 chronic, 11 ns) and mostly treated with 2nd generation AP (2 first, 6 second, 5 both, 7 ns).

Mostly explicit timing task were performed in studies where a correlation between timing task and symptoms assessment was found (11 E, 4 I), with 4 procedures looking for motor timing tasks and 11 for perceptive timing tasks.

Studies were correlations were not found performed explicit timing and implicit timing task with quite the same frequency (11 E, 9 I) with an important majority of perceptive tasks used (16 P, 1 M, 3 both).

In both group of studies (correlation found vs correlation not found) the most frequent symptoms assessment used was PANSS.

		CORRELATION NOT FOUND	CORRELATION FOUND
Total number of patients		551	472
Number of studies		20	15
Control size		544	491
Outpatients/inpatients	Outpatients	6	3
	Inpatients	2	5
	Both	6	2
	Not searched	6	5
Clinical phase	Acute	0	1
	Chronic	9	2
	Not searched	11	12
Treatment	Mostly 1° gen. AP	2	1
	Mostly 2° gen. AP	6	4
	Both	5	5
	Not searched	7	5
Explicit/implicit	Explicit	11	11
	Implicit	9	4
Motor/perceptive	Motor	1	4
	Perceptive	16	11
	Both	3	0

	Time assessment	CORRELATION NOT FOUND	CORRELATION FOUND
	Sensorimotor Synchronization Task	0	2
	Judgment of Simultaneity	6	1
	Duration Discrimination Task	4	3
	Verbal Time Estimation	2	1
	Interception Task	0	1
	Temporal Order Judgement	1	0
	Temporal Irregularity Detection	1	0
	Rhythm Production	1	0
	Temp. Order Judg. + Judg. of Simu	0	1
	Verbal Time Est + Time Prod	1	1
	Time Production + Other	1	0
	Dur. Discr. + Time Pro. + Other	0	1
	Other	3	4
	Symptomatology assessment		
	PANSS	6	6
	PANSS + CPE	8	3
	BPRS + SAPS + SANS	0	1
	SANS + SAPS + CPE	1	1
	CPE	1	1
	SANS + SAPS	1	0
	BPRS + CPE	1	0
	Other	1	3

symptomatology correlation found vs not found

Table 6: correlation found between symptomatology and timing performance, studies description

Author	Year	Time range	Sample/control	% F	A	I/O	CP	T	E/I	M/P	TA	SA	Findings
Wilquin H	2018	300-600ms	24/27	41.6	40.6 (8.0)	O	C	Both	E	M	Sensorimotor Synchronization Task	PANSS	Results suggest a clear dissociation between the preservedability to produce inter-tap intervals in schizophrenia and thedifficulties in timing self-initiated action to predictable externalevents.
Moussa-Tooks AB	2018	500ms	33/42	35.5	36.7 (10.7)	I	Ns	Ns	E	M	Sensorimotor Synchronization Task	PANSS	Specifically, shorter and morevariable ITIs were observed during the continuation phase.
Stevenson RA	2017	0-400ms	16/16	50	42.3 (8.9)	Ns	Ns	Ns	I	P	Temporal order judgment+ judgment of simultaneity	BPRS + SAPS + SANS	Unisensory auditory, but not visual, TOJ performance was predictive
Losak J	2016	50–175 ms	28/27	21.42	32.0 (6.9)	I	Ns	Mostly 2°	E	M	Interception task	PANSS	There was a significant group difference in the number of hits ($P < .001$) and early misses($P < .001$), but not late misses ($P < .29$).
Su	2015	0-1200ms	24/24	50	27.04 (7.35)	Ns	Ns	Ns	I	P	Other	PANSS + CPE	Significant deficit specifically in temporal integration rather then late attentional impairment in SCZ patients.
Papageorgiou	2013	1080-1320ms	60/35	31.66	38.2 (5.9)	I	Ns	Mostly 2°	E	M	Other (percentage of correct responses)	PANSS	The overall mean percentage of correct responses in time interval comparison was significantly greater for the control group than for the patient group.
Peterburs	2013	3000-18000ms	22/22	31.81	32.68 (7.61)	O	Ns	Ns	E	P	Other	PANSS	The present data support the notion of a deficit in anticipatory and predictive mechanisms in schizophrenia thet is modulated both by symptom manifestation and by cognitive demand of the task at hand.
Turgeon	2012	300-900ms	20/20	30	39.2 (9.3)	O	Ns	Both	E	P	Duration discrimination + time production + other (deviant detection)	PANSS + CPE	MAIN TASK 1 and 2 JND (minimum detectable phase shift) are overall larger for SZ than NC.
Tschacher	2011	0-150ms	34/34	20.58	27.9 (7.1)	Both	A	Mostly 2°	I	P	Other	PANSS + CPE	Enhanced attribution is related to increased positive and decreased negative symptoms

													(jumping to conclusion style of cognition
Lee	2009	400-800ms 1000-2000ms	38/38	10.52	37.3 (10.4)	Ns	Ns	Mostly 2°	E	P	Duration discrimination task	SANS + SAPS + CPE	Patients with schizophrenia had an increased bisection point when compared to healthy controls in the 400/800 ms condition but not in the 1000/2000 condition.
Waters	2009	960-1440ms	35/16	Ns	36.0±10.6 FRS- 33.1±7.5 FRS+	Both	Ns	Both	E	P	Duration discrimination task	SAPS + SANS + selected items from SCAN	Patients with FRS have impaired time discrimination abilities and that they experience time differently by underestimating the duration of time interval.
Foucher JR	2007	0-470ms	30/33	33.4	33.0 (9.0)	Ns	Ns	Both	I	P	Judgment of simultaneity	PANSS	Increased simultaneity thresholds in bimodal conditionscould well account for the apparent increase ofintegration of sensory information demonstrated inpatients with schizophrenia.
Todd J	2000	50-150ms	22/25	Ns	28.3	I	Ns	Both	E	P	Duration discrimination task	CPE	Results highlight the possibility of abnormalities in the process of auditory trace formation and temporal summation in schizophrenia.
Rutschmann J	1973	500-2000ms	16/16	0	18-30	I	C	Mostly 1°	E	P	Verbal time estimation + time production	Other	Sz understimated intervals-anxiety is an important variable to be considerer.
Orme JE	1966	30min	70/116	Ns	Ns	Ns	Ns	Ns	E	P	Verbal time estimation	Other	time perception could be an useful variable to distinguish between paranoid and non-paranoid Sz and to assess the personality variable extrovert-introvert.

Table 7: correlation not found between symptomatology and timing performance, studies description

Author	**Year**	**Time range**	**Sample/control size**	**% Female**	**Mean age (SD)**	**I/O**	**Clinical phase (A/C)**	**Treatment (1°/2° generation AP)**	**E/I**	**M/P**	**Time assessment**	**Symptom assessment**
Ciullo V	2018	200-1600ms	30/30	30	41.36 (9.87)	Ns	Ns	Ns	E	Both	Duration discrimination	PANSS
Zvyagintsev M	2017	0-100ms	20/20	37.50	42.2 (7.3)	I	Ns	Mostly 2°	I	P	Other	PANSS
Graham-Schmidt	2016	200-600ms	39/43	26.50	43.1 ± 1.8 (no passivity symptoms) 42.8 ± 2.5 (with passivity symptoms)	O	C	Ns	E	P	Verbal time estimation	SAPS + SANS + CPE
de Boer-Schellekens	2014	0-300ms	16/16	6.25	40.0 (8.1)	O	C	Mostly 2°	I	P	Temporal order judgment (TOJ)	BPRS + CPE
Capa	2014	0-96ms	20/20	30.00	37.2 (9.2)	Ns	Ns	Both	I	P	Judgment of simultaneity	PANSS + CPE
Chen	2014	30-310ms	28/26	60.70	40.3 (9.9)	I and O	Ns	Ns	I	P	Judgment of simultaneity	PANSS + CPE
Bolbecker	2014	300-600ms	168/73 (BDP 34, BDNP 37, SCZ 66, SA 31)	58.82 BD 56.75 BDNP 37.87 SZ 61.29 SA	Ns	Ns	Ns	Mostly 2°	E	P	Duration discrimination	PANSS
Martin B	2013	0-440ms	13/13	23.00	35.0 (7.5)	O	C	Both	I	P	Judgment of simultaneity	PANSS + CPE
Lalanne	2012	0-92ms	18/18	50.00	35.7 (6.3)	O	Ns	Mostly 2°	I	P	Judgment of	PANSS + CPE

											simultaneity	
Lalanne	2012	0-92ms	19/19	36.84	37.0 (6.5)	Ns	Ns	Both	I	P	Judgment of simultaneity	PANSS + CPE
Delevoye-Turrell	2012	Around 500ms	39/39 (24SZ / 15UHR)	41.66 SZ 33.33 UHR	40.6 (8) SZ 18.2 (2.6) UHR	O	C	Ns	E	P	Other	PANSS + CPE
Roy	2012	800-2400ms	25/25	4.00	18-35	Ns	C	Ns	E	Both	Time reproduction + other	PANSS
Carroll	2009	300-600ms 3000-6000ms	28/31	25.00	37.4 (11.3)	I and O	Ns	Ns	E	P	Duration discrimination	PANSS
Carroll CA	2009	500ms	32/31	31.25	37.3 (11.4) M 43.2 (8.3) F	I and O	Ns	Both	E	M	Rhythm production	PANSS + CPE
Giersch A	2009	0-460ms	19/19	31.50	30.6 (6.1)	O	C	Mostly 2°	I	P	Judgment of simultaneity	PANSS
Carroll	2008	300-600ms	23/22	34.78	37.6 (11.6) M 43.6 (9.3) F	I and O	Ns	Both	E	P	Duration discrimination	PANSS + CPE
Bourdet	2003	53-1116ms	22/14	Ns	34.5 (9.7)	Ns	C	Ns	E	P	Temporal irregularity detection	CPE
Posada	2001	0-1400ms	20/20	30.00	36.4 (7.9)	I	C	Mostly 2°	I	P	Other	SAPS + SANS
Tysk L	1984	30000ms	9/5	22.20	33.3	I and O	C	1°	E	Both	Verbal time estimation + time production	Other
Tysk L	1983	1000ms (task 1) 7500-27500ms (taks2) 10-30ms (task 3)	58/60	40.00	34.1 (8.9)	I and O	Ns	Mostly 1°	E	P	Verbal time estimation	Other

