Disturbances of multisensory processing in schizophrenia spectrum disorders: a behavioural and neurophysiological account

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A thesis submitted for the degree of Doctor of Philosophy (PhD)

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January 2021

Declaration

I declare that this thesis, ‘Disturbances of multisensory processing in schizophrenia spectrum disorders: a behavioural and neurophysiological account’, represents my own work, except where otherwise stated. None of the work referred to in this thesis has been accepted in any previous application for a higher degree at this or any other University or institution. All quotations have been distinguished by quotation marks and the sources of information specifically acknowledged.

Submitted by Francesca Fotia

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Chapter Three: Ferri, F., Venskus, A., Fotia, F., Cooke, J., & Romei, V. (2018). Higher proneness to multisensory illusions is driven by reduced temporal sensitivity in people with high schizotypal traits. *Consciousness and cognition*, 65, 263–270. doi: 10.1016/j.concog.2018.09.006

Chapter Four: Fotia, F., Cooke, J., Van Dam, L., Ferri, F., & Romei, V. (2021). The temporal sensitivity to the tactile-induced double flash illusion mediates the impact of beta oscillations on schizotypal personality traits. *Consciousness and cognition*, *91*, 103121. https://doi.org/10.1016/j.concog.2021.103121

Chapter Five: Costantini, M., Salone, A., Martinotti, G., Fiori, F., Fotia, F., Di Giannantonio, M., & Ferri, F. (2020). Body representations and basic symptoms in schizophrenia. *Schizophrenia research*, 222, 267–273. doi:10.1016/j.schres.2020.05.038

For any work that has been co-published (or prepared for publication), my personal contribution is outlined below:

Chapter Three: Writing, reviewing, and editing.

Chapter Four: Data collection and data curation, data analysis, writing, reviewing, and editing.

Chapter Five: Data collection, data analysis and writing.

Chapter Six: Data collection and data curation, data analysis, conceptualization, writing and editing.

Acknowledgements

My first thank you goes to the Department of Psychology, for having allowed me to study here and for funding my project. This thesis would have not been possible had it not been for the support and guidance I found here.

My deepest gratitude goes to my first and second supervisors, Dr Loes Van Dam and Dr Francesca Ferri. It has been an enriching experience for me to work under their guidance. Dr Van Dam, for her exemplary guidance, careful monitoring, and for being the key person in teaching me the learning attitude required for cutting-edge research. Also, I shall thank her for having helped me improve the quality and the composition of my thesis. Dr Ferri, for offering brilliant support and constant guidance during my PhD, for awakening my enthusiasm for carrying out this study and for sharing ideas that has expanded the depth of my thinking. Also, for welcoming me at the University of Chieti during my research period abroad, along with my second co-supervisor Dr Marcello Costantini, who I sincerely thank for the precious cooperation and for his valuable time in assisting in my work and teaching me new research skills. I owe a very special thanks to Prof. Vincenzo Romei for being the driving force behind the study presented in Chapter Four, for his assistance and suggestion throughout the years, and for his invaluable help with the EEG analyses.

I would like to give a heartfelt thanks to the staff in the outpatient clinic in Chieti mental health department (IT) and to all the patients who agreed to take part in the research presented in Chapter Five, sharing their valuable time.

I owe a deep sense of gratitude to Prof. Alberto Zuliani and Dr Marco Esposito, for offering me the first research opportunities in the inspiring environment of the NPO 'Una breccia nel muro'.

I also must thank my great colleagues Jason Cooke, Tania Garcia Vite, Achilleas Pavlou, Alistair Thorpe, Agnese Venksus, Qian Sun, Itsvàn Gyimes, Giulio di Cosmo, Brunella Donno, Matteo Frisoni, Mario Paci and Francesca Bianchi. A special thanks goes to my colleague and friend Astrid Priscilla Martinez Cedillo, for her indispensable support and for the joyful time we have spent together.

My heartfelt thanks go to Denise and Grandad, for having welcomed me in their family, for their loving support and for all the great times we have shared.

I would like to express my eternal gratitude and love towards my parents and my sister, whose value to me only grows with time. Thank you for supporting and encouraging me throughout the entire period of my PhD and for being always there for me no matter where I am. Thank you for being an example of honesty and wisdom who I shall take inspiration from.

Above all, my deepest gratitude goes to my fiancé John. Thank you for being the closest person to me during these years, for your loving support and encouragement, and for all the precious and valuable time we share. Also, thank you for having unconcealed philosophically powerful thoughts that I had not considered before, and for having encouraged me to look into intriguing research directions.

Abstract

Self-disorders have long been considered as a central nucleus of the schizophrenic experience. It has been suggested that such self-disturbances might be associated with abnormal multisensory integration and abnormal bodily self-awareness. The primary goal of this thesis was to explore the behavioural and neurophysiological markers of self-disturbances in schizophrenia and in high schizotypy (i.e. a sub-clinical trait linked to schizophrenia). Specifically, we aimed at (i) investigating the temporal acuity in individuals with low and high schizotypy (ii) measuring aspects of the neural responses to multisensory integration in low and high schizotypes (iii) exploring how body representation abnormalities in both schizophrenic patients and high schizotypes affect basic processes of self-perception. In line with previous research showing a reduced multisensory acuity in schizophrenia, results from Chapter Three revealed a significant relationship between the temporal window within which two stimuli are integrated (i.e. TWI), and schizotypal personality traits; namely, higher schizotypal traits are associated with wider TWIs. In Chapter Four, we provided evidence of a selective relationship between the TWI for visuo-tactile stimuli and the individual beta frequency (IBF), i.e, slower IBFs accounts for larger TWIs, and between the TWI and schizotypy, i.e. wider TWIs are linked to higher schizotypal traits. In Chapter Five, we have demonstrated that patients with schizophrenia possess more malleable body representations and that these abnormalities are linked to early markers of vulnerability to the disorder (i.e. basic symptoms). Finally, findings from Chapter Six revealed that the abnormalities in bodily self-awareness observed in schizophrenia might extend to schizotypy, suggesting that such abnormalities could represent a trait marker for schizophrenia proneness. All in all, our results suggest that the

abnormalities in multisensory integration and bodily awareness observed in schizophrenia spectrum disorders might produce a distortion in the structure of self-experience and contribute to the emergence of the disorder.

Chapter One

1. An introduction to schizophrenia spectrum disorders

The driving motivation of this thesis has been to examine the processes by which schizophrenia spectrum disorders arise. Grounding on a vast amount of research that has conceptualised schizophrenia spectrum disorders as “disorders of the self”, I aimed to connect the newest neuroscientific evidence with both early and contemporary theories in phenomenological psychiatry. In particular, I have focused on the contribution of multisensory processes in the construction and maintenance of *bodily self-awareness*, a component of the self that appears compromised since the very early stages of the disorder (i.e., *disembodiment* of the self). As such, the studies presented in this thesis have investigated how abnormalities in multisensory temporal integration (Chapter One), the underlying patterns of neuro-oscillatory activity in the brain (Chapter Two), body ownership (Chapter Three) and body representation (Chapter Four) may underlie a more profound dis-attunement between the self and the body, which ultimately could be predictive of schizophrenia onset.

A disordered sense of self has long been considered as a core feature of schizophrenia spectrum disorders (Kraepelin, 1913; Bleuler, 1911; Jaspers, 1913; Minkowski, 1927; Sass & Parnas 2003; Gallese & Ferri, 2013; Nelson et al., 2012; Hur et al., 2014). The unconscious, tacit quality of self-awareness rests upon the sensations deriving from the perceptive processes of one’s own body interacting with the world. Interestingly, a vast amount of empirical and phenomenological evidence has shown that schizophrenia onset is characterised by the emergence of changes concerning anomalies of corporeality and self-awareness. Indeed, clinical phenomena such as *disembodiment of the self* and impairments in self-other discrimination appear to be quite common before the first psychotic episode and are maintained after the patient is diagnosed with schizophrenia (Møller & Husby, 2000; Parnas, 2000; 2003; Raballo et al., 2011). These symptoms can manifest with a sub-delusional detachment from reality, reduced recognition of the body, disintegration of multisensory inputs, diminished self-experience or feeling of being disconnected from oneself and one's action (de Haan & Fuchs, 2010; Uhlhaas et al., 2008; Nelson, 2012). Recent research has demonstrated that self-disorders in the schizophrenia spectrum are temporally stable and are highly predictive for the emergence of the disorder in high-risk populations (Nordgaard et al., 2017; Parnas et al., 2011).

However, in the past decades, diagnostic criteria have vastly neglected these aspects of the disorder. As a result, research on schizophrenia and its neural correlates have overlooked the relevance of this subjective dimension in place of an over-reliance on the so-called "operationalized" conglomerate of psychotic symptoms and signs and, more generally, on the cognitive impairments of the disorder (Parnas, 2011). Currently, a more comprehensive account of schizophrenia spectrum disorders and their shared and core features is needed. Such an account would reunite knowledge regarding the phenomenology of the schizophrenia spectrum (i.e. the subjective experience of patients) with more recent discoveries on its specific neurological and behavioural features. Most importantly, more attention needs to be given to the early premorbid and prodromal stages of the illness as an access to a moment in which the dissolution of normal functioning is being formed. This would contribute to evaluating and describing the mechanisms that become altered in the general structure of the schizophrenic experience that are responsible for the emergence of the disorder. Ultimately, this would contribute toward indicating future directions for potential causative treatment. Several contemporary authors now agree on stressing the importance of the corporeal dimension of the self (Stangellini, 2009) and of multisensory integration (Postmes et al., 2014) as fundamental expressions of the structure of subjectivity. Both of these aspects are enclosed in the concept of minimal self.

1.1 Minimal Self and Bodily Self

At the most fundamental, phenomenological level, the notion of the "self" refers to the sense of possessing a first-person perspective and of being an individual with defined physical boundaries between oneself and the environment (Blanke & Metzinger, 2009). According to Gallagher (2000), the concept of the "self" comprises several aspects of conscious experiences from low-level bodily, to high-level cognitive or narrative aspects. On this basis, Gallagher identified three levels of selfhood. First, the *pre-reflective selfhood*, also referred to as the *minimal self*, refers to a fundamental sense of existing with a direct and immediate *'mineness'* of experience (Gallagher, 2000; Sass & Parnas, 2003, 2007). The *minimal self* could be described as the most basic level of self as it is constituted by a "consciousness of oneself as an immediate subject of experience" and as "the pre-reflective point of origin for action, experience and thought" (Gallagher, 2000, p.15). Thus, this nuclear aspect of the self is localised at the level of the body (i.e. the embodied self), and it carries potential for action (i.e. *praktognosia*) (Gallese, 2003; Gallese & Sinigaglia 2010, 2011). Second, the *reflective self* assumes a more explicit awareness of the self as a subject of experience and action extended in time and in constant relationship with the outer world; at this level, the self acquires the character of invariance. Finally, the *social* or *narrative self* involves autobiographical information or an explicit idea about one's individual identity. The second and third levels of selfhood depend and are built upon the "minimal self" (Nelson et al., 2012). While the minimal self is a self-devoid of temporal extension (it is the 'I' who is experiencing here and now), the reflective self and the narrative-self involve a sense of continuity across time.

Interestingly, many of the early studies on schizophrenia proposed that disturbances in most basic forms of selfhood are constitutive of the schizophrenia spectrum conditions (i.e."schizoidia" and "latent schizophrenia") (Bleuler, 1911; 1911; Kraepelin 1919). Recently, this view has been reinforced and expanded by empirical studies providing evidence for abnormal sense of minimal self in schizophrenia (e.g., Ferri et al., 2012; Maeda et al., 2012; Sass, 2001; Sass & Parnas, 2003). In particular, research has suggested that disturbances in the minimal self may cause and maintain "surface-level" symptoms often observed in schizophrenia spectrum disorders (Maj, 2012). Indeed, although the more elaborate components of the self, such as the "reflective self" and the "narrative self" are also affected in schizophrenia spectrum disorders, it seems that the core symptomatology relates to the very basic experience of being a self - i.e. the implicit sense of coherence, unity and immersion in the world- thus, the "minimal self" (Sass & Parnas, 2003; Maj, 2012).

The concept of the minimal self has been widely discussed in cognitive neuroscience (Metzinger & Gallese, 2003), developmental psychology (Rochat, 2004), phenomenological psychiatry (Nelson et al., 2019; Parnas et al., 2012) and philosophy (Gallagher, 2000; Gallagher & Zahavi, 2012). However, the finer details of the minimal self have yet to be fully empirically demonstrated. For instance, it is not clear what kind of experiences would contribute toward shaping this implicit sense of being oneself or what the brain's role is in mediating the interaction between the minimal self and the stimuli from the outside world. Research on this topic has emphasized the role of the human body for cognition (Varela, 1994; Gallese & Sinigaglia, 2011) and has stressed the necessity of the embodiment of the self (Cremolacce et al., 2007). According to Metzinger (2003, 2004, 2005), minimal selfhood develops as a result of pre-reflective self-modelling. This account assumes that the brain is a representational system which interprets the environment to construct and simulate a model of the world that is phenomenologically centered onto the self (Metzinger & Gallese 2003). This model would reduce the ambiguity that comes from the external world. For this system model to be successful, the self needs to be constructed in the bodily context (Metzinger, 2005). Indeed, the body *is* the context through which we feel, think, perceive and take action upon the world (Legrand, 2006; Friston, 2010; Farmer & Tsakiris, 2012). Thus, the minimal self is strictly connected to embodiment, as it represents a tacit "in the background" sense of one's first-person presence and action in the environment.

With this in mind, when we talk about the minimal self, we need to stress its fundamental bodily aspect. The body is a minimal "threshold" component of selfhood, which does not need an explicit conceptualisation to affect the agent's cognition (de Haan & Fuchs 2010). The body represents the one and only interface with the world and is characterised by its potential for movement and action (Gallese & Ferri, 2013). Moreover, the body integrates multisensory information, acts as the source of internally generated inputs and is essential for interacting with the environment (Friston et al., 2010). This relationship can be clearly observed in everyday interactions with our environment. Take, for example, the act of picking up an object: the information about the object arises from multiple senses, i.e., by looking at the object (visual) and touching/grasping (tactile) it at the same time, i.e., we need to guide our body/hand to reach the object. These various processes provide us with information about both the world and our own bodies. This implicit self-awareness is constituted by the continuous integration and organization of sensory and motor signals, which are corporeal and mapped by various and specific brain circuits. In other words, the minimal self emerges from the dynamic interrelationship between brain, body and environment and heavily relies upon combining information across the senses.

Bodily self-awareness is maintained through an interaction of multisensory experiences and a combination of top-down and bottom-up processes. As such, multisensory integration and body representation share a common currency, which is to perceive and effectively interact with the environment and to provide an online representation of the body in the world (Damasio, 1999). Evidence has suggested that our sense of embodiment is highly influenced by the processes involved in multisensory integration (Hohwy, 2010; Tsakiris, 2010). Indeed, as we perceive our environment and ourselves with all our sensory systems, multisensory inputs need to be combined to produce the basis of bodily self-consciousness (Haggard et al., 2003, Tsakiris, 2010). Unsurprisingly, disturbances in multisensory integration and in the bodily-self have been detected in schizophrenia spectrum disorders (de Gelder et al., 2003; Stevenson et al., 2016; Ferri et al., 2018; Uhlhaas et al., 2008), resulting in the weakening of the basic sense of self - i.e. disembodiment of the self – often observed in patients (Fuchs, 2005).

The following sections aim to provide the reader with an overview of the past and current theoretical and empirical literature that has shaped the current definition of schizophrenia as a disorder of the self.

1.2. Schizophrenia as a disorder of the self

Nosographic classification and phenomenological accounts of the disorder

For a long time, studies on schizophrenia have been dominated by cognitivism. Indeed, much of the research has focused on the study of the disruption of high-level cognitive structures, such as language, working memory, theory of mind (for a review, see Brüne, 2005). In the clinical field, two and three-dimensional descriptions of schizophrenia have been dominating the field since the late 1980s, particularly with the American Psychiatric Association's Diagnostic and Statistical Manual III (DSM III) and its newer edition (DSM-5) (2013). However, such an approach has neglected a vast corpus of knowledge that has been left by the fields of earlier approaches to psychopathology and phenomenological psychiatry. Early authors in these fields emphasised the role of the self and its pre-reflective relationship with the external world (Kraepelin, 1896; Bleuler, 1911; Minkowski, 1927). The specificity of the disorder was thought of as anchored to its "fundamental" clinical core, which was constitutive of the spectrum conditions (e.g. "schizotypes", "latent schizophrenia"). The symptomatology observed in "schizophrenics" was considered as a "state" or "accessory" phenomena and the diagnostic identification of schizophrenia was linked to a Gestalt recognition of these single characteristics, their qualities, developmental and temporal aspects. As such, the specific signs and symptoms were seen as an expression of a fundamental structural change of the patient's subjectivity (Parnas, 2011).

The German psychiatrist Emil Kraepelin (1856-1926) developed a classification system for mental illness, which has been influential for many years. By focusing on the search for homogenous groups of patients with a common aetiology and symptoms, he proposed a distinction between chronic and progressing "*dementia praecox*" which was thought to be caused by organic changes in the brain, and the remitting "*manic depressive disorder*". Kraeplin (1912) recognised that the emergence of schizophrenia - which he called dementia praecox - was characterised by fundamental changes in the self which manifested in the individual as a loss of the inner unity of consciousness and of will: "*the chaos in the mind is like an orchestra without a conductor*" (Kraeplin, 1912). Despite providing important insights into some of the fundamental characteristics of the illness, Kraepelin's view was profoundly influenced by nineteenth-century positivism: the idea of psychotic madness as a chronic and irreversible disease (Kraeplin, 1913).

This paradigm was broken by Eugen Bleuler (1857-1939) which, in 1908, translated the notion of *dementia praecox* into that of schizophrenia (from the Greek *split mind*) to indicate the patient's splitting of psychic functioning as a prominent symptom (Bleuler as in Cutting and Shepherd, 1987). Bleuler observed that the disorder always involved a profound suffering/affliction of the self (*Spaltung*), which manifested with incoherence of association and affect. These symptoms, which he called "*basic symptoms"*, were considered as specific to the core of the schizophrenic spectrum. On the other hand, non-specific state phenomena indexing a psychotic phenomenon - i.e. hallucinations, delusions, catatonic features - which he classified as *"accessory symptoms"* - were relegated to a subordinate status and considered less relevant for the diagnosis (since they could be present or absent). According to Bleuler, the fundamental or basic symptoms were mainly associated with anomalies of self-experiences and concerned progressive changes in the affective, expressional, behavioural domains. The inability to be normatively attuned with the world, what

Bleuler called schizophrenic autism, constituted the basic clinical essence of schizophrenia.

This dimension became even more explicit in the writings of Eugène Minkowski (1885-1972), who developed and expanded the Bleulerian intuition of autism. According to Minkowski, autism is not one of the symptoms of schizophrenia, but it is rather a peculiar mode of existence which affects intentionality (e.g., loss of meaning), the self and the dimension of intersubjectivity. Thus, he believed that schizophrenic autism represented a global structuring of a way of being which lay at a more basic experiential and existential alteration of the schizophrenic spectrum. This mode of existence was characterised by an incapability to attune to the "*common sense*" and through a progressive "*lack* of *vital contact with reality*" or what Minkowski called "*trouble générateur*", viewed as an incapacity to "*resonate with the world*" and to establish meaningful bonds with other individuals (Urfer, 2001). Such alteration would then transpire into single characteristic symptoms, shaping them and keeping them interconnected through time. Thus, Minkowski believed that a true understanding of the disorder could only be achieved by adopting a background theory of the nature of mental life, a position that he shared with Karl Jaspers. This background theory, as we will see, is represented by phenomenology.

Karl Jaspers (1883-1969) is generally acknowledged as the first major psychiatrist to bring scientific foundations to psychopathology. Moreover, he can be considered as the initiator of the phenomenological movement in psychiatry, and his contribution to the psychopathology of schizophrenia continues to be extremely relevant. Jaspers was interested in first-person experience and in what he called the "patient's attitude toward his illness" - or the active role that the individual has in understanding and responding to their individual experiences of illness - an idea that was later adopted by person-centred psychopathology (Stanghellini et al., 2013). His conceptualisation of ‘personalization’ (i.e. the I-quality of self-awareness) corresponds to what is now referred to as ‘subjective experience’: “*self-awareness is present in every psychic event…every psychic manifestation, whether perception, bodily sensation, memory, idea, thought or feeling carries this particular aspect of ‘being mine’, of having an ‘I’ quality, of ‘personally belonging’ of it being one’s own doing. We have termed this ‘personalization’” (Jaspers, 1913: 121*). In other words, the subjective experience of feelings, thoughts, memories and perceptions, including the perception of the body, possess these the quality of being mine.

In his *General Psychopathology* (1913), Jaspers observed how the alterations in self-experience observed in schizophrenia seemed to challenge Descartes’ well-known notion of the *cogito*, that the nature of thought automatically provided evidence that the self is always in possession of its own experiences. Jaspers hypothesised that at the basis of the onset of schizophrenia lies a fundamental alteration of experience, which he named “delusional mood” or “delusional atmosphere”. These changes in experience were characterised by the alteration of four experiential modalities: the awareness of my own existence and action; the awareness of unity; the awareness of identity (temporal-diachronic identity), and the awareness of being distinct from the outer world (me/not me demarcation) (Gallese & Ferri., 2013). The schizophrenic would react to these confusing experiences with what Jaspers called “perplexity”, a state in which the patient’s level of activity progressively deteriorates, and he/she gradually becomes detached from external reality. Then, through a process of self-interpretation, the schizophrenic would try to “work through” these experiences and *“laboriously develops a delusional system out of his delusional experiences*” (Jaspers, 1913, p.416). The different outcomes of acute schizophrenia would derive from the individual's "position taking" in response to these aberrations, as a top-down effort to make sense of the subjective changes, which occurs during the initial pre-delusional phases of schizophrenia (Stanghellini et al., 2013).

Moreover, Jaspers described more specific schizophrenic experiences which are very bodily-orientated, such as "*abnormal body or organ sensation*" (Jaspers, 1913, 447). On this basis, Kurt Schneider (1887-1967) described the loss of "ego-boundaries" and the feeling of being under the influence of an external agent, as characteristics of self-disorders in the schizophrenic experience. As he noted: *"Certain disturbances of self-experience show the greatest degree of schizophrenic specificity. Here we refer to those disturbances of first-personal-givenness (Ich-heit) or mineness (Meinhaftigkeit) which consist of one's own acts and states not being experienced as one's own"* (Schneider, 1950, p58). Schneider's primary focus was to teach clinicians how to reliably diagnose schizophrenia and, in contrast with Kraepelin, Bleuler and Minkowski, he defined hallucinations and delusions as the "first-rank symptoms" of schizophrenia. The Schneiderian viewpoint is integrated into the series of current major operational diagnostic systems: the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Statistical Classification of Diseases (ICD).

In the early nosographic classification of schizophrenia, as the International Classification for Diseases (ICD-8 and -9, 1893-1922), the role of disturbances of "personalities" and loss of "self-direction" was stressed. Here, it has to be noted that the term "personality" has to be interpreted in line within the customs of nineteenth-century psychiatry, which corresponds to what today we call "self" and "subjectivity". With the publication of the Third Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III, 1980), this emphasis on the self was almost completely removed, in place of a more behaviouristic approach which highlighted the measurable and observable characteristics of the disorder. In the DSM-IV and in the ICD-10, the notion of the self is not mentioned at all among the diagnostic criteria for schizophrenia. Indeed, much attention has been given to the apparent heterogeneity of schizophrenic symptoms, while less emphasis on the unifying factors that are shared by the patients. Remaining at the level of nosographic-descriptive diagnosis, the various clinical manifestations of schizophrenia have been distinguished and categorized in the DSM-IV TR into five types of schizophrenia: the disorganised type; the paranoid type; the catatonic type; the undifferentiated type; the residual type. In the latest edition of the DSM-V (American Psychiatric Association, 2013), schizophrenia disorders are classified as “schizophrenia spectrum and other psychotic disorders”, favouring a partially dimensional approach. The five subtypes of the DSM-IV have been abandoned again in DSM-V because of their "limited diagnostic stability, poor reliability and poor scientific validity" (American Psychiatric Association, 2013). Instead, symptomatology has been subdivided into three main clusters: positive symptoms, negative symptoms and disorganised symptoms. Positive symptoms include hallucinations, abnormal perceptual experiences, delusions, false beliefs and disorganised behaviour. Delusions often fall into different categories: paranoid delusions, delusions of reference or control and delusions of grandeur. Negative symptoms refer to apathy, anhedonia, social avoidance and reduced affect. The disorganised symptoms usually include confused or abnormal speech, behaviour and emotion (APA, 2013).