Symptoms and time assessment discussion

The correlation between dopaminergic transmission and schizophrenia symptoms is now well established[146]. In recent years, it has also been seen how dopaminergic transmission seems to play a fundamental role even within the neural networks involved in the perception of time[147]. Among the regions involved we find the basal ganglia and in particular the substantia nigra, as evidenced by the alterations of temporal perception found in subjects affected by Parkinson's disease[147]. Some patients on drug treatment with L-DOPA, compared to controls, have been shown to: underestimate the length of a time interval in a verbal time estimation task; wait longer in a temporal reproduction task; require a longer minimum time interval between paired stimuli to perceive two time-separated stimuli. Administration of L-DOPA significantly improved patients' performances in all three tasks [71,72]. It was also found by combining drug administration with different tasks a correlation between dopamine deficiency and the perception of shorter intervals as increased and the longer ones as decreased[70,73].

At the same time, pharmacological studies, for example, indicate that performances related to time perception are highly sensitive to dopaminergic modulation. Dopamine agonists such as cocaine or methamphetamine are able to cause a perceived lengthening of time, while haloperidol causes a subjective shortening of time [66]

Further considerations of the relationship between symptoms of schizophrenia and altered perception of time can be derived from phenomenological psychopathology studies.

Minkowski hypothesized that subjective time is altered in its flow, and is experienced as frozen, immobile, devoid of "élan vital". He described the time of people suffering from schizophrenia as characterized by the loss of immediate attunement to the situation. He also highlighted the phenomenon of the spatialization of time: time is perceived as divided into juxtaposed elements that the schizophrenic is unable to put together. The fragmentation of time has been regarded as a generating disorder of schizophrenia. Some of the most characteristic symptoms of schizophrenia (e.g. thought insertion, hallucinations or experience of passivity) have been interpreted as

manifestations of a disorder of the constitutive synthesis of consciousness, so that every moment is experienced by the person as detached from the stream of consciousness and from the sense of self. In other words deficient temporal information processing would lead to dysfunctions in timing or sequencing of mental activity and behaviour, producing some classic symptoms of schizophrenia, such as delusions and disorganized behavior[54]

To illustrate how distortions in the perception of time could produce positive symptoms, consider delusional thinking. Distortions in the perception of time intervals could lead to the failure to correctly perceive the time sequence of contiguous events. This in turn could lead to a failure to attribute voluntary control to some of one's actions (lack of agency) or confusion about the relationship between one's actions and the outcome of those actions (e.g. flipping a light switch turns on the light), giving the illusion of lack of control by the individual and control by some other entity, a common aspect of paranoid delusional thinking in schizophrenia[39,148,149]. Given the critical role of dopaminergic signalling in the perception of time, together with its documented dysfunction in schizophrenia, this interpretation may be consistent with current conceptualizations of the involvement of impaired dopaminergic signalling in producing positive symptoms via aberrant attribution of salience.[150]

Examining the results from our review about the link between symptoms domain and time perception domain, we can propose that:

Unlike what has been said about the cognitive aspects, it is more difficult to establish whether or not there is a clear correlation between the symptomatological and temporal domains. The number of studies and the absolute number of patients in which a correlation was found is very similar to that in which, on the other hand, no correlation was found, so there is no clear indication of this. It was not even possible to identify cut-off time ranges for the presence or absence of correlations and no clear indications were found on the impact of the clinical phase, which was not reported by the vast majority of studies. the same inconclusiveness is present with regard to the patient's recruitment setting (outpatient or hospital), although it seems to be slightly easier to find significant correlation data in the hospital population.

There are also no clear differences between the two groups regarding the use of first or second generation antipsychotics.

The use of implicit tasks led less frequently to highlighting significant correlations (found in 4 versus 9 studies in which they were not found). Also, when these were discovered, they were never about negative symptoms (in 3 with positives and in 1 with disorganization)

The use of a specific temporal task such as the "Judgment of Simultaneity" has never led to significant results except for one study[151] which reported a correlation with disorganization but not with positive and negative symptoms.

The correlation with negative symptoms appears to be at least partly linked to the use of tasks that involve greater use of executive functions (eg sensorimotor synchronization task, duration discrimination) and time intervals ≥ 300ms.

Considering the relationships found in recent scientific literature and partly supported by this review between increased mesocortical dopaminergic transmission, productive symptoms and accelerated perception of time lead us to some reflections:

The fact that it was not possible to find a clear correlation between the time perception tasks and the clinical manifestations of schizophrenia despite the known common alterations of dopaminergic transmission, could open an interesting option from a treatment point of view. As is known, there is a certain amount of patients who do not respond to treatments with dopamine antagonists and for which a different pathophysiological mechanism for the production of symptoms has been hypothesized[150]. It would be interesting to explore the hypothesis if alterations in the perception of time were systematically absent in this group of patients (as they were also linked to an impaired dopaminergic transmission). If this were the case, one could hypothesize the development of a predictor of a temporal pharmacological response. If the temporal alterations were found, one could expect a clinical response to the use of drugs that act on dopamine, if instead the subjects did not show alterations in the temporal perception task, one could immediately orientate on drugs that intervene on other profiles receptor such as clozapine. In support of this hypothesis there is also the confirmation that among the studies that find correlation, this is mostly present with positive symptoms (where a relationship with an aberrant transmission of dopamine is best known) and to a lesser extent with negative ones and those belonging to the domain of disorganization.

The correlation with negative symptoms appears to be at least partly linked to the use of tasks that involve greater use of executive functions (eg sensorimotor synchronization task, duration discrimination) and time intervals ≥ 300ms.

FIRST PART CONCLUSIONS

The first of the two topics I dealt with, the alterations of temporality in schizophrenia, made it possible to highlight the complexity of the dialogue between phenomenology and cognitive sciences but also the possible positive developments of the same.

When I wrote to him for his opinion on the work I was planning to undertake, Dr. Gilberto Di Petta, president of the Italian Society for Phenomenological Psychopathology, answered me like this:

"Dear Enrico, your idea is commendable, even if you take a road paved with good intentions, but with poor results. [...] So good luck ..."

Before moving on to the second part, I would therefore like, as is now almost customary for those who have dealt with the perception of time, to quote Saint Augustine:

“Quid ergo est tempus? Si nemo ex me quaerit, scio: si quaerenti explicare velim, nescio.”

“What then is time? If no one asks me, I know what it is. If I wish to explain it to him who asks, I do not know.”

PART 2: INTERSUBJECTIVITY

INTERSUBJECTIVITY IN COGNITIVE SCIENCES

In his article "*Social Cognition in Schizophrenia: An Overview*"[152] Penn et al provide a useful introduction to the concept and its various applications in psychiatry.
When we talk about social cognition we are referring to a term that took hold in the scientific debate during the so-called "cognitive revolution" which began towards the end of the 1960s.[153] The term social cognition therefore refers to the way in which people perceive themselves and others in the social world. This construct includes different components that relate to perception and causal attributions and is fed by multiple theoretical perspectives that investigate how the information in a social context.
Regarding schizophrenia, 3 main fields of study can be cited to justify social skills deficits: perception of emotions, theory of mind and attributional style.

The perception of emotions refers to the abilities and skills to recognize and identify the emotions of others, in addition to the biological and physiological processes involved. Emotions are generally thought to have three components: subjective experience, physical changes, and cognitive assessment; emotion perception is the ability to make precise decisions about another subjective experience by interpreting their physical changes through sensory systems responsible for converting those observed changes into mental representations.

The ability to perceive emotions is believed to be both innate and subject to the influence of the environment, and is also an essential component when it comes to social interactions. How emotion is experienced and interpreted depends on how it is perceived. Emotion perception impairment in schizophrenia represents a robust finding in schizophrenia that appears to be moderated by certain clinical and demographic factors.[154] .

The theory of mind refers to the possibility of imagining the experiences, thoughts and intentions of another individual. According to this theory, the observation that

other people have a mind can only occur indirectly, inferring the information by similarity of the observed behavior.

A meta-analysis using this construct would have indicated that people with schizophrenia have a stable and significant deficit of "theory of mind"[155].

Mentalization (as the process of using the theory of mind is referred to) deficit has also been demonstrated in first-degree departures of patients with schizophrenia (when they themselves scored high on a schizotypy scale).[156]

Furthermore, these deficits are not explained by a more general deficit of other cognitive functions, nor by specific symptoms that may appear to underlie an incorrect interpretation of the behavior of others (such as paranoia).[157]

Attributional style, sometimes known as explanatory style, refers to the ways in which people make assumptions on the cause of events which happen within their lives. When people experience positive or negative events, they often wonder why the event occurred. In order to answer this question, people make causal attributions based upon three basic dimensions: *internal-external*, *stable-unstable*, and *global-specific*.[158]

More often than not, people attribute responsibility for positive events to themselves while responsibility for negative events to others. Most of the work on attribution style in individuals with schizophrenia has focused on symptoms of paranoia or persecutory delusions. People with these symptoms tend to blame others rather than situations for negative events, a style of attribution known as personalization bias.[159,160]. This mechanism has been interpreted as a system for maintaining self-esteem because attributing negative intentions to people helps to maintain a positive self-image. However, this leads to the perception of an increasingly hostile environment. These negative attributions appear very resistant to correction in paranoia, even when subsequent information is obtained that conflicts with the initial assumption.

Other biases of a more strictly cognitive nature can obviously be associated with alterations in the attributional style such as the tendency to "jumping to conclusions" and "confirmatory prejudice" (that is, seeking confirmation evidence for a belief rather than disconfirmatory evidence).[161]

INTERSUBJECTIVITY IN PHENOMENOLOGY

According to the phenomenological perspective, the problem of intersubjectivity is one of the central themes of schizophrenia, however, according to this methodology, the question must be set in a different way from what is described regarding the cognitive sciences.

There are 3 criticisms of the approach used by mainstream psychiatry regarding the alteration of social cognition:

- The assumption that the behavioral component in which the deficits are emphasized is strictly evaluated regardless of their genesis

-The definition of these deficits concerns only the quantitative reduction of performance;

- the extreme heterogeneity of the contexts to which these concepts are applied

According to Stanghellini[162] because of these limitations, it is difficult for general psychiatry to distinguish social dysfunction in schizophrenia from social dysfunction in general or social dysfunction that simply emerges in the face of adversity.

The concept used by phenomenology to explore the disorders of social cognition in schizophrenia is that of intersubjectivity.

Intersubjectivity can be defined as the ability to understand other people, that is, the ability to grasp or evaluate the significance of their action and expression. As we will see later, this concept and that of embodied cognition have become important topics on the research agenda of philosophy (phenomenology, cognitive sciences and philosophy of mind), developmental psychology and neuroscience. This bridging concept will be what we will develop later in the experimental part of the thesis.

The salient points of the question of intersubjectivity were summarized by Gallagher and Zahavi[163] in 3 main reflections

- If the nature of intersubjectivity is mainly of a cognitive or perceptive nature

-If, as interpreted by phenomenology, we refer to a perceptual phenomenon, is it then a special type of perception?

- Is knowledge of others secondary to one's own knowledge? Or do we initially develop an access to our mental states that only then allows the attribution of mental states to others?

Regarding the first point, cognitive sciences have generally adopted a cognitive approach in which the understanding of others is attributed to the possession of a theory of mind (ToM), understood as the ability to make hypotheses in order to explain or predict the mental states that underlie the behavior of the other.[164,165]

Phenomenology argues that the basic process of intersubjectivity is of a perceptive nature without the use of cognitive superstructures to understand and respond to others. Most everyday relationships are based on immediate, pre-reflective face-to-face encounters with other people, whose mental states are understood directly and are typically grasped as meaningful in an emerging and pragmatic context. Mutual understanding therefore takes place immediately through an immediate perception of the physicality of other people. Mental states are not hidden in the brain but behavior (postures, gestures, expressed emotions, gazes and goal-oriented actions) intrinsically possesses an expressive unity and a significance that we can grasp directly during our encounters with others , without any cognitive mediation.

From this point of view, from the earliest stages of development it is possible to recognize others through a particular type of perception of an innate nature, this finding would be reflected in the development of the mother-child dyad and in the ability of newborns to distinguish between beings from the earliest stage. humans and inanimate objects.[166]

With regard to schizophrenia, it appears important at this point to emphasize the role that schizophrenic "autism" has had since its conceptualization by E. Bleuer[166]. This concept has disappeared from current diagnostic systems but appears useful in understanding the role of an altered intersubjectivity in people with schizophrenia.

Autism in schizophrenia was initially framed in a psychodynamic perspective as a defense mechanism for managing conflicts between desires and reality[167]. Subsequently, with a paradigm no longer based on conflict, the key elements were

identified lack of affective contact with other people, combined with irritability and hypersensitivity to social stimuli, social anxiety and avoidant behavior. The authors of classical psychopathology who have most influenced the reflections on autism in schizophrenia are Minkowski and Blankenburg[168]. Minkowski assumed that autism in schizophrenia implied a vital loss of contact with reality. Vital contact with reality provides a latent awareness of reality "making us adapt and modify our behavior in a contextually relevant way but without distorting our general goals, standards and identities". Blankenburg characterized autism as a crisis of the obvious: that is, lack of a pre-reflective understanding of the surrounding world, axioms of the "natural" attitude of harmony with the situation in which we find ourselves immersed in everyday experience).

The main characteristic of the type of autism found in schizophrenia therefore seems to reside in a specific type of disorganization of the basic structures of social life, in a qualitative disturbance of spontaneous and intuitive participation in social life.

EMBODIED COGNITION AND DIRECT SOCIAL PERCEPTION THESIS: A BRIDGE BETWEEN PHENOMENOLOGY AND COGNITIVE SCIENCE?

The concepts on intersubjectivity expressed by phenomenology find a convergence with the direct social perception thesis. Direct Social Perception (DSP) is the idea that we can perceive others' mental states. This kind of perception is direct in the sense that it does not involve inferential mediation. When an infant cries, I see immediately that she is upset. When a dog suddenly starts barking, I see that my running partner is afraid of it. As my friend reaches toward the cake, I see that she wants a piece. According to DSP, I literally perceive the distress, fear, and desire. I do not first observe the behavior and then infer the mental state. Rather, I simply see the mental state in the behavior

This concept has been exemplified from Ansuini et al[169] by dr. Jekyll/mr Hyde Paradox:

"Suppose an observer, say Dr. Watson, watches Dr. Jekyll / Mr. Hyde taking hold of a scalpel to apply it to a human body. The action is the same for both actors; however, in one case, Dr. Jekyll is using the scalpel to cure a patient, and in the other case, Mr. Hyde grasps the scalpel to inflict pain. Would it be possible for Dr. Watson to discriminate their intentions by simply observing the way they grasp the scalpel?"

I will resume here what the authors suppose in this study and which is the theoretical basis to the action observation study we have done to verify possible intersubjectivity deficits in schizophrenia. This paradigm is the one we have chosen because makes a bridge between embodied cognition hypothesis (phenomenology) and cognitive science reliability.

The paradox of dr. Jekyll / Mr Hide wants to emphasize that to understand the intention of the kinematics of movement it must be unequivocally related to the

intention itself, otherwise it cannot provide an adequate basis for understanding others. In other words, “how is it possible to tell if a person who is waving an arm while walking down the street is calling a taxi, or is crushing a wasp?”[170]. Predictive coding models predict that observers watching this scene can estimate the agent's intention based on contextual information (for example, the presence of an approaching taxi). In the absence of contextual information, however, if the observed kinematics were not specific, it would not be possible to distinguish between the two intentions[171].

Ansuini instead proposes that even in the absence of contextual information, observers can access others’ intentions from the way they move.

There are now several examples in the literature of how the intention of influence for the execution of movements of reach to grasp[172,173]. The logic of these studies was to "manipulate" the unchanged intention of the object to be grasped (ie the goal) as well as the external situation (ie the context). If against unchanged the context, the kinematic chain changes in the relation of the agent's intention, this would indicate that the intention is the motor chain.

To test this possibility, Ansuini et al.[172] asked participants to reach out, grab, and perform one of four possible actions (i.e. pour, move, throw or pass) on a bottle. Kinematic evaluation revealed that when the bottle was grabbed with the intent to pour, both the middle and ring fingers were more extended than all other thoughtful intentions. Interestingly, intentions have an effect on the kinematics of the hand not only during the carrying out of the reach movement for grasping but also on contact. For example, participants have been shown to place their thumb and forefinger in a higher position when the bottle is grasped with the intention of pouring than when it is grasped with the intention of lifting[174].Further studies have extended these effects to the domain of social intention[175–177].

The differences highlighted by these results, resulting only from the modification of the intention associated with the reaching movements suggest that the actions are planned and executed as a whole motor chain and that the different kinematic characteristics are uniquely selected depending on the prior intention.

The second point to evaluate, following the Ansuini thesis, is the question of whether observers are sensitive to information on intention conveyed by the kinematics of

movement. This was verified at the behavioral level using progressive temporal occlusion, a strategy for probing the contribution of visual kinematics to understanding intention, in which multiple points of occlusion are used to form a progressive series of temporal windows within event of interest[178].

This approach was also adapted by Naish [179] to test the amount of information needed to allow participants to correctly predict the outcome of the action consisting of a two-step sequence: eat or put. However, since kinematic information was not used to select video stimuli (not allowing to understand whether pregrasp kinematics actually differed between grasping for eating and grasping for positioning), these results do not provide conclusive evidence regarding if observers can grasp the first differences in visual kinematics. To address this confusion, Sartori[180] first analyzed the kinematics of reach-to-grasp movements performed with different intentions. Following these analyzes, they selected representative sequences of each action to be included in an intention discrimination activity. In this way it was also possible to evaluate the congruence with the kinematic information.

The results revealed that despite the lack of contextual information, observers were able to discriminate cooperative, competitive, and individual movements[180].

Finally, Ansuini addressed the question of which neural mechanisms contribute to the understanding of intention starting from movement. Mirror neurons seemed to be ideal candidates: since their discovery they have been indicated as the basis of our ability to understand the actions, goals and intentions of others, or to "transform visual information into knowledge"[180].

The first clues that the way an object is grasped may affect the processing of intention within the mirror circuit was provided by Kaplan and Iacoboni[181] using fMRI.

However, in this study it was not possible to clarify the specific contribution of kinematics to intentional discrimination. One hypothesis to consider is that mirror neurons discharge during action observation not because they are guided by visual kinematics, but because they are part of a generative model that predicts sensory input[170,171,182].