Despite giving an accurate and reliable definition of the schizophrenic symptomatology, the DSM-V fails to describe what connects and underlies the various symptoms (Maj, 2012). Indeed, despite schizophrenia having been intensively studied for over a hundred years, an account that includes a satisfactory aetiological explanation is still lacking (Parnas, 2012). Current research needs to indicate core, basic features which may underlie the whole diversity of symptoms. Such features are likely to be rooted in the most basic abnormalities of consciousness - an alteration of the “minimal self” or ipseity - that underlie and also precede the largely heterogeneous signs and symptoms observed in the schizophrenic spectrum.

According to Sass and Parnas, the core of the disorder is represented by the fact that the bodily self loses its automaticity and transparency (Parnas & Sass, 2010). To explain this, they refer to two fundamental and complementary components: diminished affection and hyperreflexivity. Both the notions of hyperreflexivity and diminished self-affection are important aspects of the intentional activity of awareness. Diminished self-affection refers to a reduced sense of existing as a vital and self-coinciding source of awareness and action, meaning that the sense of immersion in the world has lost their relevance and their vitality. These feelings are often a consequence of a more general and pervasive struggle in grasping otherwise familiar and taken-for-granted significations present in the world. In this context, the body loses its role as an intermediary for meaningful interaction with the world. This loss of self-presence occurs not only on the individual but also on the intersubjective level, typically resulting in a withdrawal from the social world. This aspect is particularly predominant in the stages preceding the onset of schizophrenia, in which the patient’s sense of agency and ownership is diminished to the point that their lived experience becomes highly passive, automated and alienated.

The concept of hyperreflexivity refers to the fact that something, which was normally tacit, becomes focal and explicit and, as a consequence, can become an object of concern. In other words, aspects of the self, which are usually tacit or implicit, are objectivised and experienced as external objects of consciousness. For instance, some patients report becoming deeply aware of the act of breathing or of different sensations while walking (Nelson & Sass., 2017). Thus, in hyperreflexivity, there is a loss of the transparency of self-consciousness. Indeed, patients with schizophrenia perceive implicit properties of their experience as explicit and clear, as if they were external objects or events. This tendency is predominantly non-volitional but rather "operative" and occurs automatically. From an experiential point of view, hyperreflexivity can manifest as intensified experience, such as prominence of proximal over distal aspects of stimuli (see, e.g., Sass, 1994, re "phantom concreteness"), or as a focal awareness of kinesthetic bodily sensations (Sass & Parnas, 2003). Some level of introspective and metacognitive types of hyperreflexivity are visible at the very onset of the disorder, particularly in the domain of bodily experiences (Alvarez et al., 2016; Parnas & Handest, 2003). The body is often experienced as an object lived in the third person, with the patient often reporting feeling like they do not own their own body anymore or like they can observe their action as a witness (Parnas & Handest, 2003). In this respect, hyperreflexivity may progressively lead to a loss of the global and unitary character of self-consciousness, which characterises minimal selfhood. As the disorder progresses, the body is not anymore experienced as "taken for granted" or tacitly given in the first-person perspective, but it rather loses its "transparent quality, its tacit experience-based function, turning into an object of observation, of thinking, of concern, and thus ends up being the "thematic" of an impediment or a problem" (Irrazàval, 2005).

At the present time, experimental psychology and neuroscience could offer a crucial contribution toward the investigation of subjective experience in schizophrenia spectrum disorders. However, the various theories and intuitions from the past have only been marginally investigated with the newest empirical methods. This represents a lacuna in the current research of psychopathology. In particular, fields like embodied cognition, phenomenologically oriented neuroscience and phenomenological psychiatry have made it possible to investigate concepts such as selfhood and intersubjectivity with neuroscientific methods and to describe them to a sub-personal level. Indeed, recent literature in this field has put an emphasis on self-disorders as an important focus that may allow the early detection and prevention of psychosis. Ultimately, this could also shed important lights on the neural processes involved in the emergence and preservation of self-disorders.

1.3 Schizophrenia related disorders

The development of schizophrenia spectrum disorders is complex and multifaceted. In general, prior to the diagnosis of schizophrenia, at-risk individuals progressively experience subtle changes in self-experience, behavioural and cognitive impairments (Klosterkötter et al., 2001). Thus, disorders of self-experience are being rediscovered as a crucial factor in the early detection of traits characterizing the schizophrenia spectrum conditions (Nelson et al., 2012; Henrisken & Nordgaard, 2016). As reported by most patients, self-disorders, such as long-time persisting feelings of identity void and self-transformation, seem to emerge in childhood or early adolescence and characterise an intrinsic feature of one’s mode of experiencing the world and the self (Koren et al., 2013). These symptoms are not experienced as isolated ruptures of everyday life, but rather belong to the entire ontological framework of the patient’s existence and characterise most aspects of their lived experience (Sass & Parnas, 2003).

In the premorbid phase, worsening of self-disturbances is often predictive of the development of schizophrenic psychosis and persist after remission of a frank first episode (Nelson et al., 2012; Parnas et al., 2011). In particular, disturbances in multimodal processing undermine the ability to experience the world in a holistic fashion, as well as impacting the unity of one's own body. Consequently, this produces a progressive decline of basic selfhood and of the sense of existing in a coherent world. The present subchapter aims to introduce schizophrenia-related disorders, with a particular focus on research that has attempted to identify the phenotypical and neural markers of the illness.

1.3.1. Basic symptoms and self-disorders

One of the first attempt to classify the very early expressions of schizophrenic symptoms come from the clinical work of Huber et al. (1979; 1983), later expanded by Gross (Gross et al., 1982) and Klosterkotter (Klosterkotter et al., 1990). Huber noted that many schizophrenics maintained a certain level of awareness of their own symptoms and could recall when and how the first symptoms first appeared; thus, he coined the term "basic symptoms". During the 1980s, Gross et al. (1982) started to examine longitudinal data and detected several types of subtle symptoms that were often present in schizophrenic patients prior to, or very early in, the illness. Most of these symptoms reflect anomalies in self-experience (e.g., depersonalization and distorted bodily experiences) and appear to be predictive of the schizophrenia onset. The researchers created the Bonn Assessment of Basic Symptoms-BSABS scale, a comprehensive, semi-structured interview that evaluates various anomalies of experience (affective, volitional, cognitive, perceptual and bodily) and that is routinely used for the assessment of schizophrenia proneness (Gross, 1987).

The BSABS scale has been vastly used in clinical and empirical research and has been found to have satisfactory reliability (Vollmer-Larsen et al., 2007). The basic symptoms identified by the BSABS scale have subsequently been included in different assessment scales utilised to detect individuals at risk of developing a psychotic disorder, such as the Comprehensive Assessment of At-Risk Mental States [CAARMS] (Yung et al., 2005), the Scale of Prodromal Symptoms [SOPS] (Miller et al., 2003), and the Schizophrenia Proneness Instrument for adults [SPI-A], (Schultze-Lutter, 2009). Following a similar approach, Parnas, Møller and Zahavi, (2005), created a semi-structured interview to examine the precursory phenomena most at risk for turning into schizophrenia: the Examination of Anomalous Self Experience (EASE) (Parnas et al., 2005). The EASE has been developed on the basis of self-descriptions provided by individuals diagnosed with schizophrenia spectrum disorders and has a strong descriptive, diagnostic and differential diagnostic value. Studies using the EASE have confirmed that self-disorders are predominant and differentiate schizophrenia from other psychotic syndromes, such as psychotic bipolar illness or non-schizotypal personality disorders (Parnas et al., 1998; Parnas et al., 2003; Møller and Husby, 2000; Raballo et al., 2011).

The centrality of self-disturbances as risk factors for the development of schizophrenia was evidenced by an important longitudinal study: the Copenhagen Prodromal Study (Parnas et al., 2011). At baseline, first admission patients were assessed with semi-structured interview comprising overall psychosocial and family history, and with the Bonn Scale for the Assessment of Basic Symptoms (BSABS): fifty-seven had a diagnosis of schizophrenia, forty-three had a diagnosis of schizotypal disorder (which is considered one of the phenotypic expressions of liability for schizophrenia), and the remaining fifty-five patients suffered from other, non-schizophrenia spectrum disorders. The diagnoses were in line with the International Classification of Diseases (ICD-10) research criteria (WHO 1992). Five years later, participants were reassessed, and all the baseline interview components were repeated. Importantly, the reassessment was blind to the information gathered during the initial part of the study. At follow-up, the rate of conversion to schizophrenia spectrum diagnosis was 37%, whereas the conversion rate from schizotypal disorder to schizophrenia was 25%. Interestingly, results revealed that alterations of the basic experience of the self - as indicated with high baseline scores on perplexity and hyperreflexivity (see section 1.2.1) - predicted a subsequent evolution of schizophrenia. Thus, the authors concluded that certain trait-like anomalous subjective experiences, particularly hyperreflexivity and perplexity, are important prognostic indicators for identifying individuals with vulnerability traits of a schizophrenia spectrum disorder (Parnas et al., 2011).

Importanly, research has observed abnormal bodily self-experiences at the time of the first psychotic episode, which is the first time a person experiences a full-blown psychotic episode, following which a diagnosis of schizophrenia is often made. Research agrees that this stage represents a critical period for treating schizophrenia. A study from Stanghellini et al. (2012) selected patients with first-episode schizophrenia from a sample of 393 psychotic patients. The researchers observed that abnormal bodily experiences were present in 30 out of 39 (76.9%) of the patients with first-episode schizophrenia. By means of a phenomenologically based qualitative method of inquiry, the authors identified two main properties that could be taken as cores of abnormal bodily experiences in the schizophrenic spectrum: dynamisation of bodily boundaries and construction, and morbid objectification/devitalisation. Dynamisation refers to violation of bodily boundaries (i.e., feeling that the body is being violated by external entities or forces); disintegration of bodily construction (i.e., loss of coherence or disaggregation of bodily structure, e.g. bodily parts are felt like moving away from usual position), externalization (i.e., projection of personal bodily boundaries into the outer space), and transformation of bodily appearance (i.e. body-dysmorphic-like experiences). Morbid objectification refers to the phenomenon in which parts of one's body that are usually tacitly present become "explicitly experienced" (e.g., hyperreflexivity). This feature is often experienced alongside feelings of devitalisation and of devitalization of body parts (e.g., body parts are felt as devoid of life and experienced as things) (e.g. diminished self-presence). Most importantly, the researchers found that patients devote significant attention to these experiences affecting their body and report great distress and feelings of anguish as a consequence. Also, the authors observed that much effort is produced to make sense of these disturbances, possibly contributing to delusional thinking (Stanghellini et al., 2012).

The concepts related to basic symptomatology and self-experiences have been highly influenced by the tradition of phenomenological psychopathology, particularly by Karl Jaspers' descriptive phenomenological method for understanding mental disorders. One of the merits of this approach has been to observe schizophrenia spectrum disorders from several points of view and at different stages of development of the pathology, with particular focus on the experiences that characterise the development of psychosis. However, the fact that most of the studies adopting this approach have implemented semi-structured interviews, which must be conducted in a clinical setting, represents something of a problem for data collection in the healthy population. Given the fact that abnormal experiences appear to start several years (e.g. since childhood) before the emergence of first frank symptoms, investigating the emergence of subtle changes in experience among healthy individuals could shed important light on the trajectory of schizophrenic spectrum disorders. To this purpose, we need to refer to a construct able to describe a set of experiences - expressed at a subclinical level - that can be found in the general population without being necessarily associated with a mental disorder. This set of experiences below the clinical threshold has been conceptualised as schizotypy.

1.3.2. Schizotypy

Schizotypal pathology refers to a latent psychological organization that underlies a liability for schizophrenia. For instance, the DSM-5 recognised that schizophrenic-like psychopathology could represent an alternative manifestation of schizophrenia liability by placing schizotypal pathology within the schizophrenic spectrum (Lenzenweger, 2018). It is likely that schizotypal pathology is determined by schizophrenia-related genetic and polygenic influences, which co-habit and are impacted by the environment (e.g. stressors and epigenetic inputs). Thus, schizotypal traits can be exhibited phenotypically in various ways, ranging from clinically diagnosable schizophrenia through pathological personality manifestation - such as schizotypal personality disorder - to more subtle, subclinical schizophrenic-like phenomenology. The term "schizotype" was coined by Meehl and Rado (1962) as an abbreviation of "schizophrenic phenotype". The authors observed that one of the main disturbances in schizotypes was represented by the tendency to form a distorted awareness of bodily self, a deficiency in the "action self" and a dysfunction of "spatial-kinesthetic-vestibular system" (Meehl, 1990).

The development of the Schizotypal Personality Questionnaire (Raine, 1991), further contributed to the development of the definition of schizotypy. Schizotypy has been conceptualised as series of cognitive and behavioural variations of schizophrenic traits which are less severe but similar in nature (Kraepelin 1919; Lenzenweger 1995, 2006, 2010; Stotz-Ingenlath 2000) and which indicates a “latent personality construct rather than a description of overt behaviours” (Lenzenweger, 1996). Schizotypy can range from low to high; thus, elevated levels of schizotypy might represent a vulnerability to psychosis (Kwapil et al., 2015). The schizotypy construct is crucial to investigate the psychosis continuum, representing a useful framework for understanding variation in behaviours and in the development, trajectory and potential risk factors for the emergence of schizophrenia. In particular, it offers the possibility to bypass all the issues given by the confounding factors associated with schizophrenia spectrum disorders (e.g. medications and hospitalisations) (Gambini et al., 1992; Kwapil & Barrantes-Vidal, 2015). Importantly, the construct of schizotypy offers the possibility to implement studies with multiple participants, that can be conducted outside of clinical settings. These types of studies have the benefit of being able to investigate subtle alterations in experience across the lifespans of the healthy population. Ultimately, this would contribute toward identifying a psychopathological continuum that stretches from sub-psychotic and sub-clinical mental states to frank psychotic experiences. This approach has already been proven successful, with much evidence supporting the hypothesis of a continuum between schizotypy and schizophrenia.

For instance, in line with the hypothesis of polygenic inheritance of schizophrenia spectrum disorders (for a review see Ingraham & Kety, 2000), adoption studies have observed a greater incidence of schizotypal traits in relatives of schizophrenic patients, regardless of environmental conditions (Kendler & Gruenberg, 1984). Additionally, a growing body of research has suggested that the abnormalities observed in both schizophrenia and schizotypy may be at least partly a result of cascading effects from multisensory anomalies, linking multisensory disintegration with disturbances of the self (Schilder, 1993; Postmes et al., 2014). Researchers have observed that both schizophrenic patients and high schizotypes often experience multimodal stimuli that are further apart in time and in space as co-occurring (Foucher et al., 2007; Haß et al., 2017; Ferri et al., 2019). Also, individuals with schizophrenia and schizotypy show altered responses to somatosensory stimuli, which seem to weaken their capacity to discriminate between the environment and the body (Ferri et al., 2016; Lenzenweger et al., 2000; Chang et al., 2005; Benson et al., 2019; Michael & Park, 2016). Correspondingly, both conditions have shown a more malleable form of body representation (Thakkar et al., 2011; Ferri et al., 2014; Michael & Park, 2016). Commonalities among schizophrenia and schizotypy have been observed at the neural level too. For instance, several studies have found abnormal patterns of neural alterations and functional dysconnectivity in both conditions (Nikulin et al., 2012; Roiser et al., 2013; Ferri et al., 2017; Siever et al., 2002). For instance, Uhlhaas et al. (2010), found a reduction of beta and gamma oscillations and their synchronization, indicating a deficit in the temporal coordination of distributed neural activity. In line with these findings, Koychev et al. (2011) found that individuals with high schizotypy exhibit reduced phase-locking factor – a measure of network synchronization - in the beta and gamma bands in fronto-central and central occipital regions, and reduced beta power in the same fronto-occipital network. Given the role of synchronised neural oscillations in facilitating the transfer of information across sensory modalities (for a review see Keil & Senkowski, 2018), the aforementioned abnormalities in synchronised oscillatory activity may exacerbate the multisensory abnormalities already observed in both conditions.

Both multisensory integration and body representation are essential for maintaining a stable sense of self; disturbances to these components may contribute to the loss of coherent perception of one's body and the external world, exacerbating the self-disturbances observed in both schizotypy and schizophrenia (Schilder, 1993; Postmes et al., 2014). Researchers suggest that self-disturbances are often characterised by depersonalisation and ‘loosening of association’ between thoughts, feelings and action (Sass & Parnas, 2003), something that has also been observed in dissociative disorders.

1.3.3. Schizophrenia and Dissociative Disorders

Dissociative disorders include a range of disorders which are characterised by a disintegration of the functions of consciousness, identity, body representation, memory, and perception of the environment (American Psychiatric Association, 2013; Butler et al., 1996; Renard et al., 2017). Dissociative disorders include depersonalization/derealization disorder, dissociative amnesia, and dissociative identity disorder. Both depersonalization and derealization refer to ongoing experiences of extraneousness, unreality and detachment from the self, the body and the external world (e.g., the sensation of observing oneself from outside). However, while in depersonalization these experiences are immersed in an intense emotional-affective climate, such as that phenomena of detachment can lead to ego boundary disturbances, derealization is instead mainly characterised by apathy towards, and reduction of, the emotional-affective involvement with interpersonal relationships, and between the body and the external world (for a review, see Salami, Andreu-Perez & Gillmesteir, 2020). Dissociative identity disorder refers to identity fragmentation and feelings of being possessed. Dissociative amnesia indicates the inability to recall significant personal information, usually of traumatic nature. An individual diagnosed with dissociative disorder might suffer from one or more of these subtypes (Spiegel et al., 2013).

Despite having been classified as distinct conditions from schizophrenia spectrum disorders, both dissociative disorders and schizophrenia spectrum disorders share some fundamental aspects of abnormal self-experiences that are worth further discussion. Indeed, common symptoms include feelings of being detached from oneself, mental absorption and fragmentation of one's own identity. Both in dissociative disorders and in schizophrenia spectrum disorders, phenomena of detachment are often described as a sort of "daydream" in which the body loses its sense of unity and can be perceived as modified and distorted (Spiegel et al., 2013; Sass & Parnas, 2003). Unsurprisingly, overlap with schizophrenia spectrum disorders and dissociative disorders have been observed in research (Moise et al., 1996; Ross and Keyes, 2004). For instance, dissociative disorders are often found in first-episode psychotic (FEP) individuals and are often associated with childhood trauma (Sun et al., 2019), suggesting that experiences of trauma or intense stress may exacerbate abnormal responses in already vulnerable individuals. Additional evidence on this association comes from clinical data reporting dissociative symptomatology in schizotypal personality disorder and in early stages of schizophrenia (Watson, 2001). For instance, subclinical dissociation is often observed in individuals with high schizotypy, a personality trait that has been linked to schizophrenia proneness (Giesbrecht & Merckelbach, 2008; Pope & Kwapil 2000; Watson, 2001). Whether dissociative symptomatology could represent a risk factor in the development of schizophrenia, is still being debated.

Although the line of demarcation between these dissociative experiences and the emergence of schizophrenia is blurred and unclear, the main point of connection can be identified within symptomatology concerning detachment and depersonalisation, aspects that are both deeply related with changes in the quality of embodied pre-reflective experiences. Indeed, a major constitutive factor of both clinical pictures is characterized by the progressive loss of the first-person perspective, which threatens the basic experience of bodily awareness and bodily boundaries. As such, both conditions imply a loss of the implicit gestalt structure of the body - or of "transparency of experience" (i.e. hyperreflexivity) (Sass & Parnas, 2000) - even though in dissociative syndromes this loss is usually transient and the agent maintains a certain level of awareness of this change.

The detection of enhanced incidences of hyperreflexivity and dissociative symptomatology among at-risk individuals posits interesting questions regarding the role of bodily disturbances as an important component of self-disturbances. This is because hyper-reflective forms of consciousness accentuate the perception of the body as an object of explicit cognition, rather than as a subject of pre-reflective experience (Krueger, 2018). Similarly, in dissociative disorders, individuals may feel like third-person onlookers, rather than first-person subjects of their own experiences. Clinical reports have observed that the progression to schizophrenia illnesses is characterised by an objectification of the body and of introspective experience, with progressive feelings of alienation between the self and the stream of consciousness, as well as forms of decentralization, disembodiment and a disturbed feeling of agency (Szczotka & Majchrowicz, 2018; Sass & Parnas, 2003). For instance, patients in the prodromal phase may start to devote full attention to their body and movements, which eventually begin to feel alien, and, as a consequence, begin to develop delusional explanations to rationalize their state. Future research could investigate the role of dissociative symptomatology in schizophrenia spectrum disorders in order to provide important insights into the pathogenesis of the illness.

From the research mentioned in this section, it emerges that that impairments in multimodal integration, body representation, and disturbances in brain processing, may induce incoherent self-experiences, including diminished sense of self (i.e., derealization), depersonalization, and a weakened self-other gradient (i.e., the boundaries between internal and external sensory inputs becomes distorted) (Thakkar et al., 2011; Postmes et al., 2014). The following chapter aims to introduce the components that seem altered in schizophrenia spectrum disorders, namely, multisensory integration, body ownership and body representation, all aspects that are directly relevant to the studies conducted in this thesis. Subsequently, the chapter aims to introduce the tasks that have been used for the four studies included in the present thesis.

Chapter Two

2. An introduction to multisensory integration and body representation

Recognizing the concept of the minimal self as a phenomenon strongly rooted in the body and dependent on multisensory integration implies that it can be experimentally manipulated. This chapter aims to introduce different but interrelated concepts that have been utilised in my studies: multisensory integration, body ownership and body representation. Namely, I will explain how these different concepts have been utilised in research and how they can be linked to the concepts introduced in Chapter One. Particularly, I will focus on the research that has investigated these aspects in schizophrenia and schizotypy. The four studies that are part of this project ground on the research presented in this chapter. More specifically, in the studies investigating multisensory integration (Chapters Three and Four respectively), we have experimentally induced multisensory conflicts to investigate how individuals with high and low schizotypy process signals coming from their direct environment. Thereafter, we have attempted to utilize multisensory stimuli to manipulate the sense of body ownership in individuals with schizophrenia, and we have linked this process to basic symptomatology and to body representation (Chapter Five). Finally, the last study has attempted to isolate a more specific component of body part representation - i.e., the body structural representation – to investigate whether individuals with high schizotypy, similarly to individuals with schizophrenia, exhibit a more malleable internal body representation model (Chapter Six).

2.1 Multisensory Integration

Multisensory integration is fundamental for several aspects of normal self-experience, such as the recognition of one's own body, actions and awareness (Gallagher, 2000; Tsakiris et al., 2007; Bermúdez, 2011). Sensory information coming from different modalities (e.g., vision and touch) needs to be integrated across time and space into a coherent percept of our dynamic environment and of our body. As such, a disrupted multisensory integration could cause feelings of detachment from one's environment and from one's self (Jauregui-Renaud et al., 2008); experientially, this would manifest with perceptual incoherence. Extensive evidence has found alterations in time perception (Elvevåg et al., 2003) and temporal processing in people with schizophrenia (Davalos et al., 2002). Moreover, research has found that individuals with schizophrenia exhibit abnormalities in both unisensory and multisensory temporal perception indicated by a reduced capacity in judging the simultaneity between purely visual, purely auditory and combined visual-auditory stimulus pairs (Foucher et al., 2007, Martin et al., 2013). In addition, structural and functional changes in the superior temporal cortex, a brain region deeply involved in multisensory processing, has been detected in schizophrenia and in individuals identified as being at risk for the disorder. Such abnormalities have been detected as reduction in grey matter volume (Gur, 1999; Honea et al.,2005; Wright et al.,2000), and abnormal activity in the superior temporal gyrus during performance of different cognitive tasks (Gur et al., 2007). Also, hypoactivity in the ventral premotor cortex has been observed in patients with First Episode Psychosis (Ferri et al., 2012; Ebisch et al., 2013). Research shows that this region is involved in integrating multisensory signals with motor representations of different parts of the body (Fogassi et al.,1996; Graziano et al.,1994; Rizzolatti et al., 2002).

In line with the hypothesis of schizophrenia as a continuum, impaired sensory integration has been observed in schizotypy (Stevenson et al., 2017; Ferri et al., 2018) and at the time of patients' first psychotic episode (Williams et al., 2010), corroborating the hypothesis that disturbances in multisensory integration represent a hallmark neurological "soft sign" of schizophrenia spectrum disorders (Heinrichs & Buchanan, 1988). These disturbances could contribute to the development of aberrant self-experiences, including depersonalisation and "loosening of associations" between thoughts, feelings and actions (Postmes et al., 2014). These experiences lie within the framework of "disorders of the self" as conceptualised by Sass and Parnas (2003), as mentioned in Chapter One. As such, in order to understand schizophrenia spectrum disorders, we need to investigate the more general components of multisensory integration.

Multisensory integration refers to the ability to consolidate the information arising from different sensory modalities into a single multisensory perception (Stein & Meredith, 1993: Rohde, van Dam, Ernst, 2016; van Dam et al., 2014). The integration of the senses is fundamental in creating a coherent representation of the world and for our ability to discriminate between self and non-self (Ramachandran & Hirstein, 1998; Gawęda et al., 2013). Perception, as already observed by Gibson (1968), is, in essence, multisensory. This multimodal aspect of perception has enormous survival value and is fundamental for shaping our bodily self-consciousness (i.e., the feeling that our body belongs to us) (van Dam et al., 2014). Consequently, multisensory integration contributes to shaping the self from its more fundamental, pre-reflective level (the *minimal self*). Minimal selfhood is believed to be formed through the combination of multisensory information of interoceptive and exteroceptive origins, and it is related to processing of bodily signals in multisensory cortical systems (Ehrsson, 2012; Gallagher, 2000). For example, the experience of owning one's own body (i.e. body ownership) can be altered by manipulating the timing of visual and tactile/proprioceptive (i.e. exteroceptive) body-related information. At the same time, individual differences in sensitivity to internal bodily signals (i.e., interoception) could affect the experience of body ownership as well.

Research in multisensory integration has identified a series of principles to explain which combination of cross-modal inputs would be most likely to cause enhanced responses (Meredith & Stein, 1986). These principles are subsumed under the concept of the "unity assumption", i.e. the assumption, or belief, that whenever two or more unisensory cues are highly consistent in one or more dimension, observers are more likely to perceive them as perceptually bound (Welch & Warren, 1980; Spence, 2017; Chen & Vroomen, 2013). The bindings of different stimuli depend on stimulus-driven factors (low-level factors), such as the spatial and temporal co-occurrence of the stimuli (Calvert et al., 2004), on cognitive factors (high-level factors), such as semantic congruency (Chen & Spence, 2010) and on prior knowledge (van Dam et al., 2014; van Dam & Ernst, 2015).

The crossmodal integration of multiple sensory signals into unified multisensory percepts has been demonstrated in studies utilising both simple stimuli (e.g. sound or tactile stimuli) as well as more complex stimuli (e.g. speech). For instance, research has shown that sound can guide attention toward a visual target. Frens et al. (1995) showed that participants had faster saccades to a visual target when an irrelevant auditory cue was spatially and temporally aligned with the target. A study from Perrot et al. (1990), observed an improvement in visual search times when an auditory click was presented at the same location as the visual target. Interestingly, such benefits are also found when the auditory and visual signals come from different locations. Van der Burg et al. (2008) demonstrated that a nonspatial auditory event (i.e. a pip) could guide attention toward the location of a synchronized visual event (a colour-changing object) that, without such an auditory signal, is very hard to find. Thus, the authors concluded that the temporal information of the auditory signal was integrated with the visual signal, creating a salient emergent feature that automatically draws spatial attention (van der Burg et al., 2008). In a similar fashion, receiving irrelevant tactile signals can speed-up the detection of faint tones presented simultaneously - as opposed to when presented non-simultaneously - and increase auditory intensity ratings (Gillmeister & Eimer, 2007). Also, several studies investigated the role of combining sensory information in speech comprehension. For instance, a study from Sumby & Pollack (1954) showed that speech comprehension is facilitated when participants can make use of both auditory and visual information in combination.

One aspect that has been widely investigated in multisensory integration research is related to the temporal coincidence within which different stimuli are presented. Subsided under the “unity assumption”, the “temporal principle” refers to the fact that temporally aligned stimuli facilitate multisensory enhancement (see Stein, 2012 for review). Thus, sensory information is more likely to be bound together when signals from the separate senses are presented in close temporal proximity (Wallace et al., 1998; Wallace et al., 2004). An important characteristic of this phenomenon seems to be linked to the individual temporal resolution in multisensory perception, namely the temporal window of integration (Stevenson et al., 2014). This window refers to the time frame within which the brain is more likely to bind together temporally asynchronous sensory information and perceive them as coming from the same multimodal event

(Wallace et al., 2004; Wallace & Stevenson, 2014). The width of the temporal window of integration appears to be robust across healthy individuals even though it can slightly change depending on the tasks and stimuli used (Stevenson & Wallace, 2013); that is, larger windows are observed for complex stimuli (e.g. speech) than for simple stimuli (e.g. a light flash, a brief sound, a brief tactile stimulation) (Stevenson et al., 2013). Unsurprisingly, an atypical temporal window of integration – e.g., too narrow or too large – have been observed in various psychological disorders (Zhou et al.,2018; Wallace & Stevenson, 2016) and in schizophrenia (Haß et al., 2017).

A task that is particularly appropriate to assess the individual's temporal window of integration is the Double Flash Illusion (Shams et al., 2000). In a typical Double Flash Illusion, when participants are presented with a visual stimulus (a single flashing disc) and tactile or auditory stimuli (a quick double-tap on their finger or a quick double beep) they can be induced into perceiving a second illusionary flash, even if there is only ever one flash (Shams et al., 2000). In this type of illusion, one sensory domain (e.g., auditory or tactile) has an influence on another, in this case, vision. In order to characterise the temporal profile of the audio-visual version of the Double Flash Illusion – and thus identify to what point the illusion starts to decay - Shams et al., (2002) varied the width of the interstimulus interval (ISI) between the beeps. A longer ISI means that the second beep is no longer sufficiently overlapping with the flash, and therefore is not integrated. The authors found that the illusion tends to decline when the average time between the beeps exceeds 100 ms. Thus, when the two beeps are spaced apart by less than 100 ms, on average participants tend to report seeing two flashes, suggesting the illusory effect is taking place. Conversely, when beeps are spaced apart by more than 100 ms, the illusory effect begins to degrade, and the participants will tend to report seeing only one flash (Shams et al., 2002). Haß and colleagues (2017) adopted this version of the illusion to investigate the temporal sensitivity of individuals with schizophrenia compared to healthy individuals. The researchers found an extended temporal window of integration in schizophrenic patients compared to healthy participants (Haß et al., 2017). In Chapter Three, we aimed at expanding these findings to schizotypy. Namely, we employed the audio-visual Double Flash Illusion to investigate the individual temporal window of integration of audio-visual stimuli of individuals with high and low schizotypy (Ferri et al., 2017, Chapter Three). Results show that individuals with high schizotypy exhibit larger windows of integration of audio-visual stimuli and a higher proneness to the illusion (Chapter Three). Moreover, in Chapter Four, we linked the individual temporal profile of the tactile-Double Flash Illusion to beta activity in the visual cortex (Fotia et al., 2021). The next section aims to introduce past and present research that has linked neural oscillatory activity with multimodal processing. In particular, I will focus on the studies that have been used as supporting literature for Chapter Four.

2.2. Neural correlates of multisensory integration

For a long time, it was assumed that different regions of the brain were independent from each other, and that each primary sensory area received information from a specific sensory modality. That is, the integration of the senses was thought to happen after the sensory signals were processed in unisensory cortical regions (Benevento, 1977). Indeed, the majority of the early investigations on sensory processing mechanisms have focused on the activity in sensory cortices in respect to their primary sensory inputs (e.g., modulation of activity in the visual cortex in response to visual stimuli). However, a number of investigations identified several systems within the brain that respond to more than one type of sensory information (so-called “convergence sites”) such as the superior colliculus (Stein & Meredith 1993), the amygdala (Nishijo et al., 1998), the striatum (Nagy et al., 2006), the fronto-temporal regions (Giard & Peronnet, 1999), the parieto-occipital regions (Molholm et al., 2002), the ventral premotor cortices, intraparietal cortices and cerebellum (Ehrsson et al., 2005). Converging evidence coming from brain imaging studies have observed cross-modal influences even in the low level, primary sensory cortical areas that were traditionally thought to be functionally independent and sensory specific, such as the primary auditory cortex and the primary visual cortex (Bell et al., 2001). This has provided further support for the hypothesis that neuronal activity in a given cortical sensory region is modulated not only by its primary sensory inputs but also by the stimulation of other sensory systems (Foxe & Schroeder, 2005).

One mechanism that allows multisensory integration across distributed cortical networks and across sensory modalities is the transient synchronization of neural oscillations (Senkowski et al., 2008; Mercier et al., 2013; Fries, 2015). Neural oscillations are prominent features of brain functioning. One of their roles is to synchronise neuronal populations at different neural sites (e.g. auditory and visual cortex) and to coordinate distributed neuronal activity and information transfer from one site to the other (Keil & Senkowski, 2018). This is in line with Hebb’s postulate of neural assemblies (1949). Hebb postulated that learning could be explained according to three hypotheses, each of which has received experimental confirmation in current research. The first hypothesis, commonly referred to as Hebb’s rule, postulates that cortical neurons strengthen their connections after they have been repeatedly activated simultaneously. The second hypothesis states that the strengthening of synapses across the cortex involves not only neighbouring neurons, but also neurons in distant cortical areas. The third hypothesis postulates that when a group of neurons is simultaneously and frequently activated, this activation will impact the functional organization of the brain. Thus, strongly connected neurons in different areas will tend to fire together as a functional unit and to form functional, synchronised patterns. Hebbian cell assemblies are not necessarily located within small cortical areas but may be dispersed over distant cortical areas. Evidence from neuroanatomical and neuroimaging studies have lent support for the Hebbian principle, indicating cortico-cortical pathways between different areas in the cortex (Barredo et al., 2016; Roland et al., 2014; Fiori et al., 2018).

The precise dynamics by which this synchronization happens are still being investigated. One hypothesis is that multisensory processing is contingent on the functional connections between areas of the brain that are involved (e.g. visuo-tactile, audio-visual). As stated within the Communication Through Coherence framework (Fries, 2005; 2015), selective interaction among neural networks is realised by coherence (i.e. synchronization) between firing rate oscillation in remote but functionally interconnected areas. In particular, this synchronization is due to the alignment of post-synaptic neural activity to pre-synaptic input, producing temporal windows for communication between the involved areas. One way to investigate this hypothesis is to focus on neuronal activity during cross-modal stimulation (Iurilli et al., 2012; Kayser et al., 2008). A non-invasive method utilised to investigate neuro-oscillatory activity is electroencephalography (EEG).

The EEG measures the extracellular current flow generated by the sum of the synchronised activity of large groups of neurons that are spatially aligned. This activity is enabled by the transmission of electrical signals, which are passed from pre-synaptic to post-synaptic cells producing a change in the membrane potential of the post-synaptic terminal. The EEG allows to detect and to visualize multiple (excitatory or inhibitory) postsynaptic potentials of relatively large groups of neurons firing synchronously. These postsynaptic potentials produce a complex waveform, which can be segmented into different frequency bandwidths, with distinct amplitudes and phases. These bandwidths are commonly referred to as neuro-oscillations or brain waves. Research has shown that these oscillations play an active role in neural communication (Fries, 2005; Engel & Fries, 2010). A number of findings suggest that neural oscillations at low (theta, alpha) and high (beta, gamma) frequency play a fundamental role in sharing temporary information across large-scale networks that characterise the neural correlates of specific aspects of sensory integration (Singer, 1999; Varela et al., 2001). Indeed, several studies have linked neural oscillations in distinct frequency bands to different mechanisms of multisensory processing, suggesting that multisensory binding is processed differently according to the domains involved (e.g. audio-visual versus visuo-tactile) (Uhlhaas & Singer, 2012; Cecere, Reese & Romei, 2015; Cooke et al., 2019). This has recently been confirmed by Cooke et al. (2019) who investigated the neural processing involved in audio-visual and the visuo-tactile Double Flash Illusion. The researchers found that the two types of cross-modal illusion were characterised by aspects in different oscillatory processes associated with the inducing domain (i.e. alpha oscillations for the auditory driven illusion and beta oscillations for the tactile induced illusion). In order to introduce this research, we first need to briefly introduce alpha and beta frequencies and the role they play in different perceptual and mental processes. This will also serve to introduce the research presented in Chapter Four.

Brainwave frequencies are produced by synchronised electrical pulses arising from groups of neurons communicating with each other. These frequencies can be divided into distinct wavebands: Alpha (7 – 12 Hertz Hz), Beta (12 – 30 Hz), Theta (4 – 7 Hz), Delta (0.5 – 4 Hz) and Gamma (25 – 100 Hz) frequencies. Expanding on the function of each individual frequency band is out of the scope of this thesis. However, to our purpose, it is important to focus on the role of alpha and beta bands. Alpha oscillation appears to be the predominant rhythm in the resting human brain (Britton et al., 2016). Increase in alpha power is usually associated with reductions in cognitive activity (Lundqvist et al., 2013). Furthermore, alpha activity has been associated with neurocognitive functions that are central to the engagement of visual information (Piantoni et al., 2017; Ronconi et al., 2018) and auditory information (Mercier et al., 2013). Beta oscillations are present over a large range of frequencies (12-30 Hz) and are commonly segmented into low, medium or high beta. Beta oscillations are often associated with the formation of largely distributed functional networks in the context of multisensory processing, sensory-motor coordination, and the maintenance of posture during normal brain functioning. Indeed, previous studies have linked tactile and somatosensory processing with beta oscillations (Foffani et al., 2005) as well as with motor and motor related tactile stimuli (Engel and Fries, 2010; for a review see Kilavik et al., 2013). Research has observed that low amplitude beta are linked with several types of cognitive and emotional processes, such as active concentration and anxious thinking (Baumeister et al., 2008). Notably, beta frequencies are involved in inhibitory cortical transmission mediated by gamma-aminobutyric acid (GABA). Research has observed a connection between oscillatory beta activity and pharmacologically modulated GABA concentration in the sensorimotor cortex, demonstrating that drugs that decrease cortical GABA tend to result in heightening cortical beta activity (Drinkenburg et al., 2004).

An investigation conducted by Cecere, Rees, and Romei (2015) found a link between individual's alpha band responses in the visual cortex and the temporal window of integration for audio-visual inputs (the Double Flash Illusion). More specifically, they found that slower alpha waves (i.e. slower alpha peak frequency) were associated with larger temporal windows of integration. Conversely, faster alpha waves were associated with shorter temporal windows of integration. Subsequently, Cecere, Reese and Romei, (2015) expanded this research by demonstrating that changing the alpha peak frequency could directly influence the individual's temporal windows for the audio-visual Double Flash Illusion. The researchers directly manipulated the speed of the individual alpha wave using transcranial Alternating Current Stimulation (tACS). When the individual alpha peak frequency was reduced, the temporal window widened, conversely when the alpha frequency was increased, the window shortened. As a result, changing the occipital alpha wave time in the visual cortex resulted in a change in the perception of the illusion.

A possible interpretation for this effect is that the auditory-induced Double Flash Illusion is driven by local oscillatory activity in the visual cortex which is associated with alpha activity (Dugue et al., 2011; Frey et al., 2014; van Dijk et al., 2008) and which set the temporal profile for the Double Flash Illusion. If this is to be the case, one would expect the same local effect of alpha activity for the visuo-tactile Double Flash Illusion. However, this is not what has been found in a subsequent research by Cooke et al. (2019). The authors replicated the relationship between the audio-visual Double Flash Illusion and the alpha frequency observed by Cecere et al. (2015). However, the researchers found that the tactile temporal window for the tactile Double Flash Illusion's (i.e., one flash and two taps) was correlated with beta frequency in the visual cortex. More specifically, the authors found that a slower beta wave is associated with a longer temporal window of integration, whereas a faster beta wave is associated with a shorter temporal window of integration. This suggests that the cross-modal effect in the Double Flash Illusion is not driven by local visual processes (related to alpha wave frequencies), but rather, it is driven by properties of functional connections between remote areas of the brain. In the auditory induced DFI, the connection between auditory and visual cortices would be linked with the oscillatory processes related to auditory processing (alpha waves); on the other hand, the tactile induced DFI is linked to beta waves, which is the frequency at which tactile stimuli are processed. Thus, the visuo-tactile Double Flash Illusion, rather than being dependent on local network rules (i.e., local occipital oscillatory resonance activity), is determined by long-range communication networks (i.e., functional connections between somatosensory and visual cortices) that influence visual cortical processing. More specifically, the temporal window for the tactile induces illusion would be mediated by beta oscillations as somatosensory processing (pre-synaptic), which is typically linked with beta activity, phase-align beta oscillations in the visual cortex (post-synaptic), defining the temporal resolution of interregional synchronization. A similar pattern has been observed for the auditory-to-visual network by the aforementioned study from Cecere et al. (2015), who found an association with the auditory-induced illusion and alpha activity (which has been linked to auditory processing) in the visual cortex. These observations have been interpreted within the “Communication Through Coherence” framework (Fries, 2005; 2015) as a way of communication between the senses for optimal multisensory binding (Cooke et al., 2019).

How does the above link to observations of neural activity in patients with schizophrenia and schizotypal disorders? Given the functional involvement of oscillatory networks in cognitive and perceptual processes, it is plausible that the disturbances observed in the spectrum might be associated with a core disturbance in the generation of coherent neural oscillatory activity. This is what has emerged in current literature (Uhlhass, 2010). Electroencephalography (EEG) and magnetoencephalography (MEG) studies have examined rhythmic activity during both spontaneous and task-related activity in schizophrenic patients or in healthy individuals with schizotypal traits. Results suggest abnormal power, amplitude and synchrony of oscillatory activity in both schizophrenia and schizotypy, especially in the beta and gamma bands (Liddle et al., 2016; Tillman et al.; Uhlhaas & Grent-Jong, 2018; Grutzner et al., 2013; Koychev et al., 2011; Spender et al., 2003; Symond et al., 2005; Uhlhaas et al., 2008). Moreover, research has found slower oscillatory activity in the alpha band in both schizophrenia (Clements et al., 1994: Omori et al., 1995) and schizotypy (Fuggetta et al., 2014). Researchers have hypothesised that the tendency towards slower oscillatory activity within a given frequency band is symptomatic of a general loss of neural code efficiency (see Ferri et al., 2018; Cecere et al., 2015). Moreover, as observed by Cecere et al. (2015) and Cooke et al. (2019), slower oscillatory activity appears to be associated with longer period of integration of information across the senses. In agreement with previous investigations which demonstrated that the abnormalities in schizotypy are similar to, but less pronounced than, those in schizophrenia (Nelson et al., 2013), both a longer window of sensory integration (Haß et al., 2017; Ferri et al., 2018) and slower oscillatory activity (Stevenson et al., 2017; Fotia et al., 2021) have been observed in both schizophrenia and schizotypy. These findings support the hypothesis that these alterations be present at the preclinical stages of schizophrenia spectrum disorder.

With this in mind, Chapter Four investigated the relationship between temporal sensitivity in the tactile-induced Double Flash Illusion, neural oscillations and schizotypy. Here, we were able to replicate the findings from Cooke et al. (2019), which demonstrated slower beta waves (i.e., reduced frequency) was associated with longer temporal window of integration, whereas faster beta waves were associated with shorter temporal windows of integration accounting for the illusion. Additionally, we found that reduction in individual beta frequency was associated with high schizotypal traits, as well as a longer temporal binding window within which they perceived the illusion. Individuals with lower schizotypal traits showed faster beta waves and shorter temporal binding windows for the illusion. Moreover, we found that the relationship between individual beta frequency and schizotypal personality traits was fully mediated by the temporal binding window. Taken together, these results suggest that a wider temporal window of integration between different sensory modalities, as have been observed in schizophrenia (Stevenson et al., 2017), likely also characterize schizophrenic-like subclinical conditions (Haß et al., 2017). Both these aspects may at least partially originate from abnormalities of the oscillatory frequency patterns associated with multisensory integration processes. Such interpretation would be in line both with reports of abnormal oscillatory activity and abnormalities in network synchronisation as measured by the “phase-locking factor” from Koychev et al. (2011), in turn leading to a deficient modulation of the sensory processing in schizotypy as observed in Chapter Four. Our results may represent a step forward in the identification of neurophysiological biomarkers of schizophrenia across different sensory domains and brain networks.

The multisensory abnormalities that have been observed in schizophrenia spectrum disorders are likely also connected to a deeper aberrancy in the structure of the self. In the phenomenological context, the self and the external world are not separable, as an individual’s sense of self is shaped through interactions with the world of objects.

This immersion and projection into the multisensory external world is mediated by the body, which is the most fundamental component to cohabit and co-determine the experiential structure from which a Gestalt emerge (Parnas, 2003). In the next section, we will focus on the representation of our body in the brain by introducing the concept of body ownership.

2.3. Body Ownership

The body plays a crucial role in shaping our fundamental sense of self. Representing our body at the brain level is extremely important for several tasks; for instance, it allows us to perceive our limbs in space and this, in turn, allows us to program our movement in the external space. Phenomenologically oriented neuroscientists suggest that the experience of the body must be assumed as the first and fundamental manifestation of the phenomenal or minimal self (Cremolacce et al., 2007; Metzinger, 2003). Research in developmental psychology has shown that at the age of 2-3 months - thus, long before mirror self-recognition has developed, which usually occurs at around 18 months – infants develop the capability to interpret invariant information about their own body as a separate entity in the environment (Rochat, 1998). This represents a fundamental step to develop a sense of one's body as a distinct entity, differentiated from the external world. Without a representation of one's own body, it is not possible to perceive and experience properties of ownership and agency. Body ownership, also referred to as 'mineness' (Gallagher, 2000), refers to the status of one's body as an invariant structure for receiving sensory stimuli that are unique to oneself (Tsakiris et al., 2007) and has been linked with neural activity of specific brain areas, such as the premotor areas, the occipitotemporal cortex, the primary/secondary somatosensory areas, and the anterior insula (Petkova et al., 2011; Ehrsson et al., 2004). Body ownership is essential to distinguish us from others (Myers & Sowden, 2008), and to develop higher-order cognitive processes (Gallese et al., 2004).

These experiences of embodiment posit an interesting question: where does body ownership come from? What grounds the experience of my body as my own? The sense of body ownership is likely to be acquired by dynamic multisensorial integration processes and their interactions with internal models of the body. Indeed, a long tradition in psychology and cognitive neuroscience have suggested that body ownership depends on multisensory integration (Bonnier, 1905; Holmes & Head, 1911; Longo & Haggard, 2012). Gibson (1979) argued that self-perception of one's body is generated by different forms of sensory stimulation, such as "amodal invariants" (e.g., synchrony, rhythm and intensity patterns) and their overlap: *"Information about the self accompanies information about the environment, and the two are inseparable. Egoreception accompanies exteroception, like the other side of a coin. Perception has two poles, the subjective and objective, and information is available to specify both. One perceives the environment and coperceives oneself"* (Gibson, 1979, p. 126). The experience of body ownership is clearly adaptive from an evolutionary perspective, and this is most likely linked to the problem of localising and identifying oneself in the sensory environment, particularly because our bodies constantly change. These fundamental components of body ownership (i.e., self-identification and self-location) are related to the processing of bodily signals in multisensory cortical systems (Blanke et al., 2015; Ehrsson et al., 2004). Thus, body ownership is highly malleable and multisensory integration, lying at the root of body unity, is the mechanism through which the experience of 'mineness' is constantly aligned with the changing body. At the neural level, the brain regions involved in multisensory integration, such as the ventral premotor cortex (Ferri et al., 2011), the intraparietal sulcus and the insula (Grivaz et al., 2017) also contribute to body ownership. Information from bodily signals, as well as visual, proprioceptive, tactile and auditory signals, reach converge zones in the cortical regions, where the binding of these body signals happens (Botvnick, 2004; Graziano & Botvinick, 2002).

The sensation of owning our own's body is also modulated by the intentional and agentic nature of voluntary action: the sense of agency (Tsakiris & Haggard, 2005). The enabling conditions for self-experience are likely to be grounded in the feeling of body ownership and agency, which both play important roles in shaping the bodily self. For instance, in voluntary action, the sense of ownership and the sense of agency often coincide. Conversely, in the case of involuntary actions, it is almost always possible to distinguish between ownership and agency. Take, for instance, a doctor that, during a medical examination, moves the arm of the patient. In this case, the subject is aware that the moved arm belongs to him (sense of ownership), but on the other hand, he does not feel he was the one who caused the movement (sense of agency) (Gallagher, 2000). This suggests that agency and ownership produce complementary – but dissociable – components of embodiment (Gallagher, 2000; Tsakiris et al., 2006). For instance, research has evidenced that the active body (related to the sense of agency) is experienced as more coherent and unified than the passive body (Tsakiris et al., 2005, Gallagher, 2005). Indeed, in action, multiple body parts are controlled as an integrated whole. Neuroimaging studies show an orderly, segregated representation of body parts in the primary somatosensory cortex (SI), whereas the representations of different body parts strongly overlap in the primary motor cortex (M1) (Hlustik et al., 2001). For the purpose of this thesis, we will focus more specifically on body awareness as proprioceptive awareness, that is, the conscious experience of the location of a specific body-part (i.e. an arm or a hand) in space.