A solution to this problem was experimented by Lestou et al[183]: by eliminating the context and verifying whether the visual kinematics modulates the processing of intentions, it is possible to verify the involvement of the mirror neuron areas. To verify this, using manipulated point displays of different types of arm movements within an fMRI repeat suppression paradigm it was observed that the rebound effects of movements that differed in their kinematics were observed within the regions where they locate mirror neurons. Notably, rebound effects in IPL and SPL were observed only for movements with different targets, suggesting that these areas may be specifically involved in kinematic coding features relevant to intentional discrimination.

Further evidence of mirror neurons involvement were provided by Vingerhoets[184] Tunik[185], Becchio[186].

It is therefore possible to conclude that observers are in tune with the first differences in visual kinematics and can use these differences to discriminate between movements performed with different intentions.

Returning to the initial example, Ansuini therefore argues that Dr. Watson would be able to discriminate against Mr. Hyde's intentions. It would be able to do so, regardless of the context thanks to the kinematic model that characterizes its range movements. Before the start of the movement, if the scene took place in an operating room, the intention estimated by the context would be "cure". However, as the movement unfolds, the intention information specified in the visual kinematics would be taken into account and override the initial intention representation. Despite the context, the intention to "hurt" would then be properly discriminated on the basis of how the action is performed and this would finally allow Mr. Hyde to reveal: "Elementary, my dear Watson."

EXPERIMENTAL STUDY: ACTION OBSERVATION IN SCHIZOPHRENIA

On this basis, our study starts from the clinical finding that despite the progress that has certainly occurred in the treatment of major psychiatric disorders (schizophrenia, bipolar disorder, major depression), the outcomes of social functioning and quality of life still often remain unsatisfactory[187].

This partial lack of overlap between the results obtained on the most evident symptoms (psychosis, mania, major depressive symptoms) and the rehabilitation objectives understood in a broader sense is related to the important relational and social difficulties that often persist in these patients. even outside the acute phases of the disease. These difficulties were particularly evident in schizophrenia[188].

In addition to these now ascertained alterations of social cognition, more recently the motor symptoms present in major psychiatric disorders[189190] have again been placed at the center of attention. The progressive overcoming of the dichotomy between the motor and cognitive systems has led to the re-evaluation of the contribution of these symptoms in the general economy of psychiatric disorders. In fact, their contribution in the genesis of the symptoms of impaired social cognition seems increasingly probable.

Social interaction skills have been described and studied in terms of empathy, theory of mind, intersubjectivity, and social cognition using different theoretical perspectives, models and methods of investigation - however, a huge discrepancy persists between recent theoretical neuroscientific gains and therapeutic practices. Beyond the reference model, the hypothesis that relational / social skills develop in a way related to the body dimension ("embodied cognition"), in particular sensorimotor, which would constitute a prerequisite[191–194].

To date, the most used interventions for the recovery of social and interpersonal skills are the use of "social skills training" programs[195]. However, although these techniques have shown benefits in treated patients, they are not theorized on the basis of specific deficits but act on the acquisition of a limited repertoire of social skills, reproduced starting from the behavior of healthy subjects. The limits of this

type of strategy in hitting the founding nuclei of the deficit have repercussions on the fact that it is precisely the patients who are most deficient and who would therefore most need rehabilitation interventions are those who instead receive the least benefit from these "pedagogical" treatments[196]. Alternative strategies, more focused on the body and movement, however, are showing positive results in the reduction of negative symptoms such as apathy and social withdrawal[197].

Recent experiments demonstrate the importance of visual detection of the kinematics of movement for decoding the intentions of others[198–200].

Of note, the ability to recognize the intentions of others are altered in autism[201,202] which presents a genetic overlap with schizophrenia as regards the "social communication difficulties"[203].

Purpose of the study

The study aims to evaluate the alterations in intersubjectivity (alterations in the interpretation of intentions) in subjects suffering from psychotic disorders.
The primary objective is to detect whether there are differences between patients with psychotic disorders and healthy controls in carrying out tasks of decoding the kinematic parameters.

Using an action observation task we attempted to answer the following questions:

1. *Can patients with psychotic disorder discriminate object size from the observation of grasping movements?*

2. *How rapidly are they able to do that? How much movement information do they need?*

3. *Does the accuracy in action observation task relate to clinical parameters?*

Methods

Study design: Case-control

Criteria for the inclusion of subjects with psychiatric disorder:

- psychotic episode
- age between 18 35 years
-Language spoken: Italian
- availability to participate in the study
- good psychopathological compensation reported by the treating psychiatrist

As regards the population affected by psychiatric pathology, patients have been enrolled on a voluntary basis and following an agreement with the treating psychiatrist among the adult population belonging to the services of the DAI-SMDP of Ferrara. In particular, participation has been offered, with the agreement of the treating psychiatrist, to patients in good psychopathological state under treatment at the public services of the province (SPT Ferrara, SPT Portomaggiore, SPT Cento, SPT Codigoro, SPT Copparo, SPDC, SPOI, rehabilitation residence "la Luna", rehabilitation residence "Basaglia", rehabilitation residence " Il convento").

Exclusion criteria for subjects with psychiatric disorder:

- presence of neurological diseases (e.g. epilepsy, Parkinson's disease)
- clinical conditions that affect the safety of the patient or staff in carrying out the procedures related to the study (eg suicidal risk, self-directed or hetero direct aggression)

Controls group description:

Controls were shared with the Ansuini study "*Grasping Others' Movements: Rapid Discrimination of Object Size From Observed Hand Movements*"[204]: 19–29 years old healthy controls took part in the experiment. All had normal or corrected-to-normal vision and were naive as to the purpose of the experiment. All participants self-reported to be right-handed.

Task and assessment

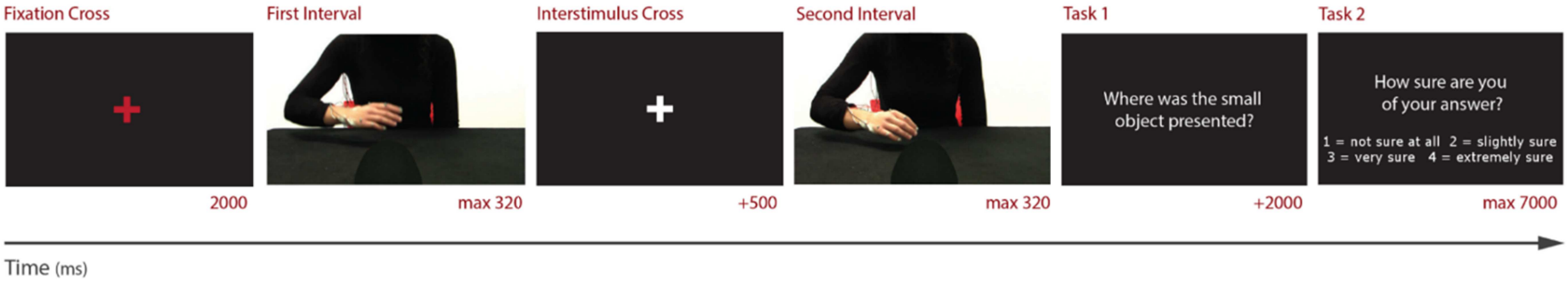
The study consisted of:

1) An *action observation task*, aimed at assessing the ability to discriminate object size over time from two different perspectives.
2) A clinical assessment of different domains (functioning, psychopathological symptoms, cognition, neurological signs; see text below for details)

Action observation task procedure

The experiment was carried out in a dimly lit room. Participants sat in front of a 17-in. computer screen (1,280 % 800 pixels; refresh rate 75 Hz; response rate 8 ms) at a viewing distance of 48 cm. At movement onset, from the frontal viewpoint, the hand and the mask were presented at a visual angle of 3.9° x 8.4° and 7.1° x 11.5°, respectively. From the lateral viewpoint, the visual angle subtended by the hand was 5.1° x 6.3°, whereas the angle subtended by the mask was 8.5° x 11.7°. Stimuli, timing, and randomization procedures were controlled using PsychToolbox script running in MATLAB R2014a (MathWorks, Inc.). A two-alternative forced-choice paradigm was employed (see Figure above). Each trial consisted of two intervals: a *target* interval (displaying a movement toward the target object, e.g., the small object) and a *nontarget* interval (displaying a movement toward the nontarget object, e.g., the large object), with a 500-ms fixation cross (white against a black background) in between. Participants were asked to decide which of the two intervals displayed a

movement toward the target object (e.g., “Where was the small object presented?”; Task 1; Figure above). Responses were given by pressing with the index fingers one of two keys on a keyboard: a left key (i.e., “A”) when the target
interval was presented as the first interval, and a right key (i.e., “L”) when the target interval was presented as the second interval. Participants were instructed to respond as accurately and as fast as possible. The maximum time allowed to respond was 2,000 ms. After this time had elapsed, participants were requested to rate confidence of their decision on a four-level scale by pressing a key (from 1 ! *least confident* to 4 ! *most confident*; Task 2; Figure 3). Participants were encouraged to use the entire confidence scale. Stimuli displaying grasping movements from the lateral and frontal viewpoints were administered to participants in separate sessions on two consecutive days. In each session, participants completed eight blocks of 30 trials: four consecutive blocks in which the target interval contained a movement toward the small object, and four consecutive blocks in which the target interval
contained a movement toward the large object. At the beginning of each block, participants were instructed about which object to consider as target, with the target interval appearing randomly either as the first interval or as the second interval. Each block included at least three repetitions of each time point. Half of the participants completed the blocks in which the target was the small object first. Participants completed a total of 240 trials for each viewpoint, with eight repetitions of each time point. Feedback was provided at end of each block to encourage participants to maintain accurate responding (e.g., “Your mean accuracy in this block was 75%”). To familiarize participants with the type of stimuli and the task, at the beginning of each experiment, we administered 10 practice trials. The practice trials were randomly selected from the main experimental videos. A performance feedback was provided at the end of the practice session. On each day, the experimental session lasted about 40 min. The order of the sessions was counterbalanced across participants.