A vast corpus of literature on body ownership is based on the Rubber Hand Illusion paradigm (Botvinick & Cohen, 1998). This paradigm has been utilised to showcase that the perception of one's own body in space critically depends on multisensory integration. The illusion offers an example of how an extra-biological object (i.e. a rubber hand) can be incorporated into the neural body map. Several studies have demonstrated that changes in body ownership occur during the Rubber Hand Illusion, both using the classical paradigm (Botvinick & Cohen, 1998; Armel & Ramachandran, 2003; Longo et al., 2008; Tsakiris et al., 2007) or modifications of the classical paradigm (Ehrsson et al., 2007, 2008; Tsakiris et al., 2006; Petkova & Ehrsoon, 2008). In the typical Rubber Hand Illusion, a participant is asked to put their hand (palm-down) on a table, while an experimenter places a screen to hide the participant's hand. Then, a rubber hand is placed on the table in a location that replaces the real, hidden hand. The experimenter strokes the rubber hand and the hidden hand in synchrony with two paintbrushes, moving the brushes at the same time on corresponding parts (e.g. corresponding fingers) of the hidden hand and of the rubber hand. This creates a multisensory visuo-tactile temporal congruency of multisensory cues from that limb. In accordance with the temporal congruency principle of multisensory integration (Holmes & Spence, 2004; Stein and Stanford, 2008), the participant begins to feel that the rubber hand is their own actual hand. The rubber hand illusion creates the sense that the false hand is connected to the body; the effect occurs because the participant watches the rubber hand being touched synchronously with their real hand. The illusion does not occur when the rubber hand is stroked asynchronously with respect to the subject's own hand.

The rubber hand illusion also depends on the spatial congruence of the sensory information involved. In accordance with the spatial principle of multisensory integration - namely, that spatial coincidence facilitates the integration of information coming from different sensory modalities (Holmes & Spence, 2004; Stein & Stanford, 2008) - a study from Lloyd et al., (2007) found that the illusion is limited by the distance between the rubber hand and the participant's real hand. Indeed, when the distance between the two hands is widened, the strength of the illusion decreases in a nonlinear way: it remained quite stable for smaller distances, and it started to consistently decay for distances beyond 27.5 cm. The decay reflects the extent of peripersonal space as estimated in electrophysiological (Fogassi et al., 1996) and neuropsychological (Ladavas et al., 1998) studies. Also, in order to elicit the illusion, the rubber hand must be as similar as possible to the subject's real hand (Tsakiris & Haggard, 2005). Interestingly, participants who experienced the Rubber Hand Illusion more strongly also perceived their hand and the rubber hand as significantly more similar as opposed to participants who did not experience the illusion (Longo et al., 2009). These effects are not limited to the hand. For instance, in the full-body illusion, watching the body of an avatar being stroked, while receiving the same tactile stimulation on one's own body at the same time, induces participants to self-identify with the avatar (Petkova & Ehrsson, 2008). Moreover, the full-body illusion can induce the participants to misperceive the location of their own body and perceive themselves as closer to the avatar's position (Ionta et al., 2011). What this ultimately suggests is that the unity between body and self can be temporarily suspended.

The changes in subjective experience elicited by the rubber hand illusion have been investigated with different methods. For instance, one widely used method consists of submitting the participant to questionnaires in the form of analogue or Likert scales, which usually include two or three statements about the important perceptual effect of the illusion (e.g. “I felt as if the rubber hand was my hand,” “It seemed as if I were feeling the touch of the paintbrush in the location where I saw the rubber hand being touched”), and five to seven statements designed to control for task compliance and suggestibility (Botvinick & Cohen, 1998). More recent literature has been debating whether these questionnaires are reliable measures of embodiment, particularly on whether the introspective account of ownership, as indicated in the questionnaires, reflects the sense of ownership or the judgement of ownership (de Vignemont, 2010). A recent investigation found that the phrasing of the questions can influence participants’ judgment. For instance, statements based on ‘feeling’ (whether the participant feels that the rubber hand belongs to them), resulted in higher agreement compared to statements based on ‘believing’ (e.g., whether the participant believes that the rubber hand belongs to them) (Tamè et al., 2018). Another indicator which has often been used as a measure of ownership is the perceived change in the location of the participant’s own hand towards the rubber hand (i.e., proprioceptive drift) (see Tsakiris, 2007 for a review). Further research demonstrated that if the rubber hand is threatened (e.g., with a hammer), unconscious fear response mechanisms are activated, and the subject reacts as though the hammer is about to be hit their real hand. Also, the participant’s blood pressure and heart rate, as well as the adrenaline levels, rise when they experience the illusion, or when the rubber hand is threatened (e.g. with a hammer, or sometimes even with a knife, in Virtual Reality (VR) studies) (Gonzalez-Franco et al., 2013).

The extent to which these various measures reflect the same or different underlying processes involved in the illusion, is still under debate (Longo et al., 2008; Gallagher et al., 2021; Abdulkarim & Ehrsson, 2016). In particular, despite the fact the proprioceptive drift often correlates with body ownership in the Rubber Hand Illusion, this is not consistent across different studies, and the relationship between these two measures still remains unclear. Rohde et al. (2011), found that subjective ratings of embodiment were higher following synchronous vs asynchronous tactile stimulation, whereas proprioceptive drift was reduced only by continuous asynchronous stimulation. On the other hand, when tactile stimulation was frequently interrupted, the authors observed similar drifts both in the synchronous and in the asynchronous conditions. Also, Abdulkarim & Ehrsson (2016), found that proprioceptive drift was affected when the participants moved their hand towards or far from the rubber hand, whereas movement did not affect the subjective questionnaire ratings. On these bases, it has been suggested that proprioceptive drift reflects self-localization, while subjective reports indicate ownership over the rubber hand (Longo et al., 2008; Serino et al., 2013). Thus, the proprioceptive drift is likely to result from a process of multisensory spatial recalibration, during which the position sense is dynamically updated to correspond better with the location of the rubber hand in the external space. However, despite the fact that the two components of ownership and localization can be dissociated, they are generally strongly linked in most experiences. Indeed, even if the sense of owning one’s body might not be reducible to the perceived location of one’s body, the two components of ownership and location most likely work together to differentiate self from other (Jeannerod, 2007).

Further insights on the relationship between the experience of the location of one’s own hand relative to the rubber hand (i.e. proprioceptive drift), and the sense of ownership over the hand (as assessed with subjective reports) come from a study from Longo et al. (2008). The authors found that the two components are dissociable but form a coherent cluster of experience, suggesting that the sense of body ownership is not a single dimension, but a composite of several different subjective components, organised with a characteristic structure. By applying principal component analysis, the authors found four major components related to the RHI: *embodiment of the rubber* (i.e. the feeling that the rubber hand belonged to the participant), *loss of own hand* (i.e. feeling that one's hand is out of one's control), *movement* (i.e. perceived motion of one's own hand and of the rubber hand), and *affect* (i.e. pleasant feelings related to the illusion). Furthermore, the authors found an additional fifth component in the asynchronous condition: *deafference* (i.e., the sensation of pins-and-needles and numbness in one's hand). A secondary analysis of the *embodiment of the rubber hand* component further revealed three subcomponents: *ownership* (i.e., the sense that the rubber hand was part of one's own body)*, location* (i.e. the sense that one's own hand was in the same location as the rubber hand), and *agency* (i.e. the sense of control over the rubber hand)*.* In particular, the authors found that both the *location* and *ownership* component were significant independent predictor of *proprioceptive displacement*, whereas the *agency* subcomponent was not. What this suggests is that proprioceptive displacement is a by-product of embodiment which relates to body ownership, but not to agency. The authors concluded suggesting at least two types of influences structuring embodiment: those associated with immediate sensations from the body (bottom-up) and those associated with stored representations of the body (top-down).

Thus, the Rubber Hand Illusion effect suggests that feelings of ownership result from both bottom-up processes (i.e. involving the multisensory integration of visual, tactile and proprioceptive information) and top-down processes (i.e. involving an internal representation of the body) (Tsakiris, 2010). Indeed, it has been noted that the spatial and temporal congruence, (e.g. between tactile and visual information) is necessary, but not sufficient, to experience the rubber hand illusion. On top of that, a pre-existing representation of the body is essential to understand several aspects of the illusion (Tsakiris & Haggard, 2005; Tsakiris, 2010). For instance, susceptibility to the illusion can be abolished by a mismatch in hand orientation (Pavani et al., 2000; Ehrsson et al., 2005), or by using a fake wooden hand instead of a rubber hand (Tsakiris & Haggard, 2005). Costantini and Haggard (2007) demonstrated that the illusion operates in a hand-centered reference frame, which is constantly updated with changes in body posture. The authors suggest that perception of current sensory stimulation on the body depends not only on feedforward integration of current inputs but also on pre-existing body representations which possess their own frame of reference and are distinct from external spatial representation. Therefore, it is likely that a prior structural-spatial body representation has a key role in elaborating multimodal stimuli and creating the experience of what is "mine". This aspect of body representation will be furtherly expanded in section 2.4. On a neural level, the rubber hand illusion has been linked to activity in multisensory areas in frontal and parietal association cortices such as the ventral premotor cortex and the intraparietal cortex (Ehrsson et al., 2004), suggesting that these areas contribute to self-attribution of body parts by integrating visual, tactile and proprioceptive signals (Gentile et al., 2013).

Unsurprisingly, research has observed that individuals with schizophrenia spectrum disorders are more susceptible to the Rubber Hand Illusion and exhibit a more rapid onset of the illusion (Peled et al., 2000; Peled et al., 2003; Thakkar et al., 2011; for a review see Klaver & Dijkerman, 2016), suggesting abnormal multisensory integration related to bodily self-experience. One interpretation is that altered proprioception outweighs visual information coming from the rubber hand (Chang & Lenzenweger, 2005). However, research which found reduced influence of visual information on proprioceptive and auditory signals in schizophrenia is inconsistent with this hypothesis (Williams et al., 2010; de Gelder et al., 2003). Alternatively, researchers have hypothesised that the higher proneness to the illusion may be caused by more flexible body representations among patients with schizophrenia. This would be consistent with anecdotal observations which found that some patients experience the illusion even before receiving tactile stimulation (Peled et al., 2000; Haggard et al., 2011). Previous work has found that body representation anomalies are pre-existing - or even predisposing – features in at-risk individuals (Chapman et al., 1978; Lenzenweger, 2010; Thakkar et al., 2011). This is also supported by evidence that found significant alterations in long-latency somatosensory evoked potential during the Rubber Hand Illusion in schizophrenic patients (Peled et al., 2003). Moreover, it has been shown that higher proneness to the Rubber Hand Illusion was detectable among healthy individuals who exhibited psychotic-like symptoms (Germine et al., 2013). With this in mind, Chapter Five aimed to investigate whether disturbances in a specific type of body representation (i.e. the body structural representation, see section 2.4.), were associated with higher proneness to the Rubber Hand Illusion and with basic symptomatology that is usually taken as phenomenological markers of schizophrenia risk (i.e. the basic symptoms, see section 1.3.1). Our results suggest that patients with schizophrenia possess more malleable body representations. Consequently, patients might be more likely to adopt faulty models of their own body’s spatial mapping and location and be more susceptible to external influences (e.g. an external visual rubber hand). Moreover, our results indicate that such aberrancies are correlated with symptoms that are considered as the first experienced phenomena of the ongoing morbid process. To test whether similar body representation disturbances are traceable in high schizotypy, Chapter Six examined the internal body representation system in individuals with high and low schizotypal personality traits. To this purpose, we utilised two tasks that target body representation directly, in the absence of multisensory cues. The next section aims to introduce different types of body representation and examine the different ways that have been employed to investigate them.

2.4. Body Representations

When we talk about body representations, we refer to the neurological and cognitive structures of the body that underlie self-representation (Waters & Badcock, 2010). Possessing a set of representations of one's body has consequences for both feelings of agency and bodily ownership, as it provides a natural reference point for understanding one's own body and its possibility to interact with the external world (Damasio, 1999). Thus, we are able to perceive our body as a coherent, holistic "me", and not merely as a disorganised collection of inputs (Tsakiris et al., 2006). This coherent experience of "me" arises from the simultaneous activation of multiple body representations, which are derived from multimodal sensory input, motor monitoring and planning sources. According to phenomenological research, the body in schizophrenia is often experienced as an object external to one's self and unrelated to events in the external world (Northoff & Stanghellini, 2016). In addition, abnormal processing of body parts and perceptual gestalts in schizophrenia spectrum disorders have been extensively documented in research (Uhlhaas & Mishara, 2007; Chan et al., 2010). These disturbances consist in the weakening of the kinetic dimension (e.g. limited sense of agency) (Van Haren et al., 2019), the kinaesthetic dimension (e.g. abnormal sensorimotor representation) (Ardizzi, 2020), and the aesthetic dimension (e.g. misperception of body's appearance) (Priebe & Rohricht, 2001; Ferri et al., 2012).

An unstable and disorganized system of body representations can include perceiving changes in proportions, size and weight of different body parts (Nelson et al., 2010) and loosening of body boundaries (Parnas et al., 2003; Noel et al., 2016; Di Cosmo et al., 2018). From a phenomenological perspective, these changes are characterised by a transformation in the subjective experience of the body. For instance, a patient might feel like they no longer inhabit their body, but rather experience it as an object (e.g., hyperreflexivity).

In phenomenology, body representations have been interpreted through the framework of intentionality, i.e., when "I" take the world as an intentional object from the position of the body. Thus, "I" am a lived body of intentions, projects and activity, but "I" am also capable of viewing my body as an objective body. This distinction echoes the phenomenological division between the body-as-object of experience or "Körper", and the body-as-subject of experience or "Leib". Whereas the "Körper" is the physical body that the agent can observe and that can be in turn observed by the others, the "Leib" is the body that the agent can pre-reflectively experience as a subject and consists in sensorimotor representation that guides actions (Merleau-Ponty, 1945). To date, there is little consensus on how many body representations exist and on how they should be functionally defined (Holmes & Spence, 2004). Several prominent theories have attempted to provide a clear conceptual distinction between two of the most pertinent types of body representation: the *body schema* and the *body image*. However, there has been confusion surrounding these definitions because of the conflation between these two concepts (Holmes & Spence, 2004; Gallagher & Zahavi 2012). Justifying the definition employed here is the fact that this definition emphasises the important distinction between the '*body as an object' (*i.e., the body image*)* and the '*body as a subject'* (i.e., the body schema), a distinction that is important for understanding the schizophrenic pathology, and, more specifically, the schizophrenic prodrome.

2.4.1. Body Image and Body Schema

Body image refers to the conscious representation of our body in space in reference to an external observer and is made up of sensory, conceptual and affective processes (Paillard, 1999; Gallagher, 2000). The body image consists of a system of perceptions, dispositions and beliefs regarding one's physical body and allows for the identification and recognition of one's body (in the objective space). Moreover, the body image often involves an abstract or partial representation of the body, as "*conscious awareness attends to one part or area of the body at a time*". The body schema is a network of integrated bodily capacities, a system of proprioceptive and sensorimotor processes that produce and regulate motor behaviour in absence of perceptual awareness (Gallagher, 1995). As pointed out by Gallagher (1995), the body schema may be best characterised as a subconscious system that plays an active role in monitoring and governing posture and movement. The body schema registers the postural changes of the body through multisensory information and produces appropriate motor control. In contrast to the abstract nature of the body image, body schema functions in a holistic way: "…*a slight change in posture involves a global adjustment across a large number of muscle systems*" (Gallagher, 1995, p. 229). Thus, we could claim that body image is perceptual in nature and body schema is enactive in nature, although they still have to work in conjunction - similarly to how perception and action work in conjunction - to shape and maintain the sense of agency and ownership. In the context of multimodal integration, the body image interprets the multisensory processes related to body perception, and the body schema interprets the multisensory processes that facilitate our motor responses.

Neuroscientific and neuropsychological findings have provided strong support for the existence of these two types of body representation: a sensorimotor representation of the body that guides actions (i.e., body schema), and a more perceptual representation – or explicit attitude - towards the body (i.e., body image). In neuroscientific literature, it has been suggested that the primary somatosensory cortex and the supramarginal gyrus are involved in mediating non-action-oriented body representations (i.e., body image). In contrast, body representations that support actions appear to be mediated by the primary motor cortex and the right extrastriate body (Di Vita et al., 2016). In neuropsychological literature, an important contribution regarding the classification of body representational systems emerges from the concept of double dissociation. In brief, a double dissociation is observed when a group of patients is impaired on a task "A", which assesses one aspect of body representation, but not on a task "B", which assesses another aspect of body representation (de Vignemont, 2009). If A and B are both body-related tasks, then one could argue that there must be two distinct processing systems of bodily information, which can be functionally dissociated by brain lesions. Several studies showcased the existence of a double dissociation between neurological patients who exhibit impairments in perceptual detection - but maintain intact sensorimotor guidance towards a stimulated location (i.e., 'numbsense') - and vice versa. Thus, some patients exhibit a specific deficit in the perceptual representation of the target (body image), whereas the sensorimotor representation remains intact (body schema). For instance, a patient might be able to verbally identify the location of a tactile stimulus but show impairments when asked to point toward the stimulus

(Paillard, 1999; Halligan et al., 1995), indicating an impairment in body schema, with a preserved body image. On the other hand, some other patients may exhibit residual tactile processing for action without perceptual awareness (Paillard et al., 1983).

Interestingly, research which has found a neurological dissociation between autopagnosia (i.e., mislocalization of body parts and bodily sensations) and body-specific aphasia (i.e. loss of lexical knowledge of body parts) have hypothesised the existence of two additional subcomponents of the body image: the body structural representation and the body semantics (Schwoebel & Coslett, 2005; Sirigu et al., 1991; de Vignemont., 2009). The body semantics corresponds to a conceptual and linguistic body representation, including body part names and functions. The body structural representation, or “visuospatial body map” consists of a structural description of the relationships between body parts, including the relative positions of different body parts relative to one another in a spatial configuration (De Vignemont, 2010). For the purpose of the present thesis, I shall focus on the body structural representation.

The body structural representation is considered to be a topological map of the body which functions as a stored representation of the relationship between body parts in relation to each other within a whole-body structure (Rusconi et al., 2009; Longo, 2016). Evidence for the existence of body structural representation comes from the study of *autotopagnosia*, a condition in which knowledge of the structural body becomes deeply impaired. Autotopagnosia is normally associated with a lesion of the left parietal lobe. Patients with a*utotopagnosia* are unable to point to parts of their body on verbal command, nor to judge the spatial relations between body parts (although their somatosensory processing remains mainly intact) (Sirigu et al., 1991). Nonetheless, they are able to describe the function of their different body parts and to utilise the body parts that they cannot localize, for instance, to perform self-initiated goal-directed tasks. (Sirigu et al., 1991), suggesting that body structural representation and body schema can be dissociated. A study from Buxbaum and Coslett (2011) described a patient who is unable to point to body parts but can perform visually guided grasping movements. Moreover, the patient could point to objects attached at different locations to the body (see also Sirigu et al. 1991). The authors interpreted these impairments as a disrupted body structural representation. Further evidence comes from a neurological condition caused by lesions in the left posterior parietal brain area: finger agnosia (Kinsbourne & Warrington, 1962). Patients with finger agnosia cannot identify their fingers, although they maintain relatively good abilities in terms of sensation and action. A study by Anema et al. (2008) examined different types of finger representations in patients with finger agnosia following a lesion in the angular gyrus (a region of the brain located in the inferior parietal lobule), and with no language or motor deficits. Patients were asked to localize a tactile stimulus delivered to the hand. Most notably, patients were assessed in three different conditions: naming the finger, pointing toward the finger on a schematic drawing, and pointing directly to the touched finger without the aid of visual feedback. The last condition is considered to involve the body schema, as it involves a sensorimotor representation of the fingers that are not consciously accessible and is used for guiding motor action (Paillard, 1999; 9, Rossetti et al., 2001). The other two tasks are believed to involve the body image – and more specifically the body structural representation - because the tactile information about the targeted finger has to be transferred to an abstract hand representation (Paillard, 1999; Dijkerman & de Haan, 2007; Anema et al., 2008). Patients performed normally only in the third condition (i.e., pointing directly to the touched finger with no visual feedback), whereas they were not able to accomplish the two other tasks (i.e., respectively naming the finger and pointing toward the finger on a hand's drawing), suggesting an impairment in the body structural representation (body image), but not in the body schema.

Moreover, neuroimaging studies have identified brain areas which are active during tasks related to body structural representation. In line with clinical literature on autotopagnosia and finger agnosia, evidence coming from fMRI studies linked body structural representation with the left superior parietal cortex, the left posterior intraparietal sulcus and the primary somatosensory cortex; the latter hosts the somatotopic map of the hand and fingers (SI) (Maldjian et al., 1999). Interestingly, alteration of the SI has been found in schizophrenia (Geyer et al., 1999). For instance, a study from Reite et al. (2003) found an anomalous asymmetry of touch-activated sources in the primary somatosensory cortex of patients and anterior and inferior displacement of such activity in their left-hemisphere. Furthermore, Minzenberg et al. (2009), found that individuals with schizophrenia exhibit hyperactivation of the left inferior posterior parietal cortex and a bilateral hypoactivation of the posterior parietal cortex. Also, abnormalities in the volume of the inferior parietal cortex (left angular gyrus) have been found as well (Buchanan et al., 2004; Nierenberg et al., 2005).

Recently, a study from Graham-Smith (2016) found a reduced acuity in body structural representations in schizophrenic patients. The researcher adopted a task widely used to investigate body structural representation in neurological patients (Kinsbourne & Warrington, 1962) and in healthy participants (Rusconi et al., 2009; Rusconi et al., 2014): the In Between Task. The task requires participants to evaluate the relationship between the spatial structure of the fingers, i.e., participants are asked to identify how many fingers are in between the stimulated fingers. This task is particularly well suited to investigate the fine-grained detail of generalised visuospatial acuity (i.e., distances between fingers). The authors found that patients with schizophrenia performed significantly worse at the task, suggesting a reduced acuity in body structural representation. This reduced acuity may be caused by a weakened internal model of the bodily self, which in schizophrenics appears more blurred and malleable (Thakkar et al., 2011).

A similar task utilised to investigate the perceived structural representation of the hand is the finger localisation task. The finger localisation task is similar to the In Between Task in that it is appropriate for investigating fine-grained body mapping. In the most common version of the task, participants are asked to identify and differentiate between stimulated fingers, first with hands in view and then with hands hidden. The Finger Localization Task has often been used to diagnose patients with finger agnosia, the aforementioned disorder which affects the ability to identify stimulated fingers (Reed, 1967; Benton, 1955; Miller & Hynd, 2004), following posterior parietal lesions (Miller & Hynd 2004). In Chapter Six, we adopted both the In Between Task and the Finger Localization Task to investigate body structural representation in individuals with high and low schizotypal traits, in the absence of multisensory stimulation. Results from Chapter Six found that a deficient body structural representation in individuals with high schizotypy and high dissociative traits (i.e., fragmentation of own identity), suggesting that abnormal body structural representation may represent a potential early marker of schizophrenia.

What this suggests is that schizophrenia spectrum disorders are rooted in a lack of anchoring to one own's body. With this in mind, we can hypothesise that the disturbances in the minimal self that are observed in schizophrenia could be – at least partially - caused and maintained by more basic disturbances of body representation, such as in the body image. Whether this aberrancy in body image representation is a consequence of an abnormal body schema is still unclear. However, the efficiency of the body schema is deeply interconnected with the successful interpretation of the different body image components. Therefore, it is more likely that both these types of body representations are affected in schizophrenia spectrum disorders, suggesting a more profound dis-attunement with the lived body, which would detrimentally affect the sense of 'mineness' (for further comments, see section 7.3.).

Chapter Three

Higher proneness to multisensory illusions is driven by reduced temporal sensitivity in people with high schizotypal traits

3.1. Abstract

A coherent sense of self, typically altered in schizophrenia, is accompanied by an ability to meaningfully integrate sensory information. According to the idea of schizophrenia as a continuum, the higher proneness to multisensory illusions observed in schizophrenia may extend to schizotypy. In the present study, this hypothesis was directly tested by means of the Double Flash Illusion in participants with low and high schizotypal traits. Results confirmed that individuals with high schizotypal traits exhibit enhanced proneness to the illusion when compared with individuals with low schizotypal traits. Importantly, such higher proneness was fully explained by a significantly reduced temporal sensitivity in the integration of sensory information. Thus, we conclude that reduced temporal sensitivity accounts for enhanced proneness to illusions in people at higher risk of developing schizophrenia and may therefore represent an early marker of the disorder.

3.2. Introduction

The development of the ability to use cues from multiple senses in concert is intertwined with the emergence of a sense of self (Bremner et al., 2012; Rochat, 2011; van Dam et al., 2014). Consistently, impairments in multisensory temporal processing that extend beyond those observed in unisensory domains have been observed in schizophrenia spectrum disorders (Stevenson et al., 2017). Such impairments are thought to contribute to abnormal self-experiences (Postmes et al., 2014) and abnormal perception of the outer environment (Tseng et al., 2015). Within this theoretical framework, it has been hypothesised that symptoms such as hallucination and delusion might emerge in this atmosphere, when, over the course of many months or even years, the patients attempt to restore perceptual coherence (Postmes et al., 2014).

Multisensory integration abnormalities in schizophrenia spectrum disorders have often been investigated using audio-visual illusion tasks, such as the streaming-bounce illusion (Zvyagintsev et al., 2017), the McGurk illusion (Martin et al., 2013) and the double-flash illusion (DFI) (Haß et al., 2017). All these illusions are determined by the brain's effort to integrate information from different sensory modalities into unified, coherent precepts. Given the characteristics of the stimuli presented, such percepts (the illusory outcome) are often incoherent with the actual sensory input. Notably, these sensory illusions reflect specific temporal constraints between the senses. Such constraints provide a contextual framework for interpreting ambiguous (e.g., the precise co-occurrence of certain audio-visual events in the streaming-bouncing illusion) or otherwise incoherent stimuli (e.g. the inconsistent correspondence between lip movements associated with a compatible but mismatched sound in the McGurk illusion; or the number and temporal disparity between low-level audio-visual events in the DFI). Thus, such illusions have been commonly utilised to assess whether multimodal processing is intact, or not, in non-clinical and clinical conditions.

Research that utilised the aforementioned, and other types of illusions, have consistently suggested that higher susceptibility to audiovisual illusions in schizophrenia is linked to reduced temporal sensitivity. Such reduced temporal sensitivity is indexed by an enlarged temporal window within which the illusion is maximally perceived, namely the Temporal Window of Illusion (TWI; Cecere, Rees, & Romei, 2015). TWI, therefore, represents an inverse index for temporal sensitivity (i.e. enlarged TWI = reduced temporal sensitivity). More specifically, the temporal window within which stimuli coming from different sensory modalities tend to be integrated, rather than segregated, appears enlarged in schizophrenia (Stevenson et al., 2017) and in individuals with high schizotypal traits (Ferri et al., 2017). Whether individuals with high schizotypal traits experience greater susceptibility to multisensory illusions is currently unknown. If this would be the case, whether this phenomenon may be fully accounted for by a more general temporal sensitivity mechanism during sensory processing, remains another relevant open question to be addressed.

According to a dimensional approach to schizophrenia, schizotypy represents a continuum throughout the general population ranging from psychologically healthy individuals (low schizotypy) to schizophrenia-prone individuals (high schizotypy) (Kwapil & Barrantes-Vidal, 2015, Nelson et al., 2013). Notably, schizophrenia-proneness does not necessarily imply schizophrenia-risk, and most schizotypes are not expected to develop schizophrenia. Nonetheless, considerable overlaps between schizotypy and schizophrenia have been found both in terms of etiological factors - at the genetic, biological, and psychosocial levels (Barrantes-Vidal et al., 2015) – and both concerning a wide range of perceptual, cognitive, and motor impairments (Ettinger et al., 2015). Most importantly, investigating multisensory processing in individuals with high schizotypy offers the advantage to bypass all the confounding variables of a complex disorder such as schizophrenia (i.e., pharmacological treatment, the severity of symptoms, compensatory strategies, distress and comorbidity). Furthermore, using the same experimental paradigms in schizotypy and schizophrenia may contribute to, first, further detailing the idea of a “continuum” between the two conditions (Ettinger et al., 2015); second, to identifying early risk markers.

The aim of this study was to investigate the susceptibility to auditory-induced visual illusions in individuals with high and low schizotypy by means of the DFI, which has been already proven to be informative in people with schizophrenia (Haß et al., 2017). We specifically chose to test very brief audio-visual stimuli as they have the appropriate temporal resolution for assessing the fine-grained temporal profile of crossmodal interactions (e.g. Murray et al., 2016, Romei et al., 2012, Romei et al., 2007) and its alterations (Bao et al., 2017, Haß et al., 2017, Noel et al., 2017, Stevenson et al., 2017, Stevenson et al., 2014). Specifically, we hypothesize that by comparing the proneness to the DFI between low- and high-schizotypal groups, a higher percentage of perceived illusion in the high-schizotypal group is expected. Importantly, in line with Ferri et al. (2017), we expect that the enhanced percentage of illusory precepts in the high-schizotypal group will be accounted for by an enlarged TWI in this group relative to the low-schizotypal group.

3.3. Materials and Methods

3.3.1. Participants

One hundred ninety-six adult volunteers, recruited via mailing lists at the University of Essex, were screened with respect to schizotypal traits using the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). The questionnaire was administered electronically via Qualtrics, a web-based data collection system. The SPQ is a 74-item forced choice (Yes/No) questionnaire based on clinical features of schizotypal personality disorder described by the DSM-III-R and DSM- IV-TR (APA, 1987; APA, 2000). All items answered "yes" are scored as one: therefore, the total maximum score is 74. Factor analysis has revealed that three main factors best represent schizotypal personality: the cognitive-perceptual (i.e., odd beliefs, unusual perceptual experiences, paranoid ideation and ideas of reference), the interpersonal (i.e., excessive social anxiety, constricted affect, no close friends), and disorganized factors (i.e. eccentric behaviour, eccentric speech) (Raine et al., 1994). These three factors structure is comparable to the three analogous factors reported for schizophrenic symptomatology (i.e., positive, negative, disorganised symptoms) (Fossati et al., 2003).

The distribution of scores was divided into quintiles, with the first quintile representing the participants rated as low schizotypes (score range 5–16, n = 32), and the fifth quintile representing the participants rated as high schizotypes (score range 36–68, n = 32). As a result, a total of sixty-four participants falling within the first and fifth quintile were selected to perform the DFI task (Cecere et al., 2015, Shams et al., 2000, Shams et al., 2002). The study was approved by the University of Essex Ethics Committee. All participants read and signed a consent form prior to their participation. All the participants included in the "low schizotypes" and the "high schizotypes" groups had normal or corrected vision, and normal hearing. They did not report any history of substance abuse or other (neuro)psychiatric disorders. Age and gender were matched across groups. Demographic details are reported in Table 1.

Table 1. Demographics.

	Low Schizotypy	High Schizotypy
SPQ score range	5–16	36–68
N	32	32
No of females	25	25
Mean age(SD)	29(9)	26(7)
British White	41%	44%
Other White	50%	50%
Asian/Indian	9%	6%

Performance of three participants in the first quintile and four participants in the fifth quintile did not fit the sigmoid function (see data analysis below), mostly due to unreliable report of the illusion (as a function of the time interval between the two sounds) and were excluded from the analysis. Therefore, a total of fifty-seven participants (29 in the low- and 28 in the high-schizotypal group) were included in the current analyses. The participants gave written consent before taking part in the experiment, and all were naïve to the actual purpose of the study.

3.3.2. Apparatus and stimuli

Apparatus and stimuli were the same as Cecere, Reese and Romei, (2015). On each trial, the visual stimulus consisted of a solid white circle subtending 2 degrees of visual angle, presented in a dimly lit room at 57 cm viewing distance on a 17′ CRT display (ViewSonic Graphics Series G90FB, refresh rate 85 Hz) for the duration of one refresh frame (~12 ms). Auditory stimuli were stereo, sinusoidal pure tones (frequency: 3.5 kHz; sampling rate: 44.1 kHz) of the duration of 7 ms presented by a pair of stereo PC speakers placed either side of the monitor. This arrangement allowed coincident spatial perception of visual and auditory stimuli as they were perceived spatially aligned with the location of the visual stimuli on the screen (Macaluso, George, Dolan, Spence, and Driver, 2004). Stimulus presentation and behavioural response recording were controlled by a PC running E-Prime software (version: 2; Psychology Software Tools, Pittsburgh, PA).

3.3.3. Procedure

The procedure was adapted from Cecere et al. (2015). All trials started with a small fixation cross continuously displayed at the centre of the screen. After a random time-lag of 500–1500 ms, a single visual flash of a diameter of 2 cm, and an auditory stimulus pair were presented. Each visual stimulus flashed for 12 ms, and each auditory stimulus had a frequency of 3500 Hz and a duration of 7 ms. While the flash was always displayed simultaneously with the first auditory stimulus, the second auditory stimulus was played at 15 different stimulus onset asynchronies (SOAs) from the first auditory stimulus onset ranging from 36 to 204 ms (with each interval corresponding to an increment of one refresh frame: 12 ms) (see Fig. 3.1). According to Apthorp et al. (2013), although a frame is generally reported as 12 ms for an 85 Hz refresh rate, the actual duration of the flash is estimated to be much shorter, due to the phosphor decay rate of the cathode ray tube monitor (Elze, 2010). Therefore, the present investigation will refer to SOAs rather than inter-stimulus intervals, as the onset timing of each stimulus is known more precisely than the offset.

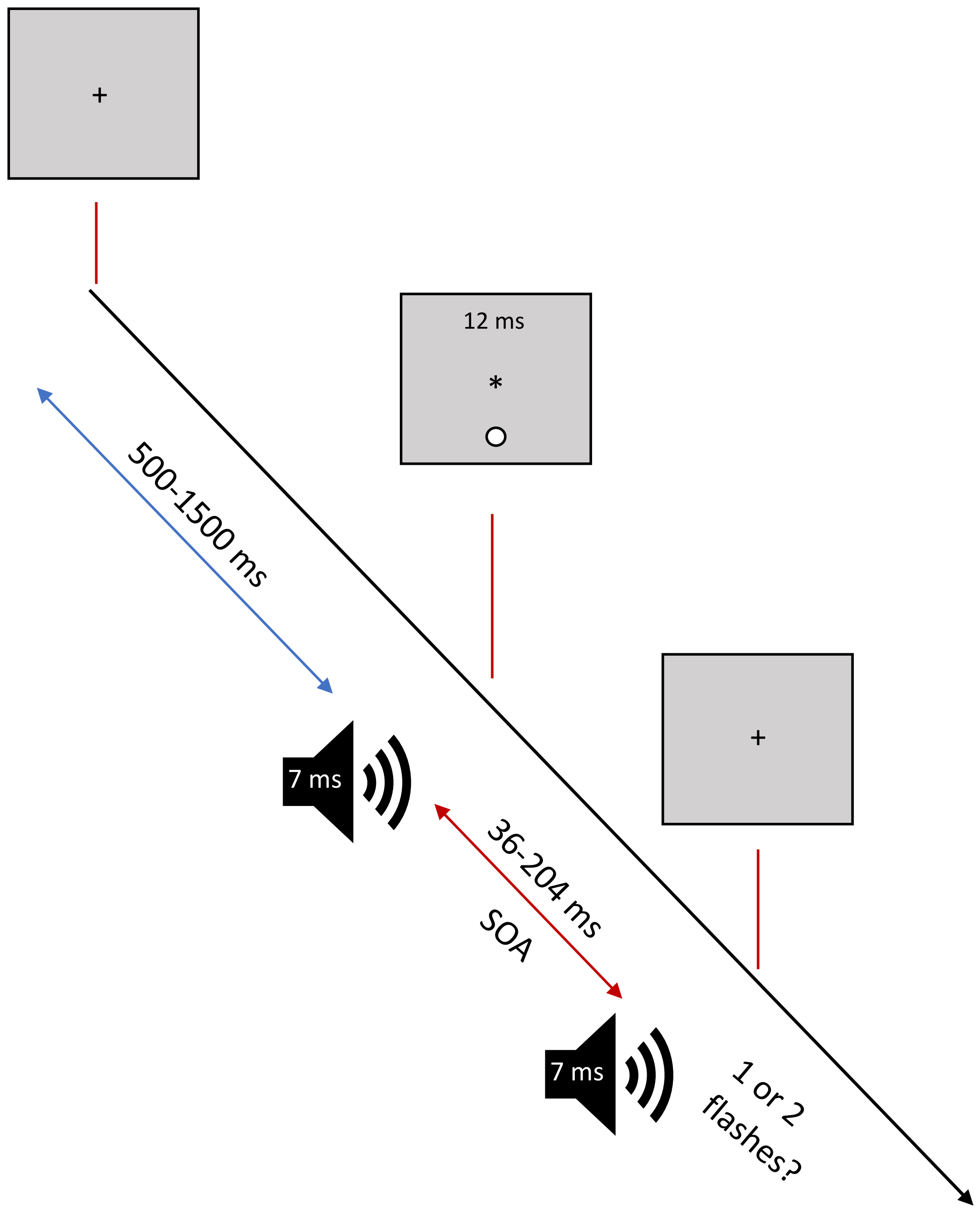

Fig. 3.1. Schematics of the experimental paradigm. For each trial, participants were instructed to fix a white fixation point in the middle of a grey screen lasting for a period randomly ranging between 500 and 1500 ms. Subsequently, they were presented with one (and always one) visual flash lasting for one refresh rate (12 ms) accompanied by two (and always two) brief (7 ms) auditory stimuli. The onset of the first beep was always temporally coincident with the onset of the visual flash, whereas the onset of the second beep could be presented at 15 different delays, with onset ranging between 36 and 204 ms in 12 ms steps from the first auditory stimulus onset. Participants were explicitly asked to report whether they perceived one vs two visual flashes.

The presentation of the auditory pair together with the single flash was aimed at inducing the perception of a second visual illusory flash while there was only ever one flash. In particular, the shorter the SOA, the stronger the illusion was expected to be (Cecere et al., 2015, Shams et al., 2002). This range of SOAs and its sampling interval has been shown to be optimal to determine the time frame within which the DFI illusion is maximally perceived while also extending beyond this time frame (Cecere et al., 2015). Therefore, it might likely provide a sufficiently sensitive time window within which any difference in TWI between low and high schizotypy could be investigated.

Participants were instructed to pay attention to visual stimuli only and to ignore the sounds. Moreover, as correct responses were favoured over speeded responses, participants were instructed to verbally report after each trial whether they perceived one or two flashes. The experimenter inputted the participant’s verbal response by pressing the corresponding button on a keyboard, which in turn started the subsequent trial. The experimental block consisted of 150 trials, with each of the 15 SOAs being randomly presented for ten times.

3.4. Data Analysis

3.4.1. Proneness to the DFI

Recent findings have shown that patients with schizophrenia have a higher proneness to the DFI (Haß et al., 2017). According to the continuum hypothesis, we tested whether a similar observation can be made for participants with high-schizotypal traits. To this aim, the percentage of “two” responses across all SOAs out of 150 (Overall proneness to the illusion [OPI]) were counted for each individual independently of their

SOAs. This percentage was compared across the low- and high schizotypy groups, testing the specific hypothesis that participants in the high schizotypy group are expected to show higher proneness to the illusion. A one-tailed independent sample t-test was used to examine the difference between the total amount of perceived illusion in the low and high schizotypy groups. Finally, a linear regression analysis was performed to investigate the contribution of each factor of the SPQ (i.e., perceptual-cognitive, interpersonal and disorganized factors) to the variance in the proneness to DFI. We expected the cognitive-perceptual factor, also referred to as positive schizotypy (Ettinger et al., 2014), more than the other factors, to significantly account for higher proneness to DFI in people with high schizotypy. This hypothesis was based on prior evidence that both positive schizotypy (e.g. Benson and Park, 2019; Bressan & Kramer, 2013; Van Doorn et al., 2018) and positive symptoms of schizophrenia (e.g. Peled et al., 2000) are commonly associated to proneness to perceptual illusions.

3.4.2. Temporal window of illusion (TWI)

In order to calculate for each individual and group the TWI, i.e. the temporal window within which participants maximally perceive the DFI, and thus the point from which the illusion starts to degrade, the number of trials in which the illusion was perceived (total percentage of “two” responses out of 10) was plotted for each SOA separately for individuals in the low- and high schizotypy groups. A psychometric sigmoid function $y = a+b/(1+exp(-(x-c)/d))$; a = lower asymptote for high values of x; b = amplitude of the psychometric curve (a+b forms the upper asymptote for low values of x); c = inflection point; d = slope] was fitted to the individual observations. Note, that parameter *d* determines also the direction of the function and, generally, can be either positive (upward sigmoid) or negative (downward sigmoid). The parameters estimation was done using the *curve fitting* option in Matlab. The fitting procedure assigns random values on the interval (0,1) as starting points for the parameters (a,b,c,d), that by default are unbounded. Normally, a starting point of 100 for the parameter c (i.e. the inflection point) was given, as 100 is near the average TWI for two simple stimuli (Cecere et al., 2015; Cooke et al., 2019). The sigmoid function is then fitted to the data, giving us a downward function (i.e. with a negative d and a positive b, or viceversa). The estimated SOA (in ms) corresponding to the inflection point (centre) of the fitted sigmoid was considered as the individual TWI within which the illusion was maximally experienced. According to our hypothesis, we expect the TWI to be enlarged in the high- relative to the low schizotypy group. Therefore, a one-tailed independent sample t-test was used to examine the difference between the mean inflection point and statistically compare the TWI of individuals with low- and high-schizotypal traits. Finally, linear regression analyses were performed to investigate the contribution of each factor of the SPQ (i.e. Perceptual-Cognitive, Interpersonal and Disorganized factors) to the variance in the TWI. We expected the Perceptual-Cognitive factor, also referred to as positive schizotypy (Ettinger et al., 2014), more than the other factors, to significantly account for larger TWI in people with high schizotypy. This hypothesis was based on prior evidence that positive schizotypy is associated with larger temporal binding window (Ferri et al., 2017).

3.4.3. Relationship between proneness to DFI and the TWI

An outstanding question to investigate is whether an enhanced proneness to the DFI can be determined by an extended TWI or whether, alternatively, might be the result of more general noise in sensory processing (Javitt, 2009, 2015). To test this hypothesis, we first ran a regression analysis between individual TWI and the individual overall proneness to DFI (OPI) using both parametric (Pearson) and non-parametric (Spearman) correlations. Moreover, to test their robustness we computed skipped parametric (Pearson) and nonparametric (Spearman) correlations (Wilcox, 2004) using the Robust Correlation toolbox (Pernet, Wilcox, and Rousselet, 2012) and conducted null hypothesis statistical significance testing using the nonparametric percentile bootstrap test (2000 resamples; 95% confidence interval, corresponding to an alpha level of 0.05), which is more robust against heteroscedasticity compared with the traditional t-test (Pernet et al., 2012). Next, we tested whether any positive correlation between these measures can be simply explained by the relative number of trials falling within a temporal window, and therefore more sensitive to the perceived illusion. In other words, if participants with high schizotypy have an enlarged TWI relative to participants with low schizotypy, they will perceive the illusion in a comparatively higher number of trials encompassing a wider range of SOAs. To specifically test this hypothesis, we normalized the measure of proneness to the DFI to each individual TWI by calculating the percentage of perceived illusion falling in the 3 SOAs preceding the inflection point. In this way, the absolute number of SOAs sensitive to the illusion was kept constant across participants, and any differential effect of proneness was now controlled for by any individual difference in TWI. A one-tailed independent sample t-test was calculated now comparing this newly obtained weighted proneness to the illusion (WPI) for low and high schizotypy groups. Finally, parametric and nonparametric correlations were performed to test whether any positive relationship still exists after normalizing the proneness to the DFI to each individual TWI.

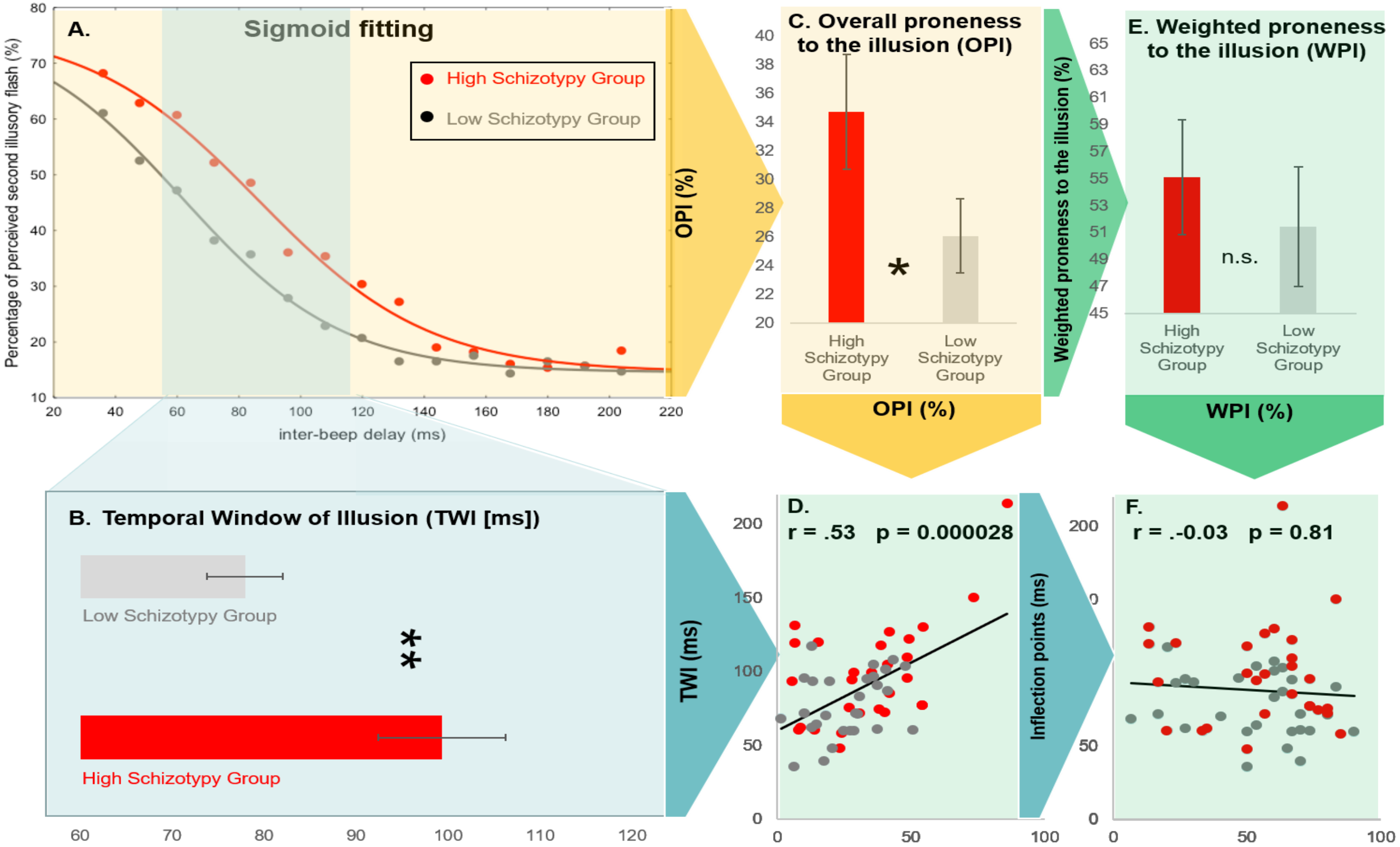

Fig. 3.2. Relationship between temporal sensitivity and proneness to the illusion in low- and high schizotypy. (A) Average probability of perceiving the illusion plotted as a function of SOA for low- (grey dots and curve) and high-schizotypal groups (red dots and curve). The curves represent the sigmoid fit determining (B) the temporal window of illusion (TWI), i.e. the temporal window within which the illusion is maximally perceived, corresponding to the inflection point of the sigmoid. (C) The proneness to the illusion across all inter-beep delays (Overall Proneness to the Illusion [OPI]) is significantly higher in high-relative to low-schizotypal individuals and (D) positively correlates with their TWI. (E) When individual differences in TWI are taken into account, and the proneness to the illusion is normalized for the individual TWI, no significant differences in weighted proneness to the illusion (WPI) and (F) no positive correlation between WPI and TWI can be found.

3.5. Results

3.5.1. Proneness to the DFI

First, as expected, in line with the idea of a continuum with schizophrenia (see Haß et al., 2017), we found that participants with high schizotypy show a higher overall proneness to the illusion (34.71%) relative to participants with low schizotypy (25.24%) (one-tailed independent sample t-test $t(55) = 2.06$; $p=0.02$) (Fig. 3.2C). Interestingly, only two factors of the SPQ, the Interpersonal (8%) and the Perceptual-Cognitive (7.4%) factors, accounted for a significant proportion of the variance in the proneness to DFI.