Fixation Cross
First Interval
Interstimulus Cross
Second Interval
Task 1
Task 2
Where was the small object presented?
How sure are you of your answer?
1 = not sure at all 2 = slightly sure
3 = very sure 4 = extremely sure
2000
max 320
+500
max 320
+2000
max 7000
Time (ms)

Clinical assessment:

Demographic data

Substance abuse

Ongoing pharmacological therapy

Brief psychiatric rating scale (BPRS): a rating scale which a clinician or researcher may use to measure psychiatric symptoms such as depression, anxiety, hallucinations and unusual behaviour. Each symptom is rated 1–7 and depending on the version between a total of 18–24 symptoms are scored. The scale is one of the oldest, most widely used scales to measure psychotic symptoms and was first published in 1962.

Brief Negative Symptom Scale (BNSS) a 13-item instrument designed for clinical trials and other studies that measures 5 domains: blunted affect, alogia, asociality, anhedonia, and avolition. The Brief Negative Symptom Scale (BNSS) is a 13-item instrument designed for clinical trials and other studies that measures these 5 domain

Calgary Depression Scale: a scale which was designed for the assessment of depression in schizophrenia. The scale was derived from two existing scales by factor analysis and reliability analysis.

The Positive and Negative Syndrome Scale (PANSS): a medical scale used for measuring symptom severity of patients with schizophrenia. It is widely used in the study of antipsychotic therapy. The scale is known as the "gold standard" that all assessments of psychotic behavioral disorders should follow.

The name refers to the two types of symptoms in schizophrenia, as defined by the American Psychiatric Association: positive symptoms, which refer to an excess or distortion of normal functions (e.g., hallucinations and delusions), and negative symptoms, which represent a diminution or loss of normal functions. Some of these functions which may be lost include normal thoughts, actions, ability to tell fantasies from reality, and the ability to properly express emotions.

*The specific levels of functioning (SLOF***)** scale assess the level of functioning on four different subscales: interpersonal, social acceptance, activities, and work. Participants completed the SLOF during one of their testing sessions and provided the name of a knowledgeable informant

The Extrapyramidal Symptom Rating Scale (ESRS) was developed to assess four types of drug-induced movement disorders : Parkinsonism, akathisia, dystonia, and tardive dyskinesia.

The Edinburgh Handedness Questionnaire is a measurement scale used to assess the dominance of a person's right or left hand in everyday activities. The inventory can be used by an observer assessing the person, or by a person self-reporting hand use.

The Neurological Evaluation Scale (NES) is designed to standardize the assessment of neurological impairment in schizophrenia. The battery consists of 26 items.

The CCAS/Schmahmann syndrome scale: is a useful tool for expedited clinical assessment of CCAS in patients with cerebellar disorders. Cerebellar cognitive affective syndrome (CCAS; Schmahmann's syndrome) is characterized by deficits in executive function, linguistic processing, spatial cognition, and affect regulation

Trails Making Test (TMT) is a neuropsychological test of visual attention and task switching. It can provide information about visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning.

*BUSS and Perry Aggression questionnaire***:** a 29-item test that presumably measures four aggression-related dimensions (physical aggression, verbal aggression, hostility, and anger).

The Adult Attachment Questionnaire. AAQ yields continuous measures of three attachment styles in romantic relationships: secure, avoidant, and anxious

Statistics:

We have run ANOVA analysis comparing the two groups on “accuracy” and “dprime” data. We have considered as within factor the “bin factor” (which represent the 8 time windows of showed videos) and as between factor the “group factor” (psychiatric patients vs controls).

T-test analysis were performed as well comparing “accuracy” values with random value (0,5) and comparing “dprime” values with 0 (which means inability to detect the signal.

Concerning the demographic and clinical variables we have run correlation test (Pearson r) to verify linear correlation between the cognitive and psychopathological assessment and the performances on “accuracy” and “dprime” at the experimental task.

Ethical aspects:

The study has been approved by the ethical Ethics Committee “Area Vasta Emilia Centro” of the Emilia-Romagna Region (CE-AVEC) based at the University Hospital of Bologna, S. Orsola-Malpighi Polyclinic.

The following procedure has been approved by the ethics committee and executed for each participant:

1) Check inclusion criteria and informed consent. The participant will be informed about the general purposes of the research, the methods used, the contraindications, the inclusion criteria, the processing of personal data, and the possibility of withdrawing from the study at any time. Only after verifying that the participant has fully understood all these aspects will the informed consent form be read and signed. We estimate the total duration of this phase to be 10-15 minutes.

2) Test phase to be carried out at DAISMDP clinics in the presence of medical personnel. Subjects suffering from psychiatric disorder will be subjected to an in-depth study aimed at describing in the most thorough and objective way possible their current symptom and cognitive profile. The administered tests are used routinely in clinical practice and do not present any risk. The estimated time is about 2 hours, which can also be divided into several sessions depending on the patient's needs.

3) Behavioral tasks. In perceptual tasks, the participant will be asked to to observe visual stimuli (e.g. an actor picking up an object with his hand). The participant will have to provide perceptual evaluations on the stimuli presented.. We estimate the total duration of this phase to be 30-40 minutes.

4) Conclusion of the experiment and explanation of the experimental aims. At the end of the experiment, each participant will be informed about the purposes of the research, the measurements made and the methods of analysis of the same. We estimate the total duration of this phase to be 10-15 minutes.

During the execution of the tasks by the group affected by psychiatric pathology, psychiatrist or psychiatric medical staff or specialists in psychiatry will be present for any but unforeseen need for greater patient reassurance.

RESULTS

We recruited 11 patients who completed the object observation tasks and the clinical assessment and 19 healthy controls (from Ansuini et al., 2016). 4 were females (12 females in controls) and the mean age was 28.6, age range=22-35 (mean age 22, age range 19-29 in controls). All patients were right handed. 1 patient had precedent contact with infancy and adolescent neuropsychiatric service when younger than 18. 9 patients lived by themselves, while 2 lived with their families. 7 were unemployed at the moment of the study, 2 had a part-time occupation and 2 were studying. The average years of education were 14.73 (min-max 9-18, std 2.8). All of them were prescribed with medications at the moment of the study. BPRS, BNSS, Calgary and PANSS results are described in table 1. Neurological and cognitive evaluations are described in table 2.

Table 1

	N	*Min*	*Max*	*Mean*	*Std deviation.*
BPRSTOT	10	26,00	55,00	38,3000	11,80442
BNSSTOT	11	,00	51,00	20,5455	17,06671
CalgTOT	5	,00	16,00	8,0000	7,61577
PANSS_TOT	11	32	67	49,64	13,909

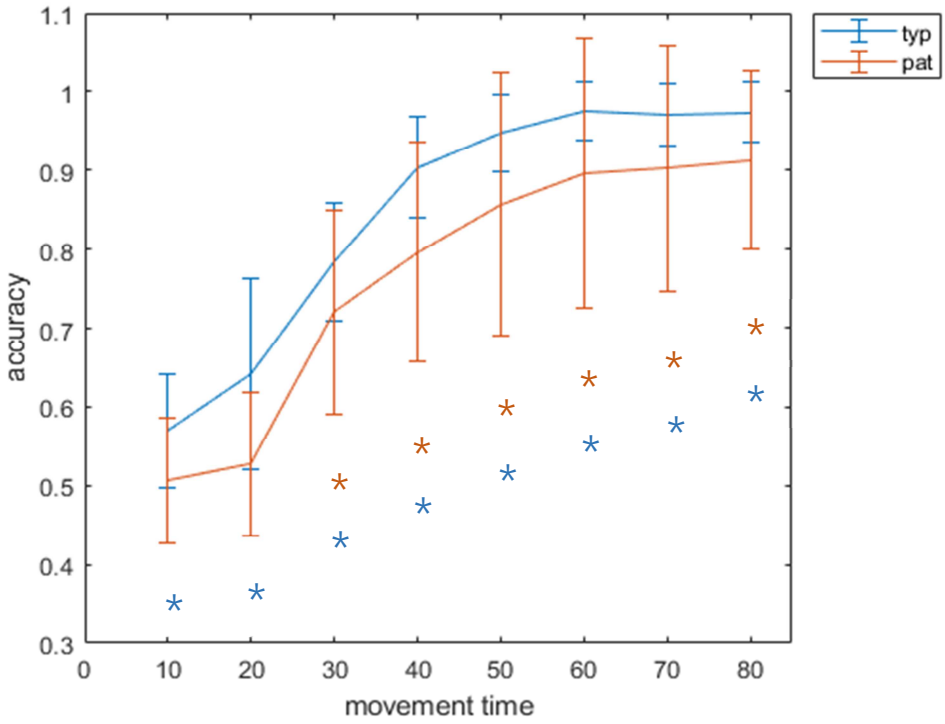
Table 2

	N	*Min*	*Max*	*Mean*	*Std deviation*
EPS_tot	10	,00	25,00	5,5000	9,65229
NES_TOT	11	,00	10,00	2,6364	2,76668
SchmaTot	11	83	114	100,00	9,508
TMTA	11	29	88	47,81	19,840
TMTB	11	47	221	100,71	55,444
TMTB_A	11	0	163	57,45	51,079

At the action observation task We found that patients with psychotic disorders were less accurate in discriminating object size than healthy controls under all occlusion conditions ($p<0.001$). While healthy controls are able to discriminate object size from the observation of grasping movements already at 10% of movement duration[204], at

10% and 20% of movement duration, patients with psychotic disorders performed at chance(T-tests show accuracy and d-prime above chance level for movement time only from 30% to 80% in patients). Accuracy was found to be related to confidence rating both in patients and in controls.