3.5.2. Temporal window of illusion (TWI)

Second, our results revealed for the first time that high schizotypy individuals show a significantly enlarged TWI (98.45ms) relative to low schizotypy individuals (77.14ms) (one-tailed independent sample t-test: $t(55) = 2.78$; $p < 0.004$; see Fig. 3.2A and B). Interestingly, only two factors of the SPQ, the Disorganized (9.6%) and the Perceptual-Cognitive (7.1%) factors accounted for a significant proportion of the variance in the TWI.

3.5.3. Relationship between proneness to DFI and the TWI

We reasoned that the difference in proneness might be mediated by the significant difference in TWI between the two groups. If this is the case, one might expect a trivial positive correlation between the proneness to the illusion and the TWI. However, by normalizing proneness to each individual TWI, the between-group difference in proneness to the illusion should disappear as well as their correlation. In order to test for the specific hypothesis that any effect of higher proneness to DFI may be more simply explained by a larger TWI in high schizotypy, the individual proneness to the illusion was computed for each participant both across all SOAs (Overall proneness to the illusion, OPI) and as a function of each individual TWI (Weighted proneness to the illusion, WPI). With regards to the WPI, we computed for each individual the proneness to the illusion for the three SOAs delays preceding their individual infection point, i.e. the largest SOA defining the TWI, so as to first normalize the proneness to the illusion to each individual TWI and second, to compute this weighted measure on a comparable number of trials across participants. As expected, a first trivial finding was that individual TWI positively correlates with the overall proneness to the illusion (OPI) (Pearson $r=.53$; $p < 0.0001$; Spearman $r=0.43$; $p < 0.001$) and such relationship survived robust correlation (skipped Pearson $r=0.451165$; CI = [0.203726 0.653286]; skipped Spearman $r=0.492489$ CI = [0.234016 0.691173]) (2D). Crucially, when the data were normalized, low- and high schizotypy groups did not show any significant difference in the amount of proneness to the illusion (low schyzotypy: 51.14%; high schyzotypy 55.12%; $t(55) = 0.61$; $p=0.54$). Accordingly, when controlling for the TWI, no significant correlation was found between the proneness to the illusion and TWI (Pearson $r=-0.03$; $p=0.81$; Spearman $r=-0.08$; $p=0.53$).

3.6. Discussion

Grounding on previous research that demonstrated an enlarged audio-visual TWI in schizophrenia (Haß et al., 2017), the present study aimed to expand this finding to schizotypy. Therefore, the DFI was used to investigate audio-visual multisensory integration in schizotypy. In agreement with the hypothesis of a schizophrenia continuum (DeRosse et al., 2015; Kwapil & Barrantes-Vidal, 2015; Nelson et al., 2013), results revealed that high schizotypy individuals, similar to schizophrenic patients (Haß et al., 2017), show a significantly enlarged TWI, relative to low schizotypy individuals. Interestingly, this larger TWI was less dramatically enlarged relative to comparable data collected in schizophrenic patients (see Haß et al., 2017), thus further supporting the hypothesis of a progressive continuum between high schizotypy and schizophrenia. Notably, when looking at the contribution of the SPQ factors accounting for both proneness and TWI of the DFI, we found only the Perceptual-Cognitive factor to clearly account for both phenomena. This suggests, in line with previous literature (Ferri et al., 2017), that alterations in perceptual and cognitive factors are those accounting for the reduced temporal sensitivity and the increased proneness to DFI in the high-schizotypy group in our experiment.

Accordingly, as in schizophrenia (Haß et al., 2017), results revealed that individuals with high schizotypy exhibit greater proneness to the DFI, as compared to participants with low schizotypy. However, in the study of Haß et al. (2017), it was not clear whether such an enhanced proneness was the direct consequence of an extended TWI of schizophrenic patients or instead, independently of it, the result of an impoverished ability to segregate information, because of a more general noise in sensory processing (Javitt, 2009, 2015). Indeed, several studies would suggest that sensory noise may lead to modulation of the sensitivity to illusions, independently of timing issues (Javitt, 2009; Moro & Steeves, 2018; Perez et al., 2015). Nevertheless, in our study, the normalization of the individual proneness to illusion to each individual TWI allowed us to disambiguate between these two possibilities, at least in our high schizotypy group. After normalization, the between-group difference in proneness to the illusion disappeared, as well as its correlation with individual TWI.

Therefore, based on these findings, we can discard the alternative hypothesis that our results reflect a general problem in sensory processing per se (Javitt, 2009, 2015) that is independent of the individual TWI. Instead, our novel findings point to the idea that a reduced temporal sensitivity as indexed by an enlarged TWI fully mediates the proneness effects of the crossmodal induced illusion observed in the high- (vs low-) schizotypy group. It can still be argued that the effects we observe here may be the result of a temporal sensitivity issue in the visual system per se, rather than a multisensory binding problem. In this regard, Kostaki & Vatakis (2016) have shown that a decreased ability to distinguish two visual flashes in time enhances the amount of double-flash illusions. Therefore, difficulties in the timing of unisensory processing may lead to a general increase in the amount of illusions. Our current dataset does not allow us to assess this specific hypothesis. However, a difficulty in distinguishing events in time even in the unisensory modality would not be in contradiction with the general hypothesis of a wider window of temporal integration, nor with the literature in patients with schizophrenia, who have difficulties with both unisensory and multisensory processing (Foucher, et al., 2007; Giersch et al., 2009; Stevenson et al., 2017). Indeed, the main issue we have identified here is a temporal sensitivity reduction in people with high schizotypy in the context of a crossmodal experimental design.

All in all, our results suggest that the difference in the proneness to the illusion in low- and high schizotypy groups is likely driven by an enlarged temporal window of crossmodally-induced visual illusion, ultimately accounted for by an overall reduced temporal sensitivity in the high schizotypy group. Finally, evidence of abnormal temporal processing in both sub-clinical and clinical samples may shed light also on the nature of anomalous multisensory self-experiences (Postmes et al., 2014) that are predictive of schizophrenia onset (Nelson et al., 2012), such as diminished sense of body ownership and agency (Postmes et al., 2014). Indeed, both these basic aspects of self-experience depend upon the temporal proximity of multisensory events (Costantini et al., 2016; Moore & Fletcher, 2012). Consequently, interventional strategies aimed at enhancing temporal resolution in sensory processing in schizotypy and schizophrenia may, at the same time, improve self-perception.

Chapter Four

The temporal sensitivity to the tactile induced Double Flash Illusion mediates the impact of the beta oscillations on schizotypal personality traits

4.1. Abstract

The coherent experience of the self and the world depends on the ability to integrate vs segregate sensory information. Optimal temporal integration between the senses is mediated by oscillatory properties of neural activity. Previous research showed reduced temporal sensitivity to multisensory events in schizotypy, a personality trait linked to schizophrenia. Here we used the tactile-induced Double-Flash-Illusion (tDFI) to investigate the tactile-to-visual temporal sensitivity in schizotypy, as indexed by the temporal window of illusion (TWI) and its neural underpinnings. We measured EEG oscillations within the beta band, recently shown to correlate with the tDFI. We found individuals with higher schizotypal traits to have wider TWI and slower beta waves accounting for the temporal window within which they perceive the illusion. Our results indicate reduced tactile-to-visual temporal sensitivity to mediate the effect of slowed oscillatory beta activity on schizotypal personality traits. We conclude that slowed oscillatory patterns might constitute an early marker for schizophrenia proneness.

4.2. Introduction

Identifying biomarkers for the early diagnosis of schizophrenia has become a crucial goal of current research. Schizophrenia is a highly debilitating disorder which affects about 0.5% of the worldwide global population (Sukanta et al., 2005). Schizophrenia often emerges in late adolescence or early adulthood, and its symptoms are non-remitting. Interestingly, the emergence of the disorder is typically preceded by a 3-4-

year prodromal phase in 75% of patients (Hafner et al., 2003; Sorensen et al., 2009). During this phase, subtle changes and sub-threshold psychotic symptoms usually emerge (Klosterkötter et al., 2001). As such, recent research has increasingly focused on identifying those individuals at a higher risk of developing schizophrenia and has strived to identify appropriate strategies for risk prediction and early intervention (Fusar-Poli et al., 2013, McGorry et al., 2009). Researchers have identified a series of cognitive and behavioural variations of schizophrenic traits which, while of reduced severity, share salient characteristics similar in form. These variations are thought to form a single personality trait: schizotypy (Lenzenweger 2018; Stotz-Ingenlath 2000). Schizotypy seemingly shares a factor-structure with schizophrenic symptoms; namely the positive, negative and disorganised subscale. It has been hypothesised that elevated levels of schizotypy represent a vulnerability to schizophrenia (Kwapil et al., 2013). As such, it could be argued that schizotypy and schizophrenia are *qualitatively* close but *quantitatively* distant. Areas of overlap between schizotypy and schizophrenia have indeed been shown both at the behavioural and neural levels (Koychev et al., 2011; Ettinger, U. et al. 2015) in several domains.

At the behavioural level, for example, both schizophrenia and schizotypy have been associated with altered responses to somatosensory stimuli (Lenzenweger et al., 2000; Chang et al., 2005; Benson et al., 2019; Michael & Park, 2016). Proprioception and touch allow for the proper discrimination between the outer environment and the sense of one's bodily boundaries. As such, a distorted haptic or proprioceptive sense could invalidate proper self-other boundary recognition. Related to this, Ferri et al. (2016) investigated the role of touch remapping in people with high and low schizotypy. They demonstrated altered remapping of environmental stimuli in the bodily space in the high- relative to the low schizotypy group. Dysfunctions in somatosensory processing and its integration with other senses seemingly lead to a more malleable body representation and increased proneness to multisensory bodily illusions both in schizophrenia and schizotypy (Thakkar et al., 2011; Ferri et al., 2014; Michael & Park, 2016). This heightened proneness to multisensory illusions might also be accounted for by another perceptual dysfunction seemingly shared by both schizophrenia and schizotypy, namely a dysfunction in the temporal profile of multisensory integration. Researchers have indeed observed that both schizophrenic patients (Foucher et al., 2007; Stevenson et al., 2017; Haß et al., 2017) and high schizotypy individuals (Ferri et al., 2017; Ferri et al. 2018) often experience stimuli that are further apart in time and in space as co-occurring, possibly leading to higher proneness to multisensory perceptual illusions, something that has been observed in Chapter Three.

At the neural level, neurophysiological evidence suggests that schizophrenia is associated with abnormalities in oscillatory activity and functional connectivity, especially in the beta- and gamma band frequencies and that these impairments are linked to both perceptual and cognitive deficits (Uhlhaas et al., 2008). Moreover, such observations, already described in schizophrenia, have been extended to schizotypy (Koychev et al., 2011). Interestingly, evidence is now emerging linking neural oscillations in distinct frequency bands to different mechanisms of multisensory processing (Senkowski et al.,2008; Ronconi et al., 2017). An investigation conducted by Cecere, Rees, and Romei (2015) using the audio-visual Double Flash Illusion task (aDFI) in healthy individuals, found a relationship between individual's alpha band oscillations in the visual cortex and the Temporal Window of Illusion (TWI). In a typical aDFI, a participant is presented with a single flash as the visual stimulus paired with two auditory beeps presented in quick succession. The pairing of the two auditory stimuli often results in the perception of a second illusory flash, even if only one flash is ever presented (Shams et al., 2000). In particular, Shams et al. (2002) adopted a version of the illusion, which uses a wide range of inter-beep intervals, well-suited to determine the size of the TWI (Shams et al., 2002; Cecere et al., 2015). Using electroencephalography (EEG) to measure brain activity, the researchers found a link between the TWI and the individual alpha frequency. More specifically, they found that slower alpha frequencies were associated with longer TWIs and vice versa. The authors interpreted these findings as a sampling mechanism gating sensory information into temporal units. These findings have been recently replicated (see Cooke et al., 2019; Keil & Senkowski, 2017). Moreover, Cooke et al. (2019) investigated the neural dynamics related to the tactile version of the DFI, that is the tactile-induced DFI (tDFI), where the two auditory stimuli are replaced by two tactile stimuli (as in Violentyev et al., 2005). The researchers found that the TWI induced by the tDFI does not relate to the individual alpha frequency but to the individual beta frequency instead. More specifically, they found that slower beta frequencies are associated with longer TWIs and vice versa.

Taken together, these results suggest that prolonged periods of temporal integration between different sensory modalities, which have been observed in schizophrenia (Stevenson et al., 2017) and also characterize schizophrenic-like subclinical conditions (Haß et al., 2017), may at least partially originate from a slowing-down of those oscillatory frequency patterns associated with the temporal dynamics of multisensory integration processes. In other words, prolonged periods of temporal integration between different sensory modalities would mediate the impact of specific oscillatory pattern changes on individual levels of schizotypy. The overarching goal of our work is to test this model with the final aim of providing a neuro-behavioural early marker for schizophrenia risk. This goal will be achieved through the validation of the following empirical points:

(i) extending the findings of Ferri et al. (2018), who showed enlarged TWI in high schizotypes using the aDFI, to the somatosensory domain, hence using the tDFI;

(ii) replicating the findings of Cooke et al. (2019), who showed that the individual TWI for the tDFI positively correlates with the individual beta frequency (IBF) in the occipital cortex;

(iii) investigating the potential association between schizotypy and IBF.

We expect people with high schizotypy to show an enlarged TWI for the tDFI, in turn predicted by a slower individual beta frequency. Most importantly, the association between the individual beta frequency and the individual scores in a self-report measure of schizotypy, should be mediated by the size of the TWI.

4.3. Material and Methods

4.3.1. *Participants*

An a-priori sensitivity power analysis (G*Power) was performed to determine the sample size that would provide ≥80% power to find correlations between behavioural and EEG data corresponding to an effect size $r = 0.50$. The analysis returned a sample of 26 participants. This effect size estimate was chosen based on a recent study showing that both the speed of individual alpha oscillations predicts the temporal window of the auditory-induced illusion and that the speed of individual beta oscillations predicts the temporal window the tactile-induced double flash illusion with an effect size $r > 0.50$ (Cooke et al., 2019). Studies reporting correlations between auditory- or tactile- induced illusions and SPQ scores were not available. A total sample of 55 participants (33 females, mean age 25) volunteered to take part in the study after having been screened with respect to their schizotypal traits using the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991). The questionnaire was administered through Qualtrics, a web-based data collection system. The study was approved by the University of Essex Ethics Committee. All participants read and signed a consent form prior to their participation. None of the participants reported any history of substance abuse or other neuropsychiatric disorders. Furthermore, they reported normal or corrected-to-normal vision.

4.3.2. Apparatus and procedure

All visual stimuli were presented on a 17.5” cathode ray tube monitor via a Dell Optiplex 960 computer (Windows XP, resolution: 1280x1024) with a refresh rate of 85Hz. The tactile stimulation was provided by a Heijo Research Electronics tactile stimulator taped onto the participant’s left index finger. The stimulator would produce a suprathreshold tap by pushing a plastic tip against the participant’s skin whenever a current was passed through the solenoid. White-noise (approximately 50db) was continuously played to participants through speakers during the tactile stimulation, to cover the mechanic noise produced by the tactile stimulator (Experimental stimuli were presented via E-prime (version 2.0; Psychology Software Tools, Pittsburgh, PA). The electroencephalogram (EEG) was recorded at 500Hz from 64 Ag/AgCl electrodes mounted on an elastic cap (Easycap, Herrsching, Germany) alongside the ground electrode (position: AFz) and the reference electrode (placed upon the right mastoid bone). The EEG signals were amplified using BrainVision Recorder (BrainProducts GmbH, Gilching, Germany). All the electrodes were set at an impedance of a maximum of 10k. In all trials, participants were presented with a flashing disc of a diameter of 2 cm displayed against a grey background. The disc always flashed once for 12 ms and was located below a small fixation cross continuously present at the centre of the screen. During the task, the disc presentation was always paired with a double tactile stimulation (double tap) to the left finger. Each participant was told to fixate the central cross at all times and to verbally report the number of flashes they saw on the screen, regardless of what was felt under the finger. The experimenter responded according to the participants' report (1 or 2 flashes) by pressing "1" or "2" (respectively) on the keyboard. Following the experimenter inputting the participant's response, a varying time interval between 500 and 1500 ms passed before the following visuo-tactile stimulus pair was presented. The second tactile stimulus always followed the first visuo-tactile pair. The two tactile stimulations were delivered one after the other at varying Stimulus Onset Asynchronies (SOAs) ranging between 36 and 204 ms with increments of 12ms. Each block of trials had 15 different time intervals between taps (repeated ten times) with a total of 150 randomly ordered trials per task. This range of SOAs appears to be well-suited to define the time frame within which the illusion is perceived (Cecere et al., 2015; Cooke et al., 2019).

4.3.3. Experimental Design

Each participant was instructed to fixate the central cross and report the number of flashes they saw on the screen while ignoring the tactile stimulations (taps). Participants were seated 57 cm away from the computer screen with their visual angle aligned with the centre of the screen. Participants were asked to place their left index finger below the presentation of the flashing disc to maximise spatial co-occurrence of the visual and tactile stimuli processing. Each visual stimulus flashed for 12 milliseconds and always occurred with a seven-milliseconds tap aligned with the onset of the flash. The second tap was randomly presented in one of the 15 inter-tap intervals. The double taps were intended to produce an illusory effect and trick the participants into seeing two flashing discs while there was only ever one presented. In particular, the quicker the taps, the stronger the illusion was expected to be. The responses were indicated by participants saying `1`, if one flash was perceived, or `2` if two flashes were perceived. The experimenter then pressed the corresponding key on the keyboard (See Figure 4.1).

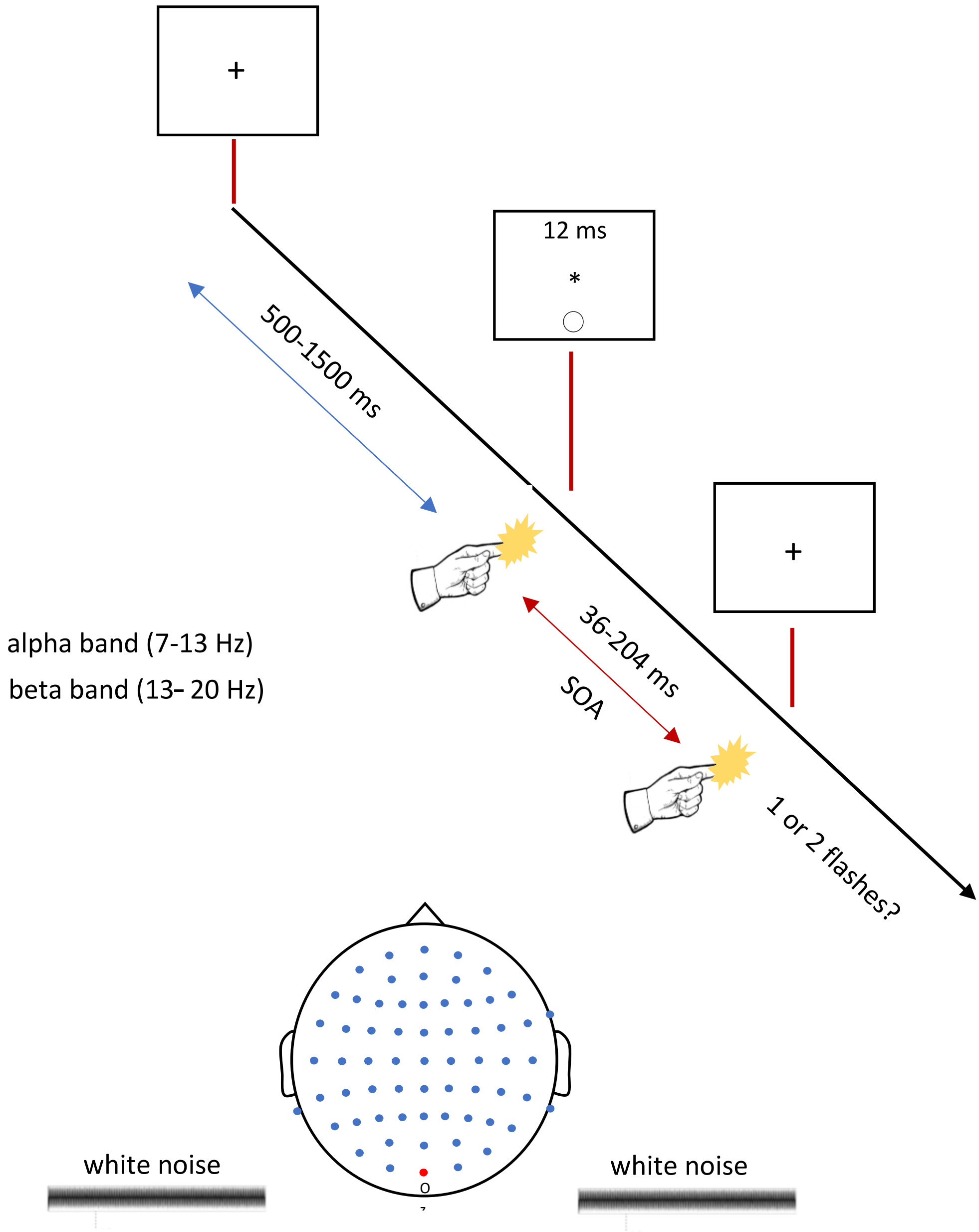

Figure 4.1. Paradigm. A schematic of the experimental paradigm. In each trial, participants were told to fixate a central cross for a period randomly ranging between 500 and 1500 ms. Thereafter, they were presented with one visual white disc (flashing for 12 ms) accompanied by two brief tactile stimuli (7 ms each). The first tactile stimulus (tap) was aligned with the onset of the flash, whereas the second tap was randomly presented at 15 different delays (randomly ranging between 36 and 204 ms). Participants were required to verbally report whether they perceived one or two flashes. The verbal report was then entered by the experimenter via the "1" and "2" key on the keyboard which prompted the new trial to start after a variable inter-trial interval. During the tactile stimulation, white noise (approximately 50db) was played to participants through speakers to mask the noise produced by the tactile stimulator. During the experiment, EEG was continuously recorded.

4.4. Behavioural data analysis

The temporal window within which the visual illusion was maximally perceived was calculated using the participants' perceived illusory flashes across the different SOAs. The percentage of trials in which the tactile-induced Double Flash Illusion (tDFI) was perceived (total "two" responses out of 10) was plotted for each participant's inter-tap interval to obtain the TWI induced by the tDFI (i.e. the point in time after which the illusion starts to degrade). A psychometric sigmoid function $y = a+b/(1+exp(-(x-c)/d))$; a = lower asymptote for high values of x; b = amplitude of the psychometric curve ($a+b$ forms the upper asymptote for low values of x); c = inflection point; d = slope] was fitted to the individual observations. Note, that parameter *d* also determines the direction of the function and, generally, can be either positive (upward sigmoid) or negative (downward sigmoid). The parameters estimation was done using the *curve fitting* option in Matlab. The fitting procedure assigns random values on the interval (0,1) as starting points for the parameters (a,b,c,d), that by default are unbounded. Normally, a starting point of 100 for the parameter c (i.e. the inflection point) was given, as 100 is near the average TWI for two simple stimuli (Cecere et al., 2015; Cooke et al., 2019). The sigmoid function is then fitted to the data, giving us a downward function with a negative d and a positive b, or viceversa. The inflection point was of particular interest as it corresponds to the point of the fitted curve dividing those trials in which the participant maximally perceived the illusions from those trials within which the illusion tended not to be perceived, thus representing the most representative measure of the TWI for each participant.

As the inter-individual variability in the susceptibility to the illusion is high (de Haas et al., 2012), it would usually be more convenient to pre-screen participants and include only those that reliably perceive the illusion (and especially so when the dependent variable is the inflection point). However, as we were examining a personality trait, we decided to initially include all participants without taking into account their susceptibility to the illusion. Indeed, if we were to exclude participants merely based on their perception of the illusion, in principle, we might have missed important information on how the perception of the illusion is distributed as a function of the schizotypy score. After having analysed each participant's fitting, we have based our exclusion criteria on fitting procedures (i.e., whenever data could not be fitted, participants were excluded), which led to the exclusion of 18 participants and R square values (whenever individual fitting R-scores values were lower than 0.6), which led to the exclusion of another 4 participants. Importantly, we explored whether participants whose performance could not be fitted (because of noisy data in reporting the illusion over time, or because they never – or always – experienced the illusion independently of SOAs) were clustered towards one extreme of the distribution of the SPQ score. However, our excluded participants' SPQ scores were equally distributed on a continuum; thus, we are confident that their exclusion has not hindered our experimental observation.

It must be noted that such a rejection rate is relatively high (corresponding to 40% of all the original participants) when compared to the one observed in previous reports (corresponding to 20% of all the original participants) (Cecere et al., 2015; Cooke et al., 2019). However, both in Cecere et al. (2015) and in Cooke et al. (2019), participants were pre-screened with a practice trial to ensure, as a prerequisite to taking part in the study, that they could reliably perceive the illusion. Those participants who could not perceive the illusion from the start were thus not included in the study, which resulted in a reduced rejection rate. When applying the same criteria to the current study, again, around 20% of the participants would have possibly been excluded because of fitting issues, and the other 20% because of lack of illusion, thus consistent with previous reports by our group. Thus, in agreement with the sample size estimated by the power analysis, the total number of participants included in the study was n= 33 (18 females, mean age 25).

4.5. EEG data analysis

EEG scans were performed during all trials to investigate pre-stimulus oscillatory activity both in the alpha and beta bands (see Cooke et al., 2019). For each participant, 64 channels EEG was recorded at a sampling rate of 500Hz. The EEG signal was re-referenced offline to the average of all scalp electrodes. EEG data was subsequently segmented into 2000ms stimulus-free and artifact-free epochs time-locked to and preceding the visual stimulus onset. Given that a total of 150 stimulus trials were presented, this resulted in 150 epochs of pre-stimulus oscillatory activity. Each single epoch was inspected to determine the data and reject any artefacts created by involuntary movements (minor muscle contractions or eye blinks) or interference. A total of 41.45% (±3.88%) of the epochs were rejected due the presence of eye movements and muscle artifacts. This relatively high number of rejected epochs contaminated by eye movements and muscle artefacts may be due to residual artifact induced by the verbal response provided by the participants.

The individual alpha and beta peak frequencies were calculated with spectral analysis based on Fast Fourier Transform (FFT) with no overlapping windows and nominal resolution of 0.1 at channel Oz for each 2-sec epoch and subsequently averaged. For each frequency peak calculation, signals were band-pass filtered within the frequency of interest using infinite Impulse Response (IIR) filter applied to separate individual wave bands in the visual cortex before undergoing FFT. This allowed filtering out frequencies that may have contaminated the calculation of the frequency of interest. Thus, peak frequency was determined as the frequency having the largest spectral values in the ranges 7-13 for alpha and 12-25 for beta (as measured at channel Oz). Once the frequency peak was calculated for each individual, the same value of cycles per seconds (e.g. 20Hz) was transformed in the corresponding duration of one single cycle (e.g. 50ms). In order to ensure that extracted peaks in alpha and beta oscillatory bands represent independent components in our EEG analysis, we performed a correlation analysis between alpha and beta frequency peaks which returned a nonsignificant correlation between individual alpha and beta peaks ($r=-0.02$, $p>0.05$).

4.6. Statistical analyses

4.6.1. Relationship between schizotypal personality trait (SPQ) and temporal window of illusion (TWI)

To test for the possible association between the individual schizotypal traits and the individual TWI measured during the tDFI task, we ran Pearson's correlation analyses between SPQ total scores and TWI, as well as between the SPQ subscales (i.e., perceptual-cognitive, interpersonal and disorganized) scores and TWI. Moreover, to test for their robustness, we computed skipped parametric (Pearson) correlations (Wilcox, 2004) using the Robust Correlation toolbox (Pernet et al., 2013) and conducted null hypothesis statistical significance testing using the nonparametric percentile bootstrap test (2000 resamples; 95% confidence interval, corresponding to an alpha level of 0.05), which is more robust against heteroscedasticity compared to the traditional t-test (Pernet et al., 2013). Finally, we corrected for multiple comparisons (Bonferroni correction) whenever appropriate.

4.6.2. Relationship between temporal window of illusion (TWI) and individual frequency peaks (IBF, IAF).

To confirm the beta frequency-specificity accounting for the TWI measured during the tDFI (Cooke et al., 2019) in our participant sample, we ran Pearson's correlation analysis between IBF and individual TWI as well as between IAF and TWI. Moreover, as above, to test for their robustness we computed skipped parametric (Pearson) correlations (Wilcox, 2004) using the Robust Correlation toolbox (Pernet et al., 2013) and conducted null hypothesis statistical significance testing using the nonparametric percentile bootstrap test (2000 resamples; 95% confidence interval, corresponding to an alpha level of 0.05).

4.6.3. Relationship between schizotypal personality trait (SPQ) and individual beta frequency peak (IBF).

Given the existing evidence of abnormal neural oscillations in the schizophrenia spectrum since its early stages (Uhlhaas et al., 2008), we tested the association between IBF and SPQ total scores, as well as between IBF and the SPQ subscales (i.e. perceptual-cognitive, interpersonal and disorganized) scores, using Pearson's correlations. As above, to test for the robustness of the correlation, we computed skipped parametric (Pearson) correlations (Wilcox, 2004) using the Robust Correlation toolbox (Pernet et al., 2013) and conducted null hypothesis statistical significance testing using the nonparametric percentile bootstrap test (2000 resamples; 95% confidence interval, corresponding to an alpha level of 0.05).

4.6.4. Mediation analysis

A mediation analysis (model 4 in the SPSS PROCESS macro80) was performed to probe any effects of IBF on individual schizotypal personality traits, mediated by its effects on TWI. All the analyses were carried out with standardized values for all the variables. Consistent with published guidelines (Memon et al., 2018), we report 95% confidence interval (CI) based on 5000 bootstrap iterations (bias-corrected) for all major effects.

4.6.5. Median split analysis

Since participants have been enrolled in the experiment independently of their SPQ scores, we have used a median split approach according to the individual SPQ score to test whether low and high SPQ scores show significant differences both in the TWI and beta peaks.

4.7. Results

4.7.1. T*he individual SPQ score accounts for the size of the TWI*

Recent work (Haß et al., 2017) has found a significantly enlarged temporal window within which schizophrenic patients (relative to a healthy control group) experience the auditory version of the DFI. This observation was extended to a schizotypal sample (Ferri et al., 2018). Here we tested whether the individual SPQ score could predict the size of the tactile-induced TWI. To this aim, a two-tailed correlation analysis between the individual SPQ scores and the individual TWI was conducted. We found a significant positive correlation between the size of TWI and the individual SPQ score ($r = .56$, $p <.001$, two-tailed), which also survived the robust skipped correlations method ($r = 0.48$, CI = [0.13, 0.76]) (See Figure 4.2.D), indicating that the wider the

TWI, the higher the SPQ score. In other words, individuals with higher schizotypal personality traits show wider TWIs. Moreover, in order to understand whether specific characteristics associated with the schizotypal traits do preferentially account for the size of the TWI, we investigated the relationship between the different SPQ subscales and the individual TWI. Results of these analyses showed that each of the three SPQ subscales significantly and positively correlate with the individual TWI, also surviving the skipped correlation method and the p-value correction for multiple correlations: cognitive-perceptual subscale (r=0.43, p=0.01, two-tailed; skipped r=0.44, CI = [.12 .69]), disorganised subscale (r=0.44, p=0.01, two-tailed; skipped r =0.44, CI= [.13 .68]), interpersonal subscale (r=0.50, p=0.01, two-tailed; skipped r=0.23, CI [.12 .55]). As there was no preferential contribution from any subscale, we used the total SPQ score in the subsequent analyses.

4.7.2. Individual beta peak frequency accounts for the size of the TWI

Recent research has shown a significant relationship between the size of TWI induced by the tDFI and the individual beta frequency (Cooke et al., 2019). We expected here to reproduce this relationship selectively for the beta but not alpha frequency. To this aim, individual oscillatory frequencies were converted from cycle units (Hz) into millisecond units (period=1000/frequency) so as to correlate TWI and oscillatory activity on the same measure scale (of time) and the same unit (ms). We found a significant positive correlation between the TWI and the duration of an individual beta frequency (r = 0.37, p = 0.015, one-tailed, based on an a priori hypothesis, see Cooke et al., 2019), which survived the skipped correlation method (r = 0.42, CI= [.16 .65]) (See Figure 4.2.C), replicating previous findings by Cooke et al. (2019). This result indicates that participants with wider TWIs (i.e. more prone to perceive the illusion) also have a slower beta cycle. As expected, no significant correlation was found between the TWI and the peak alpha frequency (IAF; see Figure 4.2.B) (r=0.16, p=0.37 two-tailed).

4.7.3. Individual beta peak frequency accounts for the individual SPQ score

So far, we have observed that larger tactile-induced TWIs relate both to higher SPQ scores and slower IBF. However, before testing the mediation role of the tactile-induced TWI for the impact of IBF on SPQ, another association needs to be tested, that is the one between IBF and individual SPQ scores. To this aim, a two-tailed Pearson's correlation analysis between IBF and the SPQ total score was performed, which revealed a significant positive correlation (r=0.36; p=0.04, two-tailed), which survived the skipped correlation method (r=0.36, CI = [.06 .61]). Specifically, the results of this correlation indicate that people with slower beta oscillations also have a higher SPQ total score (See Figure 4.2.I). Again, as expected, no significant relationship was found between the IAF and the SPQ score (r=0.19, p=.28; Figure 4.2.H).

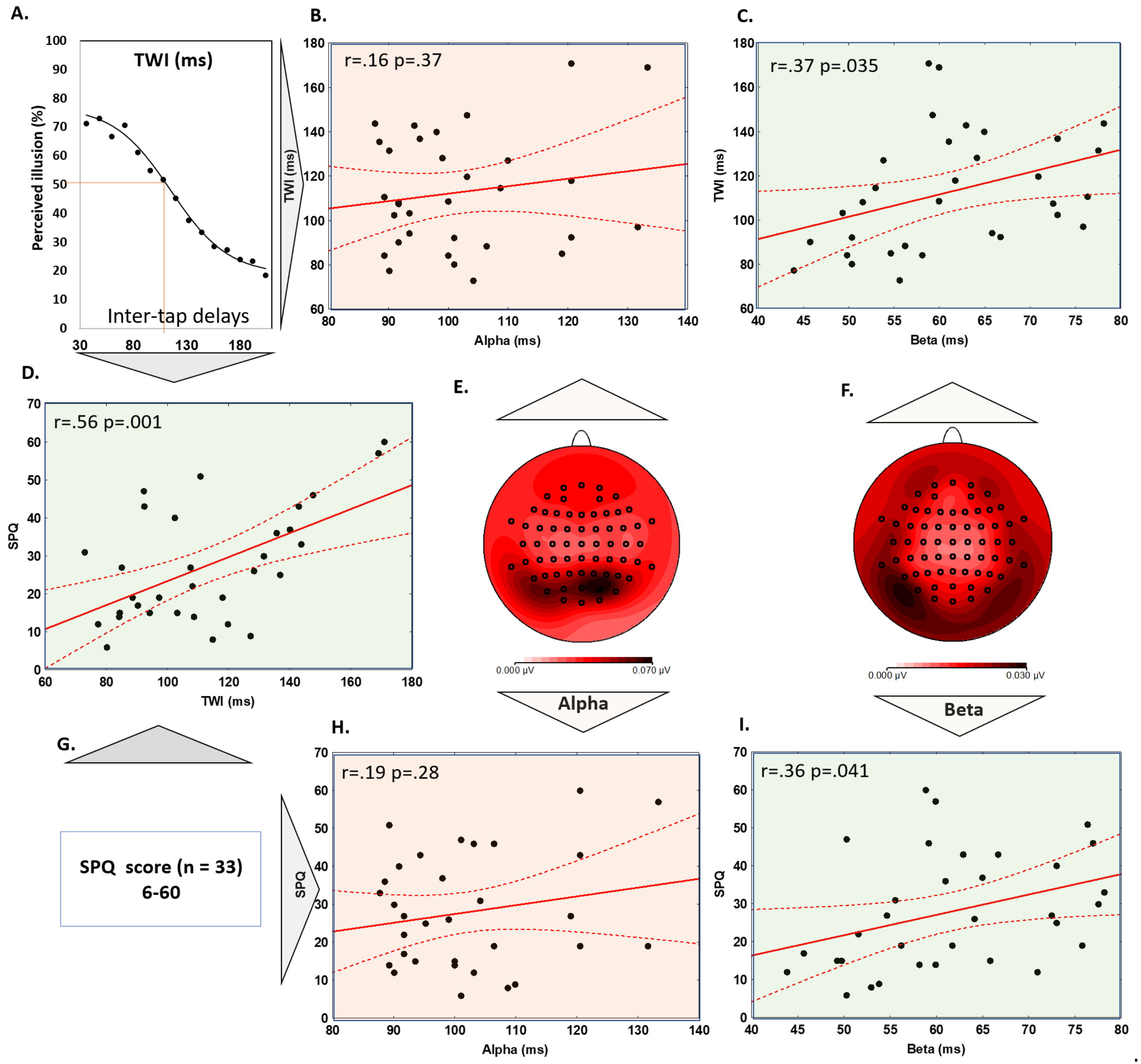

Figure 4.2. Correlation analyses. A. The sigmoid curve represents the best fit of the average probability of perceiving the illusion plotted as a function of inter-tap delays. The sigmoid fit determines the temporal window of illusion (TWI), i.e. the temporal window within which the illusion is maximally perceived, corresponding to the inflection point of the sigmoid**. B.** Correlation plot depicting the relationship between the TWI for the tactile DFI and the individual peak frequencies in alpha and **C.** beta oscillatory bands. **D.** Correlation plot between the individual SPQ's score and the width of the TWI. **E.** Oscillatory activity at individual peak signal averaged across participants in the alpha and **F.** beta oscillatory bands. **G.** Range of SPQ scores. **H.** Correlation plots depicting the relationship between individual SPQ's scores and individual peak frequencies in the alpha and **I.** beta oscillatory bands. Across the panels, significant correlations are reported on a green background together with r values and corresponding significant level p. Non-significant correlations are reported on a salmon colour background.

4.7.4. Mediation Analysis

To better understand the relation between SPQ, TWI and IBF, we used a mediation model to examine a possible mediation role of the TWI for the effect of IBF on SPQ. We found a significant mediation effect (0.291, 95% CI: 0.0633 – 0.715), whereby relatively enlarged TWI mediated a positive association between IBF and SPQ (i.e., slower IBF in individuals with higher SPQ scores). Results of this analysis showed that there was no significant residual direct effect of IBF on SPQ (0.192, 95% CI: -0.322 – 0.708) suggesting that the impact of IBF on SPQ are fully mediated by the TWI. Standardized parameter estimates are reported in Figure 4.3.

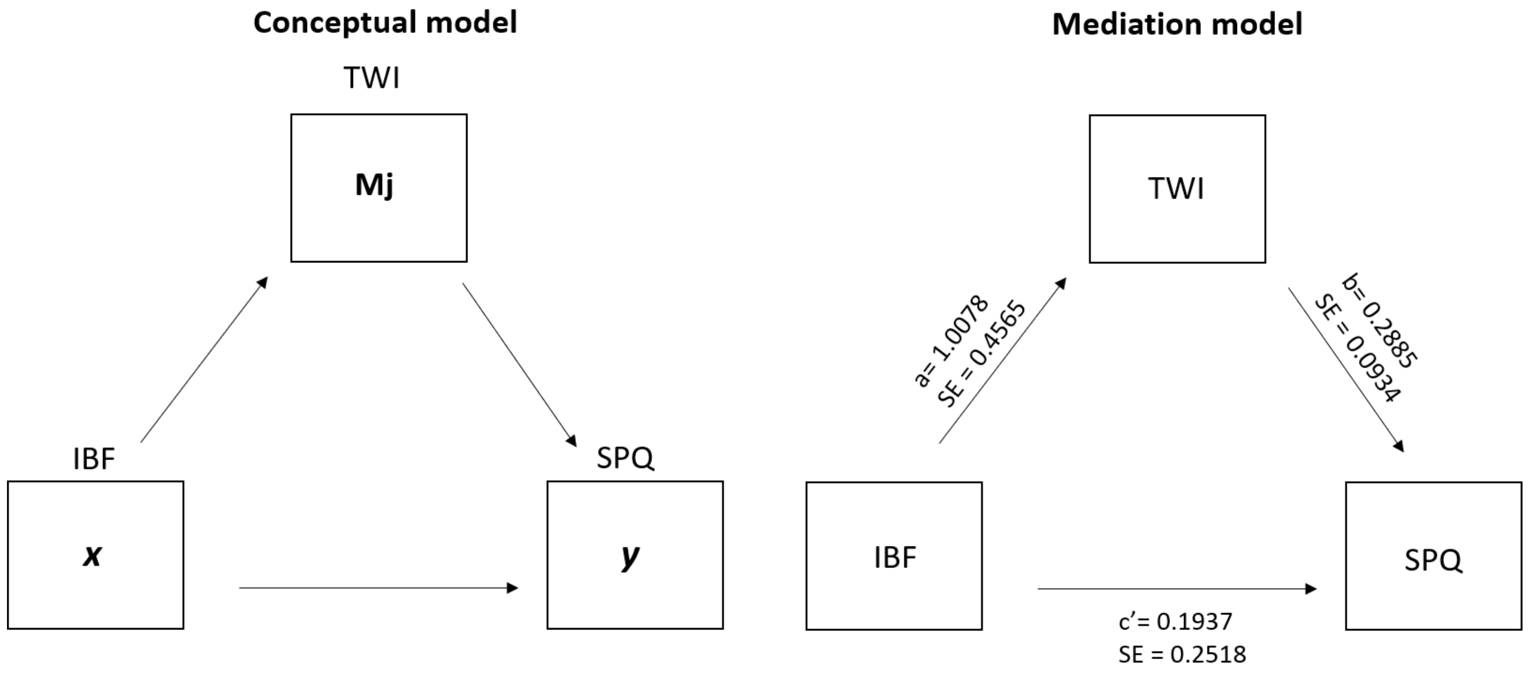

Figure 4.3. Mediation model. Standardized parameter estimates and standard errors are reported. No significant direct effect of IBF on SPQ was found, suggesting that the impact of IBF on individual schizotypal personality traits is fully mediated by the TWI.

4.7.5. Median split analysis

These findings highlight the relevant role played by oscillatory activity in accounting for individual differences in multisensory interactions, which are in turn able to predict SPQ scores, and in principle able to differentiate people with low and high schizotypy scores. To test this directly, we applied a median split analysis to contrast people with low and high SPQ scores on their IBF and TWI measures.

In line with our expectation, we found that the average TWI (103.6 ms) for the lower end of the median split (approximating the profile of a low schizotypy group) was significantly shorter than the average TWI (123.0 ms) for the upper end of the median split (approximating the profile of a high schizotypy group) ($t(32) = 2.04$; $p = 0.03$, $d = -3.21$). Finally, we measured whether the median split could also significantly differentiate groups according to their beta frequency. Indeed, we found that the IBF for the lower end SPQ score group was significantly faster ($M = 57.8$, $SD = 9.5$) than the IBF for the upper end SPQ score group ($M = 65.5$, $SD = 9.1$) ($t(32) = 2.04$; $p = 0.02$, $d = -0.86$). Interestingly, when looking at frequency specificity, our control analysis did not show any significant difference for the IAF between the lower end ($M = 101.5$, $SD = 11.4$) and upper end ($M = 102.4$, $SD = 14$) of SPQ score group ($t(32) = 2.04$; $p = 0.83$).

4.8. Discussion

In the current study, we aimed to describe the temporal profile and the oscillatory dynamics of the tactile-induced DFI in relation to schizotypal personality traits and their interplay. Chapter Three had previously shown a tight relationship between the auditory version of the DFI and the SPQ scores (Ferri et al., 2018), such that individuals with higher SPQ scores showed larger TWIs. Here, we were able to extend this observation to the tactile version of the DFI. Indeed, we found a positive correlation between the TWI, as measured with the tDFI, and the SPQ scores, thus confirming that the higher the SPQ score the larger the TWI.

This first characterization of the temporal profile of the tDFI accounting for low- and high-schizotypal profiles was followed by an investigation of their potential neural underpinnings. Relevant to this initiative is the work from Cooke et al. (2019) which demonstrated a relationship between the TWI for the tDFI and the IBF; namely, larger TWIs were associated to slower IBFs and vice versa. In the present study, we replicated the findings from Cooke et al. (2019) and crucially assessed, for the first time, whether IBF could account for the different size of the TWI as a function of the individual SPQ score. Results confirmed the presence of a significant relationship between the size of the TWI and the SPQ score, which was also associated with the IBF values. Specifically, slower IBFs were associated with larger TWIs, characterizing participants with the high-schizotypal profile, while faster IBFs were associated with shorter TWIs, characterising participants with the low-schizotypal profile. Moreover, we confirmed that IBF significantly correlated with the SPQ scores such that the slower the IBF, the higher the SPQ score. These results are in line with the notion that slower oscillatory activity is associated with prolonged periods of integration of information across the senses, as indicated by an enlarged TWI accounting for high schizotypal traits.

The hypotheses tested specifically revolved around the neural underpinning of the temporal dynamics of the illusion. Previous research looking at the relationship between the Double Flash Illusion and oscillatory activity have generally observed a link between oscillatory brain activity prior to stimulus onset and subjective perception of the illusion. For instance, Keil et al. (2014) have found that beta band power is increased in the left temporal gyrus prior to perceiving the auditory induced DFI. Similarly, Lange et al. (2013) and Cecere et al. (2015) found that higher alpha power is associated with lower perception of the auditory induced illusion. Moreover, Cecere et al. (2015) found that the individual alpha peak frequency correlates with the temporal window of illusion, such that the slower the alpha frequency, the larger the temporal window of illusion. Interestingly, Cecere et al. (2015) found that alpha power did not account for the temporal dynamics of the illusion (i.e. the interindividual difference in the length of the temporal window of illusion), which were instead explained by the alpha frequency peak, a finding that was replicated in further research (Cooke et al., 2019).

This suggests that pre-stimulus power accounts for the general proneness to the illusion, and not for the temporal dynamics of this process, which are best accounted for by individual peak frequency (Cooke et al., 2019; Cecere et al., 2015). For this reason, here we refrained from performing power data analysis as it was not within the scope of our study, as research observed that the oscillatory power in visual cortex predicts whether participants will perceive the illusion or not rather than describing the temporal dynamics of the illusion.

Thus, our findings provide novel, compelling evidence on the functional role played by oscillatory activity in neural code efficiency. They add to the body of evidence (Cecere et al., 2015; Cooke et al., 2019; Keil and Senkowki, 2017) supporting the notion that oscillatory activity in different frequency bands may play a crucial role in orchestrating sensory binding within critical windows of integration. A general view here is that a tendency towards slower oscillatory activity within a given frequency band is symptomatic of a general loss of neural code efficiency (see Ferri et al., 2018; Cecere et al., 2015; Cooke et al., 2019). Specifically, we found that individual beta frequency, previously associated with somatosensory-to-visual functional connectivity (Cooke et al., 2019) accounts for the individual TWI, which in turn predicts the individual SPQ score. Thus, oscillatory indices, as the IBF, measured during a multisensory task, as in the present study, may represent an important biomarker in the development of schizophrenic symptoms and represents a prodromal early biomarker of high schizotypy.

Investigating the pattern of neural alterations in high schizotypy is fundamental to elucidate the possible existence and nature of a continuum between schizotypy and schizophrenia. Research has now emerged suggesting that the abnormalities in oscillatory activities and functional connectivity found in schizophrenia, may also extend to schizotypy. A study by Koychev et al. (2011) found abnormalities in a measure of network synchronisation, the "phase-locking factor", and a deficient modulation of the sensory processing by higher-order structures in schizotypy. A study from Ferri et al., (2017) found that people with high schizotypy display abnormal long-range temporal correlation patterns that are similar to those observed in patients with schizophrenia (Nikulin et al., 2012). In our study, individuals with high schizotypy showed a general reduction in the speed of beta frequency (i.e. lengthening of the beta wave time) in the visual cortex, which effectively lengthened their temporal window of integration for the tDFI. This pattern could contribute to the multisensory impairments often observed in schizotypy and schizophrenia. Moreover, it could be associated with abnormalities in the neural dynamics that coordinate brain activity in large-scale networks. Indeed, as observed in Cooke et al. (2019), the tDFI phenomenon, rather than being dependent on local network rules (i.e. local occipital oscillatory resonance activity), is likely to be determined by long-range communication networks (i.e. functional connections between somatosensory and visual cortices) which influence visual cortical processing. As such, the tDFI's TWI would be mediated by beta oscillations as somatosensory processing (pre-synaptic), which is typically linked with beta activity, phase-align beta oscillations in the visual cortex (post-synaptic), defining the temporal resolution of interregional synchronization within which the TWI phenomenon arises. This pattern has previously been observed in the auditory-to visual network by Romei et al. (2012) who demonstrated that a simple auditory stimulus could phase align oscillatory alpha activity within the visual cortex. These observations have been interpreted (Cooke et al., 2019) within the "Communication Through Coherence" framework (Fries, 2005; 2015) as a means of communication between the senses for optimal multisensory binding. Such an interpretation would be in line both with reports of abnormal oscillatory activity and abnormalities in network synchronisation as measured by the "phase-locking factor" from Koychev et al. (2011), in turn leading to a deficient modulation of the sensory processing in schizotypy as observed in the present study.