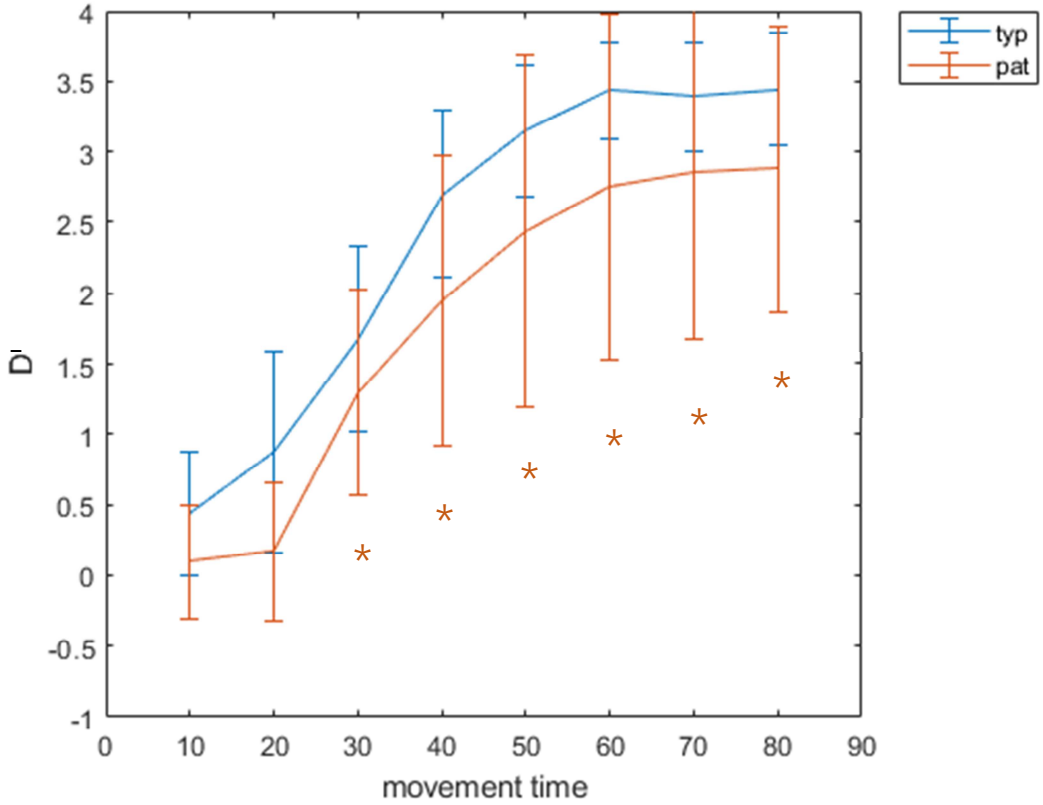
ACCURACY



ANOVA-accuracy

	Sum of squares	*Df*	*Mean Square*	*F*	*p*	n^2
Overall model	5.4996	15	0.36664	32.469	<.001	
bin	4.8641	7	0.69487	56.973	**<.001**	0.591
Paz/typ	0.6183	1	0.61835	50.698	**<.001**	0.075
bin paz/typ*	0.0171	7	0.00245	0.201	0.985	0.003
residuals	2.7320	224	.01220			

DPRIME

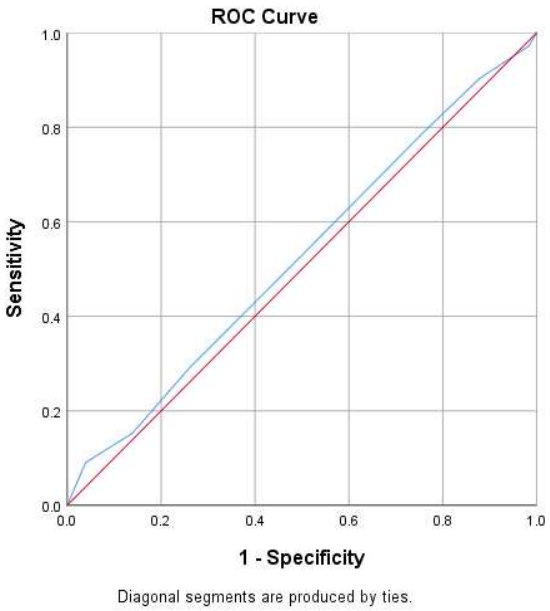


ANOVA-dprime

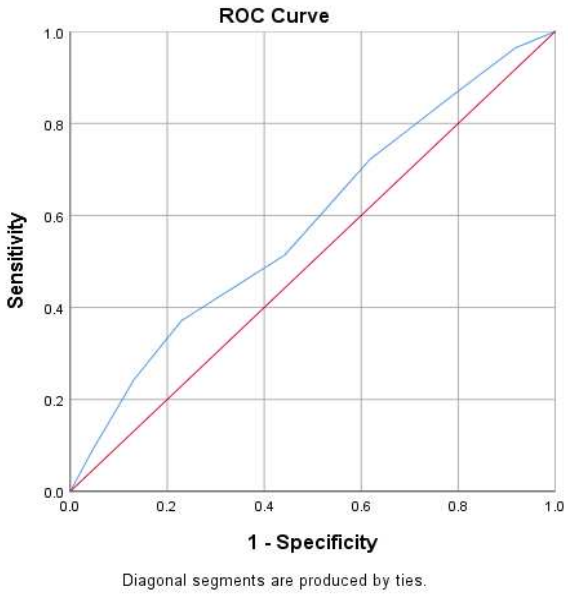
	Sum of squares	*Df*	*Mean Square*	*F*	*p*	n^2
bin	256.75	7	36.679	58.357	**<.001**	0.596
Paz/typ	31.50	1	31.496	50.111	**<.001**	0.073
bin paz/typ*	1.78	7	0.255	0.405	0.898	0.004
residuals	140.79	224	0.639			

ROC CURVES

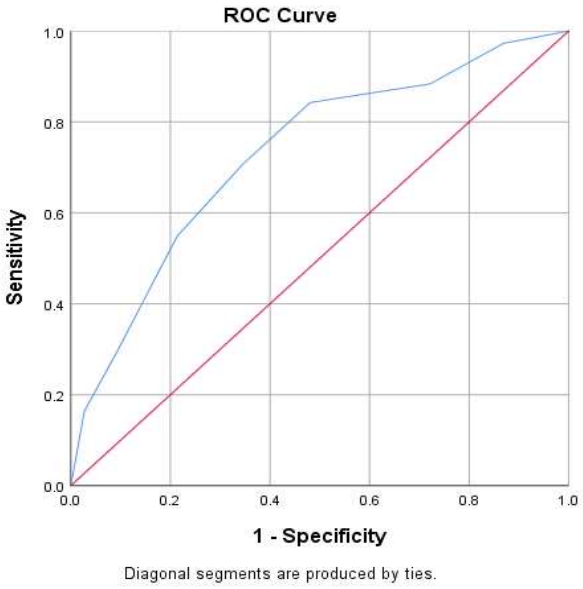
10% of movement



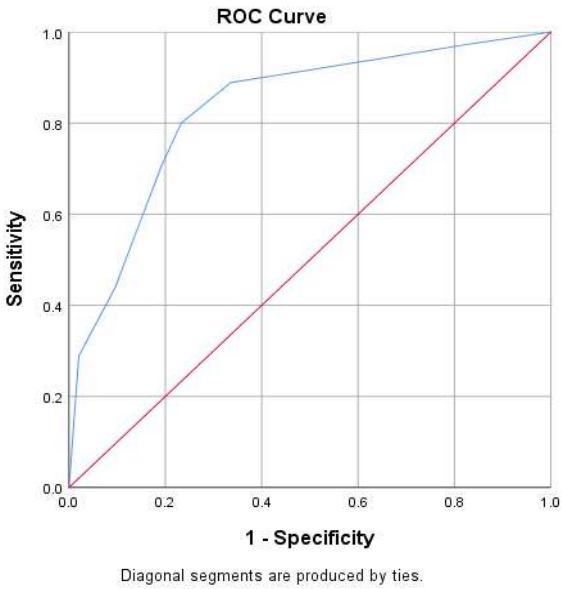
20% of movement



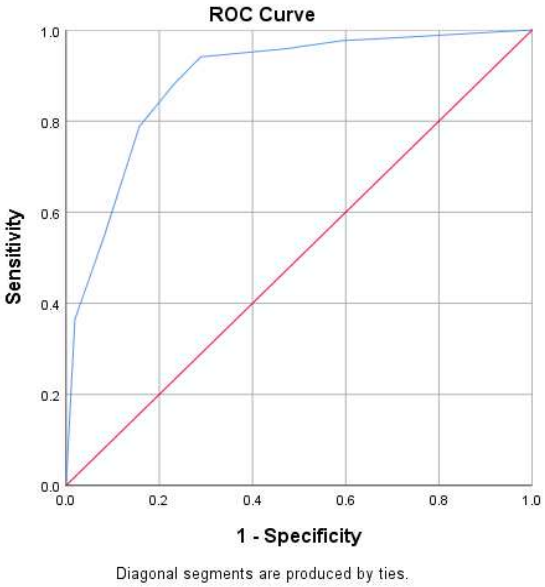
30% of movement



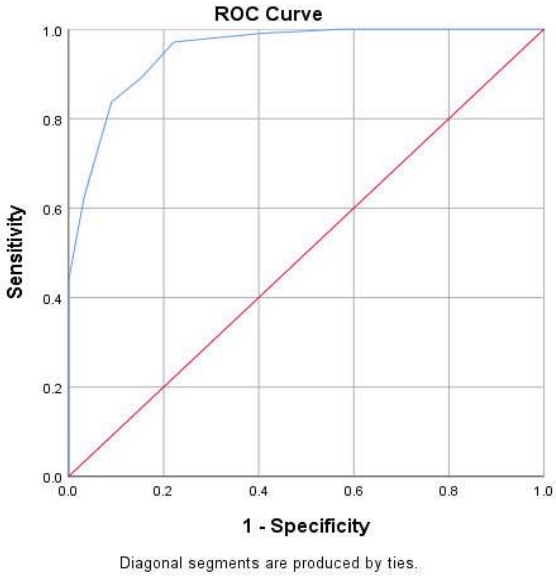
40% of movement



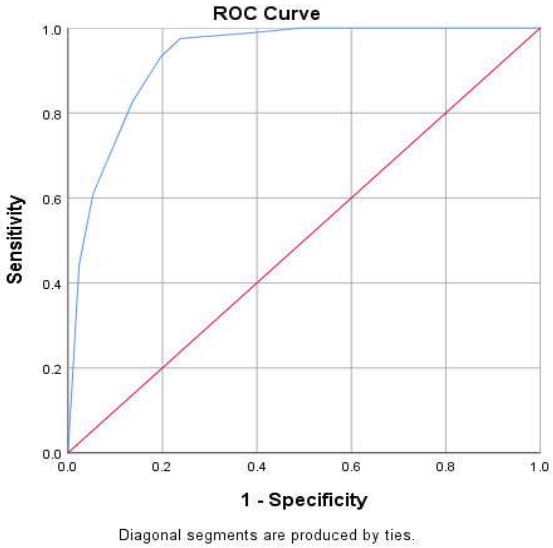
50% of movement



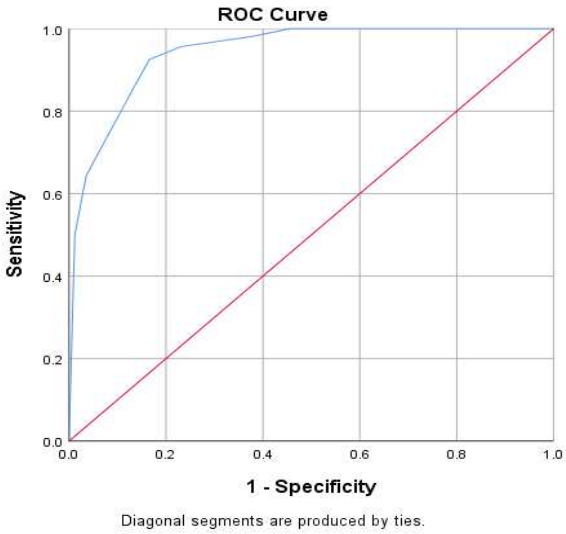
60% of movement



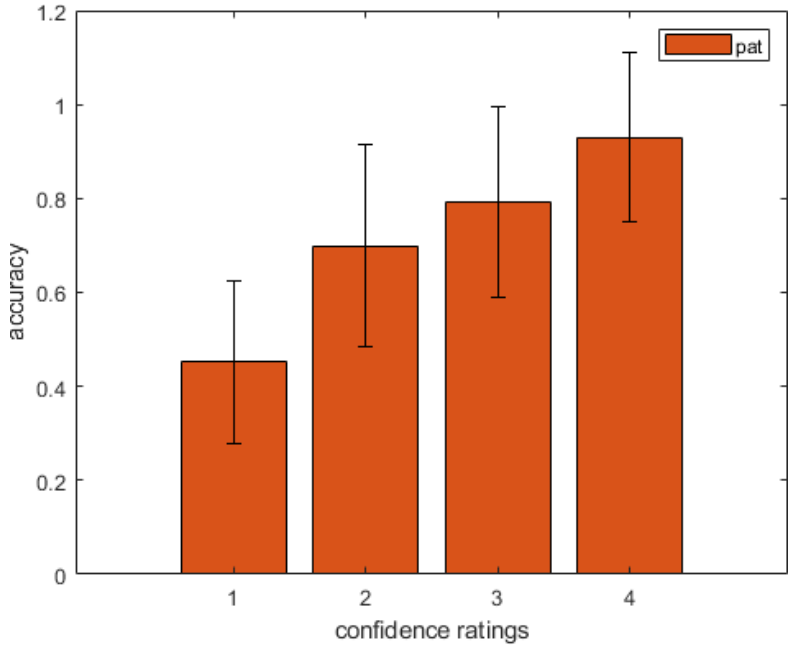
70% of movement

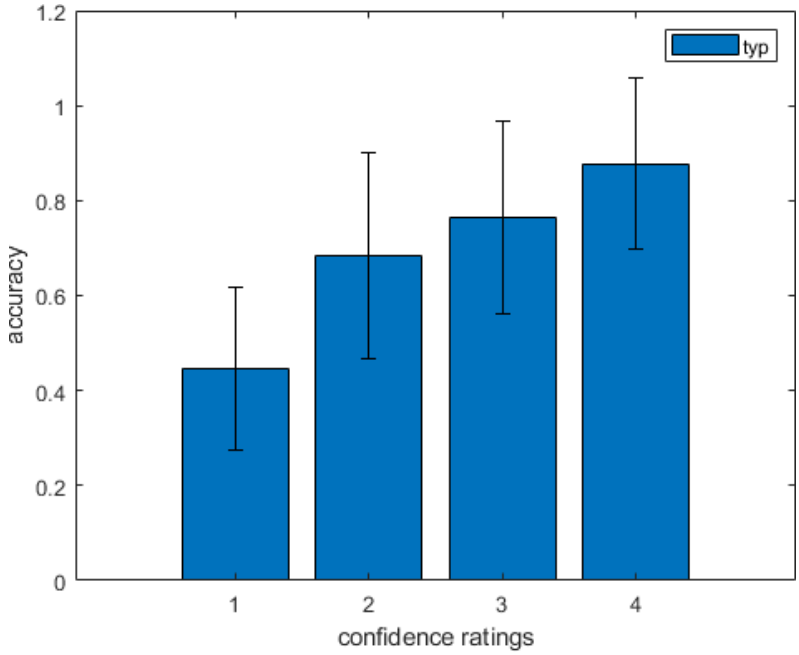


80% of movement



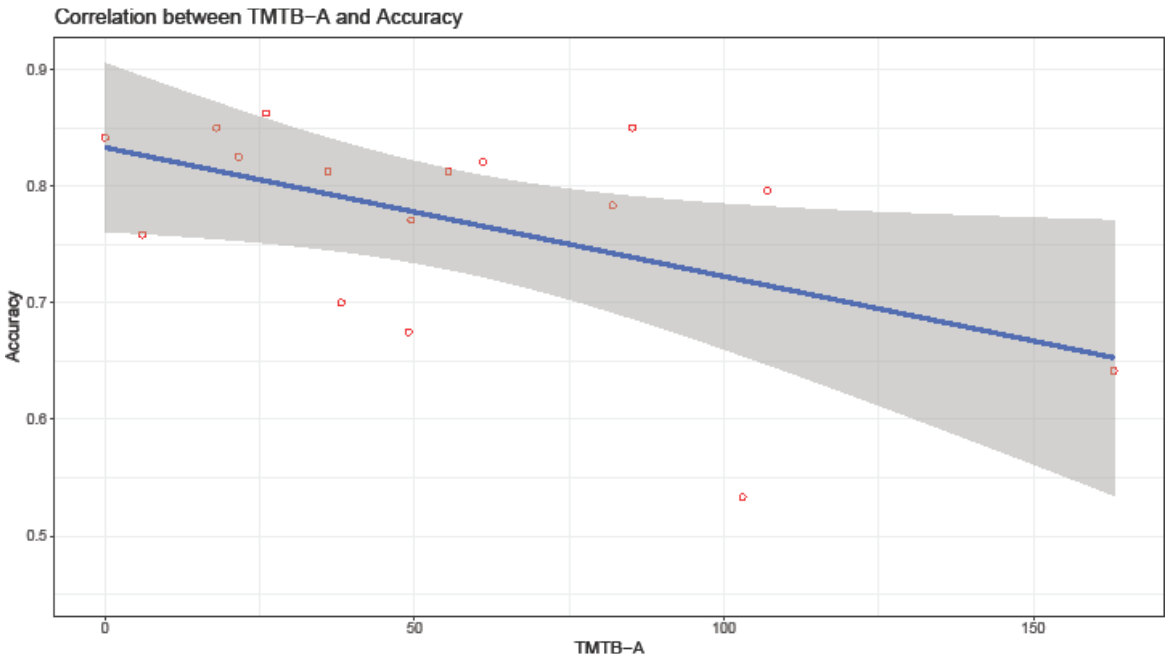
ACCURACY AS FUNCTION OF CONFIDENCE RATING





No significant correlation was found between accuracy/d-prime and demographic data, substance abuse, ongoing pharmacological therapy, Brief psychiatric rating scale (BPRS), Brief Negative Symptom Scale (BNSS), Calgary Depression Scale, The Positive and Negative Syndrome Scale (PANSS), The specific levels of functioning (SLOF), The Extrapyramidal Symptom Rating Scale (ESRS), The Edinburgh Handedness Questionnaire, The Neurological Evaluation Scale (NES), The CCAS/Schmahmann syndrome scale, BUSS and Perry Aggression questionnaire, TheAdult Attachment Questionnaire.

A significant reverse correlation was found with accuracy/d-prime was found between TMT B ($p<0.01$) and TMT B-A ($p<0.05$)



		TMTA	TMTB	TMTB_A	ACC_TOT	d_prime_tot
TMTA	Pearson correlation	1	,142	-,061	-,259	-,241
	Sign. (two-tailed)		,586	,817	,334	,368
	N	17	17	17	16	16
TMTB	Pearson correlation	,142	1	,960**	-,670**	-,718**
	Sign. (two-tailed)	,586		,000	,004	,002
	N	17	17	17	16	16
TMTB_A	Pearson correlation	-,061	,960**	1	-,525*	-,578*
	Sign. (two-tailed)	,817	,000		,037	,019
	N	17	17	17	16	16
ACC_TOT	Pearson correlation	-,259	-,670**	-,525*	1	,992**
	Sign. (two-tailed)	,334	,004	,037		,000
	N	16	16	16	17	17
d_prime_tot	Pearson correlation	-,241	-,718**	-,578*	,992**	1
	Sign. (a due code)	,368	,002	,019	,000	
	N	16	16	16	17	17

** The correlation is significant at the 0.01 (two-tailed) level.

*The correlation is significant at the 0.05 (two-tailed) level.

Our results point out that patients have greater difficulty than controls in interpreting the behavior of others, especially when presented with fragmented or partial information. At At 10% and 20% of movement duration, patients with psychotic disorders performed at chance, when in healthy controls are able to discriminate object size from the observation of grasping movements already at 10% of movement duration[204]. These data are in accordance with the known problems of social competence. The absence of correlation with the pharmacological load and the psychopathological picture also confirms what has been clinically observed: the social deficits in fact appear poorly responsive to standard treatments and persist over time despite symptomatic remission. On the other hand, the correlation between accuracy and the cognitive abilities investigated with the TMT should be highlighted

This tool is used to study visual attention and task switching, furthermore it can provide information about visual search speed, scanning, processing speed, mental

flexibility, as well as executive functioning. Indeed, these functions appear necessary in the proposed action observation task.

It would be interesting to evaluate possible changes in action observation scores following cognitive remedy training, evaluating the impact also on the real social difficulties experienced by patients. In our study, in fact, no correlations emerged between social functioning and the accuracy of the action observation task. However, the indicators we have used for social functioning can be considered highly non-specific (employment status, number of friends) and the sample of subjects examined remains extremely limited.

Another fundamental point that emerged from our research is that, in the same way as healthy controls, patients have a good awareness of their performance, as evidenced by the correlation between accuracy and confidence ratings.

This element, if translated into clinical detail, could be useful to encourage the patient's motivation for treatment. Given the possibility of little insight into other areas affected by the pathology, the possibility of working with the patient to improve his perceptive skills is an interesting element of connection.

A limitation of our study is that sample size and age of participants is not comparable between groups. The collected data therefore need to be expanded to confirm the validity of the findings.

A further point that needs to be deepened is the correspondence with cognitive alterations. The test battery used was mainly focused on the positive and negative psychopathological aspects and on motor and cerebellar neurological aspects. While these have not so far shown correlation with accuracy in the action observation task, the data collected by the TMT has proved more interesting. The cognitive component of our assessment was however limited to TMT while given the preliminary results, the possibility of evaluating the correlation with different cognitive assessment tools appears very promising.

Finally, it remains to be ascertained whether the fact that patients are less accurate in the proposed task is a specific element or a more generalizable fact. Indeed the study is based upon an action observation task, aimed at assessing the ability to discriminate object size over time, and the main results are that patients are less able

than controls in discriminating it from the observation of grasping movements. This is an interesting finding, but it is still only inferential that the kinematics of movement are per se valid to specifically understand the underlying “intention”.

CONCLUSIONS

It is complex for me to conclude this work for both the themes dealt with and the human and personal meaning that the end of this work entails. From the point of view of the contents, it is the complexity of concluding an ongoing discourse, made up of different languages, those of phenomenology and of cognitive neuroscience, in dialogue to try to build a common knowledge. From a personal point of view, writing these conclusions marks the culmination of my university career that will end with this doctorate. A path that has seen me grow and transform, just as knowledge itself , which is living and human matter, transforms itself.

The conclusions are therefore written with words that are not mine, but of which I make myself the bearer because they are words of openness, so that the foundations are built for a more human knowledge, aimed at returning “to the things themselves”.

“If one begins by thinking of cognitive science as it was first formulated in opposition to behaviorism, in terms of computational analysis and information processing, it is difficult to see how phenomenology might participate in the “cognitive revolution.” On this formulation, the scientific study of cognition is a study of how the sub-personal, nonphenomenological mind manipulates discrete symbols according to a set of syntactical procedures, and how this might be cashed out in neurological terms. This, however, is no longer the current view of cognitive science. Faced with a variety of problems implicit in this view, the cognitive revolution took a different turn in the late 1980s. This corresponded to a new emphasis on neuroscience, and connectionism, which challenged the prevailing computational orthodoxy by introducing an approach based on nonlinear dynamical systems. With this formulation there was a shift away from an emphasis on reductionism to an emphasis on the notions of emergence and self-organization. The question was how higher-level personal structures emerged from lower level sub-personal, self-organizing processes.

The current situation in the cognitive sciences is characterized by a growing interest in the ecological-embodied-enactive approach. This approach takes up the connectionist emphasis on dynamical mechanisms and self-organizing emergence,

but it further insists that cognition is best characterized as belonging to embodied, situated agents—agents who are in-the-world. On this understanding of the cognitive sciences, just as neuroscientists and neuropsychologists work together with researchers in artificial intelligence and robotics, so also phenomenologists and philosophers of mind work together with the empirical scientists in order to develop a fuller and more holistic view of cognitive life—a life that is not just the life of the mind, but of an embodied, ecologically situated, and enactive agent. This recent redefinition of the cognitive sciences, if it is to include a place for phenomenology, requires that we also conceive of phenomenology in a different way. Or at least we need to see that there is a section of the phenomenological map that can be redrawn along lines that reach across the theoretical divides that separate phenomenology from the sciences. One way to think of this is to think of naturalizing phenomenology. For many phenomenologists this will seem self-contradictory, an antilogy. Phenomenology just is, by definition, non-naturalistic. For many others, the difficult question is how it might be accomplished without it losing the specificity of phenomenology. Everything, however, depends on what one means by naturalization. There is no question of considering here all possible proposals in this regard. But consider two among many. 1. The subjective data developed in phenomenology should be made objective, and thus amenable to scientific analysis. This suggestion is similar to Nagel's idea of an "objective phenomenology" that would allow for a level of abstraction from the particularism of individual reports, or to Dennett's idea of a "heterophenomenology" that would treat phenomenological reports as part of the objective data of science. 2. Naturalization in the minimal sense means "not being committed to a dualistic kind of ontology". This includes the idea that phenomenology has to be explanatory and not just descriptive. Phenomenology would help to resolve the "explanatory gap," and contribute to an explanation of how brain and bodily processes can give rise to phenomenological properties that are not non-physical properties. The first proposal is problematic in several ways. It equates phenomenology with folk psychology, and understands phenomenological data to mean anything that a subject happens to report. In effect, because there is no concern about phenomenological method, this kind of approach, whether it follows a reductionist strategy or pursues the intentional stance, fails to take phenomenology seriously. Naturalization means, in this case, getting rid of phenomenology. Furthermore, if in such naturalizing strategies one does not employ

phenomenological method, the very objectivity that is sought will be seriously compromised. For example, in translating a subject's first-person experience into third-person data, it would not do for the scientist to rely on her own subjective experience as an interpretational guide, since this would simply lead to a pollution of the subject's first-person data with the scientist's first-person data. A scientist would have to resort to objectively, formalized meanings established within the framework of behavioral science in order properly to interpret the subject's reports. In that case, however, one needs to ask where these formalized meanings (generalizations and abstractions) originate. One comes quickly to the realization that at some point, a controlled form of phenomenological experience is required to justify the formalized meanings used as interpretational guides. In effect, an objective interpretational framework depends upon a reflective, methodically guided phenomenological analysis, without which the procedure may simply impose the results of previous uncontrolled and anonymous phenomenological exercise. The second proposal, requires a phenomenological practice guided by method. What allows Husserlian phenomenology to escape from a naturalistic framework (the natural attitude) is a change of attitude achieved through a methodical practice (the phenomenological reduction). To move in the opposite direction, that is, to bring phenomenology to bear on the naturalistic enterprise of the cognitive sciences, involves another change of attitude. This does not mean abandoning phenomenological methods, but taking what we learn about first-person experience within the phenomenological attitude and using it in the context of naturalistic explanation. Although Husserl defined phenomenology as a non-naturalistic discipline, the idea that the results of his transcendental science might inform the natural sciences is not inconsistent with his own intent. He suggested, quite clearly, that "every analysis or theory of transcendental phenomenology—including the theory of transcendental constitution of an Objective world—can be produced in the natural realm, when we give up the transcendental attitude'[205]

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ACKNOWLEDGEMTES

I thank Professor Luigi Grassi for the intellectual freedom he has granted me and for the great support he has given me during the years of my specialization in psychiatry and my PhD. The wisdom and humanity with which he leads the Ferrara school of psychiatry were gifts that I hope to have put to good use.

I thank Dr. Martino Belvederi Murri for the continuous contribution of friendly advice, comparisons and healthy criticism without which my PhD course would have certainly been poorer.

I thank Professor Giulia Nanni and Dr. Rosangela Caruso for making me feel the psychiatry institute like a second home, familiar as well as always culturally stimulating.

I sincerely thank Dr. Marta Basaldella, Dr. Eleonora Curtarello, Dr. Marta Gancitano, Dr. Benedetta Gullotta and Dr. Marco Marella, Dr. Gabriele Simonelli and dr. Luigi Zerbinati for the great help they gave me in carrying out these researches. Without their contribution this work would certainly not have been the same, and the path to carry it out would certainly have been even more difficult.

Finally, I thank Simona for the joy and color with which she has filled my life in recent years, enduring the grumbling that notoriously accompanies my work at the desk.