Finally, the current data provide support to the hypothesis that the disruption of neural dynamics that coordinate brain activity in large-scale networks could be one of the possible causes for the emergence of schizophrenia. In particular, abnormal brain dynamics could impact the multisensory experiences in schizotypy and in schizophrenia. Brain stimulation could represent an emerging approach to target and intervene in abnormal neural dynamics and abnormal multisensory integration. Evidence has now emerged that different brain areas can be entrained at specific frequencies (Romei et al., 2016). Furthermore, transcranial direct current stimulation (tACS) or transcranial magnetic stimulation (TMS) could be implemented to modulate the TWI of both schizophrenic and schizotypal individuals. At the network level, further research could adopt a novel cortico-cortical paired associative stimulation (ccPAS) TMS paradigm based on the Hebbian principle of cortical plasticity (Hebb, 1949; Romei et al., 2016; Veniero et al., 2013 Chiappini et al., 2018). This protocol adopts a repeated stimulation of pre- and post-synaptic relevant neural population over specific brain networks aimed at enhancing functional connectivity between different brain areas and thus enhance effective multisensory integration.

Chapter Five

Body representations and basic symptoms in schizophrenia

5.1. Abstract

Recent research on the early detection of schizophrenia spectrum disorders has placed much attention on the subtle and subclinical abnormalities present in body experiences that go beyond positive and negative symptoms. According to the Basic Symptom model of schizophrenia, abnormalities in bodily self-awareness constitute an important predictor of the changes in self-experience that are observed in schizophrenia. The present investigation first assessed the body structural representation (BSR), a specific component of bodily self-awareness, and its association with basic symptoms in patients diagnosed with schizophrenia. By adopting a Finger Localization Task, we found that patients are significantly less accurate than healthy controls when asked to identify pairs of fingers touched by the experimenter (with the hand hidden from view). Most notably, patients' performance at the Finger Localization Task was negatively associated with basic symptoms: the worse the individual accuracy, the higher the Schizophrenia Proneness Instrument for adults (SPI-A) total score. Furthermore, performance at the Finger Localization Task was linked to the malleability of the sense of body ownership: the less the individual ability to localize fingers, the stronger the Rubber Hand Illusion. These results support the hypothesis that self-disorders in schizophrenia reveal a more profound disattunement with the lived body - i.e. disembodiment of the self - that can be traced back to abnormal body experiences.

5.2. Introduction

A disturbed sense of self has been identified as a core characteristic of schizophrenia spectrum disorders. An important aspect of selfhood pertains the domain of the bodily self, which refers to the sense of inhabiting one own's body and possessing a coherent representation of it. Disturbances in bodily self-awareness are observable from the pre-onset phase and deteriorate during the acute phases of the illness (Nelson et al., 2012). For instance, patients can feel as if their body has undergone some morphological changes (Chapman et al., 1978), or can experience their body parts as alien and devoid of life (Mancini et al., 2014). Often times, a weakening of self-other boundaries are commonly observed across different stages of the disorder (Di Cosmo et al., 2018; Holt et al., 2015; Park et al., 2009). For instance, some patients report feeling physically invaded or penetrated by other's people gestures or actions (Mancini et al., 2014). Moreover, individuals in both the pre-onset or acute phases might feel as if once automatic motor actions require conscious attention and effort to be accomplished (Nelson et al., 2008). Thus, the body is not anymore inhabited as a subject of experience, but rather becomes experienced as an object of observation. Such focus on typically automatic aspects of body awareness implies a loss of a pre-reflective form of self-awareness (i.e. the minimal self), something that appears to be deeply disturbed in schizophrenia (Sass, 2003; Sass & Parnas, 2005).

Body perception abnormalities arise months or even years before the first formal diagnosis. Importantly, body perception abnormalities are included among the basic symptoms of schizophrenia. Basic symptoms are subtle, subjectively experienced disturbances which mostly reflect anomalies in self-experience, and which are present in schizophrenic patients prior to, or very early in, the illness (Parnas, 2012). These symptoms include disturbances of the self, of affection, thought, perception, proprioception and motor action. Basic symptoms can be regarded as the earliest form of self-experienced symptoms – hence the name “basic” – and they are different from attenuated and overt symptoms, which develop later during the course of the illness (Schultze-Lutter, 2009; Magini & Raballo, 2004). Despite the fact that they are generally applied to the assessment of people who may be at risk to develop schizophrenia, it is acknowledged that they persist after its onset and for the whole duration of the illness (Klosterkotter, 1992). Basic symptoms can be evaluated using the Bonn Scale for the Assessment of Basic Symptoms (BSABS). The BSABS is a comprehensive, semi-structured interview that assesses various anomalies of experience (affective, volitional, cognitive, perceptual and bodily) and which is routinely used for the assessment of schizophrenia proneness (Gross, 1987). The basic symptoms identified by the BSABS scale have more recently been included in a semi-structured interview: the Schizophrenia Proneness Instrument for adults (SPI-A, Schultze-Lutter, 2009). Despite the fact that the former allows a more detailed examination of the basic symptoms, it is also less manageable, and patients often experience a progressive affliction, with consequent reduction in their capability to describe their own mental state. For these reasons, the SPI-A is currently more often used to assess basic symptoms.

In accordance with the clinical reports, a recent empirical study has found that schizophrenic patients show impairments in tasks designed to detect a specific component of body representation: the body structural representation (BSR) (Graham-Schmidt, 2016). The body structural representation is considered to be a topological map of the body which functions as a stored representation of the relationship between body parts in relation to each other within a whole-body structure (Rusconi et al., 2009; Longo, 2016). Evidence for the existence of BSR comes from the study of autopagnosia (Sirigu et al., 1991) and finger agnosia (Kinsbourne & Warrington, 1962). In both conditions, patients are unable to point to parts of their body on verbal command or to judge the spatial relations between body parts but remain able to describe the function of their different body parts and to perform self-initiated goal-directed tasks. Also, their somatosensation remains relatively good (Anema et al., 2008; Sirigu et al., 1991; Buxbaum & Coslett, 2011). These conditions have been interpreted as evidence that the structural body representation differs from sensorimotor representations, such as the body schema (Gallagher 2005; Longo 2016). The BSR remains a vastly neglected component of body representation research. To date, the extent to which patients with schizophrenia exhibit altered BSR and how these deficits are related to abnormalities of the sense of body ownership has only been marginally investigated.

The present study aimed to investigate BSR in patients with schizophrenia. First, we asked patients to perform a Finger Localization Task and tested the association between their performance and the SPI-A total scores. Second, we assessed the possible relation between patients' BSR and their sense of body ownership (BO). Thus, we utilised the Rubber Hand Illusion (RHI), a task in which the synchronous touch of a rubber hand and the real hand – vs their asynchronous touch - leads to the experience of owning the rubber hand (Botvinick & Cohen, 1998). In order to avoid potential inaccuracy of patients’ self-report, due to their poor insight (Nair et al., 2014), we utilised the proprioceptive drift (see section 2.3) to quantify the induced illusion of ownership over the fake hand. Furthermore, we manipulated the posture of the rubber hand, based on previous findings showing that an incongruent position of the rubber hand with respect to the participant's hand prevents the induction of the illusion (see section 2.3.) (Costantini & Haggard, 2007; Tsakiris & Haggard, 2005).

5.3. Materials and method

5.3.1. Participants

Twenty-two schizophrenic patients (SCZ) diagnosed according to the structured clinical interview for DSM-V, and twenty-two healthy controls (HV) were included in the present study (Table 1). Schizophrenic patients were rated for symptom severity using the scale for assessment of positive symptom (SAPS) and the scale for assessment of negative symptom (SANS; Andreasen,1989 (Table 1). The study was approved by the University of Chieti-Pescara Ethics Committee. All participants (SCZ and HC) reported normal or corrected to normal vision and were right-handed. Exclusion criteria for all participants comprised significant medical or neurological illness, substance abuse or dependence in the previous six months, and an IQ < 85. Moreover, an additional exclusion criterion was included for the HC group, i.e. a personal history of Axis I/II disorders, or a history of schizophrenia in first-degree relatives. SCZ patients were recruited from outpatient services at Chieti mental health department and from inpatients at the psychiatric clinic “Villa Jolanda”. Chlorpromazine equivalents (Woods, 2003) were calculated for antipsychotics (Table 1). Most of the patients took atypical antipsychotic drugs, which are not burdened with side effects that affect the motor system (extrapyramidal side effects, EPS). Also, for patients taking haloperidol in addition to atypical antipsychotics, the neurological clinical examination revealed no signs of motor stiffness, tremors, or other EPS. Also, the movements made by the patients were observed and controlled during the task execution and no involuntary movements were detected. Finally, an accurate clinical examination was performed for all patients to exclude severe attention deficits.

Both SCZ and HC took part in the Finger Localization Task, while only SCZ took part also to the rubber hand illusion task. The study was approved by the Ethics Committee of Chieti University. Written informed consent was obtained from all participants after full explanation of the procedure of the study, in line with the Declaration of Helsinki.

Table 2. Demographic information about schizophrenia group (SCZ) and healthy control group (HC). Mean and SD of total score on SPI-A (basic symptoms), SAPS (positive symptoms) and PANNS (negative symptoms) is reported below.

	Schizophrenic patients (N = 22)	**Control participants (N = 22)**
DSM-V schizophrenia type:		
Paranoid, no (%)	11 (50%)	n.a.
Disorganized, no (%)	6 (29%)	n.a.
Catatonic, no (%)	0 (0%)	n.a.
Undifferentiated, no (%)	4 (19.05%)	n.a.
Residual, no (%)	1 (4.7%)	n.a.
Age (mean ± SD)	42 ± 10	39 ± 13
Male sex (N)	22	22
Handedness		
Right, no (%)	22 (100%)	22 (100%)
Left, no (%)	0 (0%)	0 (0%)
Education, in years (mean ± SD)	11.6 ± 3.6	14.6 ± 4.1
Illness duration, in years (mean ± SD)	11.9 ± 9.2	n.a.
SCID-II	n.a.	Negative
SAPS (mean ± SD)		
Hallucinations	4.3 ± 5.4	n.a.
Delusions	8.1 ± 7.0	n.a.
Bizarre behaviour	2.7 ± 3.3	n.a.
Formal thought disorders	6.7 ± 6.7	n.a.
SANS (mean ± SD)		
Affective flattening	10.4 ± 8.1	n.a.
Alogia	4.6 ± 4.5	n.a.

	Schizophrenic patients (N = 22)	Control participants (N = 22)
Avolition – Apathy	6.3 ± 3.2	n.a.
Anhedonia- Asociality	10.6 ± 4.2	n.a.
Attention	3.2 ± 2.6	n.a.
SPI-A (mean ± SD)		
A. Affective-dynamic disturbances	14.6 ± 4.2	n.a.
B. Cognitive-attentional impediments	12.1 ± 4.8	n.a.
C. Cognitive disturbances	10.5 ± 5.8	n.a.
D. Disturbances in experiencing self and surroundings	8.2 ± 4.0	n.a.
E. Body perception disturbances	3.3 ± 4.3	n.a.
F. Perception disturbances	3.8 ± 3.5	n.a.
O. Optional symptoms	15.9 ± 10.4	n.a.
TOT	68.4 ± 24.8	n.a.
Chlorpromazine Equivalent (mg/die)	404.0 ± 268.2	n.a.
Typical Antipsychotic, N (%)	2 (9.5%)	n.a.
Haloperidol	1 (4.8%)	
Levopromazine	1 (4.8%)	
Atypical Antipsychotic, N (%)	13 (61.9%)	n.a.
Clozapine	2 (9.5%)	
Risperidone	8 (38.1%)	
Quetiapine	3 (14.3%)	
Atypical + Typical Antipsychotic, N (%)	6 (28.6%)	n.a.
Quetiapine + Haloperidol	3 (14.3%)	
Risperidone + Haloperidol	2 (9,5%)	
Risperidone + Chlorpromazine	1 (4.8%)	

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5.3.2. Assessment of basic symptoms

Basic symptoms were assessed using the Schizophrenia Proneness Instrument (SPI-A; Klosterkotter et al., 2001) in nineteen patients. Basic symptoms refer to a set of mild self-experienced subclinical disturbances that involve different areas of psychic functioning (see Table 1). Such symptoms are assumed to play a crucial role in self-disorders and disabilities of patients with schizophrenia. Being part of the earliest manifestation of schizophrenia, they represent a *"novum"* which indicates the emergence of the illness. Most notably, basic symptoms are thought as arising from the self, rather than happening to the self without its participation (Mishara et al., 2016). Thus, the basic symptoms approach is close to models of self-disorders (Sass & Parnas, 2003; see section 1.1.3), which emphasize that they are pre-psychotic 'as if' phenomena.

5.4. Procedure

5.4.1. Finger Localization Task

Participants sat in front of a table with a box, which served to hide the participant's hands, and a drawing (outline) of a human hand. In the outline drawing, the fingers of each hand were given a number (see Fig. 5.1) that participants could use to identify the corresponding finger on their own hand. Participants were asked to put their hands on the table, with their palms facing downwards and their fingers stretched and slightly separated. Participants provided their responses by naming the fingers that were stroked referring to the outline drawing of a hand with numbered fingers. Correct responses were recorded with pen and paper. The test consisted of three tasks (ten trials on each hand per task). The first task required participants to identify the finger of the left or the right hand touched by the experimenter (Fig. 5.1a). The second task required participants to identify the finger of the left or the right hand touched by the experimenter, with the hands hidden from view (Fig. 5.1b). Finally, the third task required participants to identify pairs of fingers of the left or the right hand touched by the experimenter with the hand hidden from view (Fig. 5.1c). In the third task, responses were counted as correct when both fingers were accurately identified. The maximum total score was 60 across tasks A, B and C (20 for each task).

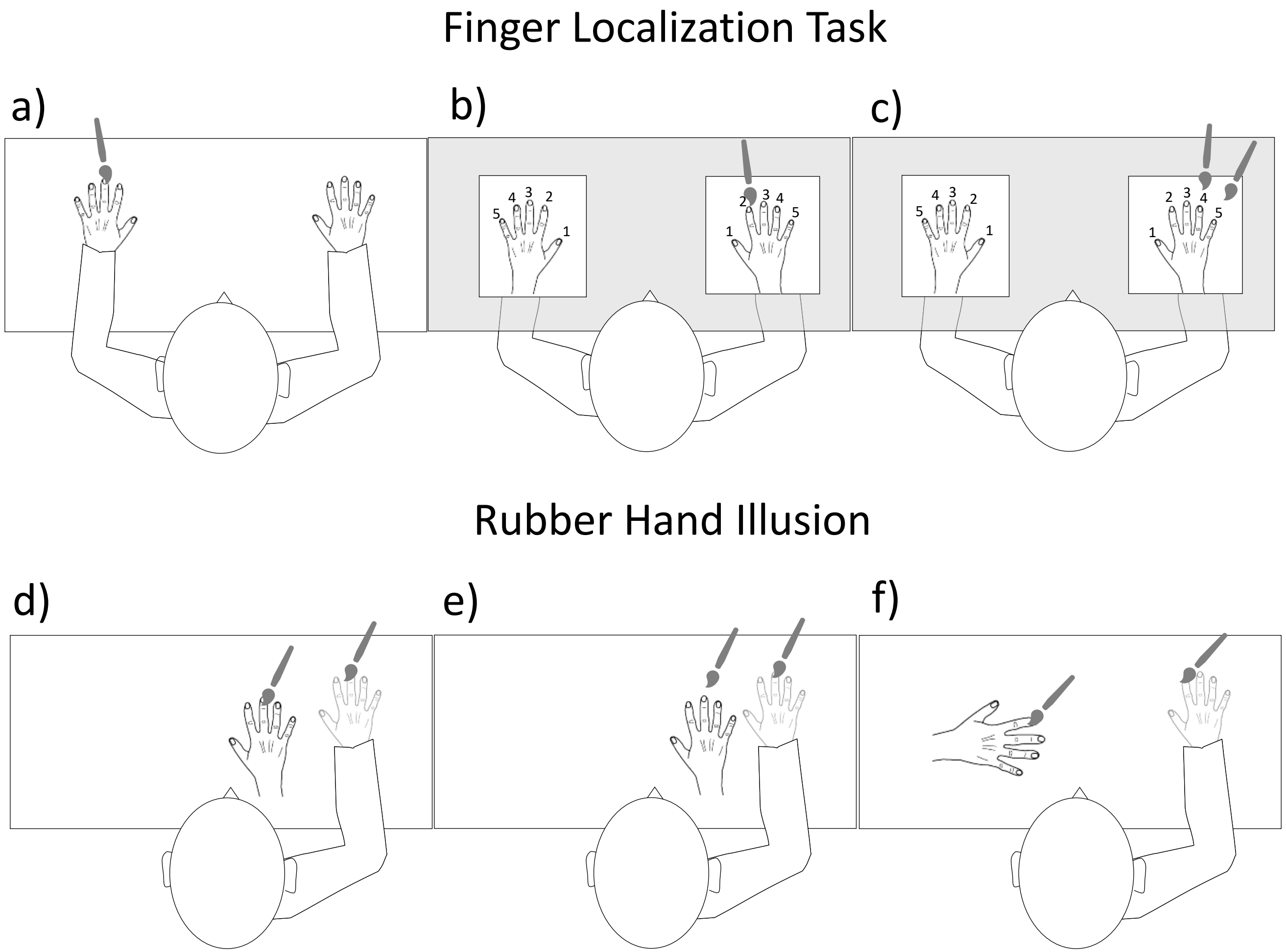

Fig. 5.1. (a, b, c) Experimental conditions of the Finger localization task. Participants had to identify the finger touched by the experimenter, with the hands visible **(a)** or hidden **(b)** from view. In a third condition, they had to identify pairs of fingers touched by the experimenter, with the hand hidden from view **(c). (d, e, f)** Experimental conditions of the Rubber Hand Illusion. Participants saw a rubber hand in a congruent posture with synchronous **(d)** or asynchronous **(e)** stroking. In a third condition, the synchronously stimulated rubber hand was in an incongruent posture **(f).**

5.4.2. Rubber Hand Illusion

Each participant performed three experimental blocks, each representing a distinct experimental condition (Fig. 5.1d–f). In two blocks, the rubber hand was aligned with the participants' hand, and the stimulation could be either synchronous (con-syn; Fig. 5.1d) or asynchronous (con-asy; Fig. 5.1e). In the third block, the rubber hand was rotated by 90 degrees (Fig. 5.1) hence inducing a mismatch between the representation of the subject's hand and the representation of the rubber hand (inc-syn; Fig. 5.1f). The block order was counterbalanced across participants. The index fingers of the rubber hand and the participant's hand were brushed by the experimenter with two paintbrushes with a frequency of approximately 1 Hz. In the synchronous condition, the hands were brushed at the same time, while in the asynchronous condition, they were brushed out of phase. For each condition, after 2 min of stimulation (either synchronous, asynchronous or incongruent), the post-induction proprioceptive location was taken. Each condition was followed by a brief rest period. A brief rest period followed each condition. During rest periods, participants were encouraged to move their hand and body so to prevent transfer of the illusion across conditions.

Participants were seated in front of a specially constructed multi-chambered wooden box. The box measured 100 cm in width, 20 cm in height and 40 cm in depth and was placed in a darkened room. To prevent participants from seeing their hands during the experiment, a semi-silvered mirror was placed on the top of the box. Two lights were installed in the apparatus, one light was used to illuminate the rubber hand during the stimulation phase, and the other was used to illuminate a sliding ruler used to measure the proprioceptive drift. Participants sat in front of a table and placed their right hand at a fixed point inside the box, while their left hand was left in their lap. A lifelike right rubber hand was placed in front of the subject's body midline. The participant's right hand and the rubber hand were positioned 20 cm from each other, with a wall between them to avoid any light over spilling into the actual hand chamber.

For each experimental condition, the experimenter turned the light on in the rubber hand chamber during the 2 min stimulation phase, so that the participant could see the rubber hand. A ruler with the numbers printed in reverse was maintained between two poles 20 cm above the box. When illuminated from above, the mirrored surface of the box allowed the numbers to be reflected in their proper orientation; thus, the numbers could appear at the same gaze depth as the rubber hand. Participants were asked: “Using this ruler, where is your index finger”? They were instructed to judge the position of their finger by projecting a parasagittal line from the center of their index finger to the ruler. Participants were required to respond by verbally reporting a number on the ruler. During the judgments, there was no tactile stimulation, and participants were prevented from seeing the rubber and the real hands or any other landmarks on the work surface, by switching off the light under the semi-silvered mirror. The participants were also cautioned not to move their hand during the stimulation phase, nor during the judgment phase. The experimenter monitored this closely. The ruler was always placed with a different random offset for each judgment to prevent participants from memorizing and repeating responses given in previous conditions.

The experimenter recorded the offset position and deducted that from the reported position, yielding the perceived finger position both before (baseline) and after (drift) the induction period of each experimental condition. The difference between the baseline and the drift estimations represents the change in the perceived position of the hand due to the stimulation, i.e. the proprioceptive drift. When positive, it indicates a mislocalization toward the rubber hand. We decided to use the proprioceptive drift to index the RHI in SCZ, rather than the questionnaire (Longo et al., 2008), as an implicit measure is more reliable than subjective reports when testing patients with schizophrenia.

5.5. Data Analysis

5.5.1. Finger localization and basic symptoms

Correct responses from the Finger Localization Task were analysed using a 2 by 2 by 3 ANOVA with laterality (left hand vs right hand), and task (first vs second vs third) as within-subject factors, group (healthy controls, HC vs schizophrenic patients, SCZ) as between-subject factor. Post-hoc analyses (Newman-Keuls) tested for between-group differences.

For the SCZ group, Pearson's correlation analysis was performed between the individual accuracy at the Finger Localization Task, computed across the three tasks, and the SPI-A total score.

5.5.2. Rubber Hand Illusion Task

Proprioceptive drifts from the RHI task- i.e., the changes in the perceived position of the hand, computed as the difference between the perceived position before (baseline) and after (drift) the induction period for each block – were analysed using a repeated measure one-way ANOVA. The within-subject factor “mode of RHI induction” had three levels (congruent-synchronous (CS) vs congruent-asynchronous (CA) vs incongruent-synchronous (IS)). Post-hoc analyses (Newman-Keuls) tested for within-group differences.

5.5.3. Rubber Hand Illusion and Finger Localization Task

To test for the effect of the structural representation of the hand on the sense of body ownership in patients, we ran a linear correlation (Pearson's) between the individual accuracy at the Finger Localization Task, computed across the three tasks, and the RHI index (computed as the difference between the proprioceptive drift induced by the CS condition and the average proprioceptive drift induced by the control conditions (CA and IS).

5.5.4. Rubber Hand illusion and basic symptoms (SPI-A)

To test for the relationship between basic symptoms and the effect of body ownership over the rubber hand, we computed a linear correlation (Pearson's) between the RHI index (computed as the difference between the proprioceptive drift induced by the CS condition and the average proprioceptive drift induced by the control conditions (CA and IS), and the SPI-A total score.

5.6. Results

5.6.1. Finger Localization and basic symptoms

An analysis of variance showed that the factor group was significant ($F (1,42) = 8.69$, $p = .005$, $\eta 2= 0.171$), as the HC group ($M= 57.18$, $S.E = 0.64$) showed higher accuracy than the SCZ group ($M= 53.63$, $S.E = 1.02$). Also, the factor task was significant ($F (2,84) = 57.04$, $p < .001$, $\eta p2 = 0.576$), with higher accuracy on the first

(M= 19.8, S.E = 0.93) and second (M = 19.27, SE = 0.17) tasks than on the third task (M = 16.3, SE = 0.49), where two fingers were touched simultaneously while hands were hidden from view. The main effect of task was further qualified by the group by task interaction ($F(2,84) = 8.08$, $p < .001$, $\eta p2 = 0.161$), accounted for by significantly higher accuracy of HC group's performance (M = 17.7, SE = 0.51), as compared to SCZ group's performance (M = 14.91, SE = 0.76), only in the third task ($p = .004$). Notably, the fact that patients and controls differed only on the third task rules out the hypothesis that these effects are due to reduced tactile acuity in patients. Indeed, if such difference was due to a reduce tactile sensitivity per se, then we would have seen an effect on all the three tasks. Instead, the fact that patients and healthy control only differed in the third task (i.e. the most complex one) suggests that such difference is mainly driven by the higher complexity of the body structural representation being tested. Finally, the factor laterality was not statistically significant, nor were its second and third level interactions with the other factors (all ps > 0.36) (Fig. 5.2a).

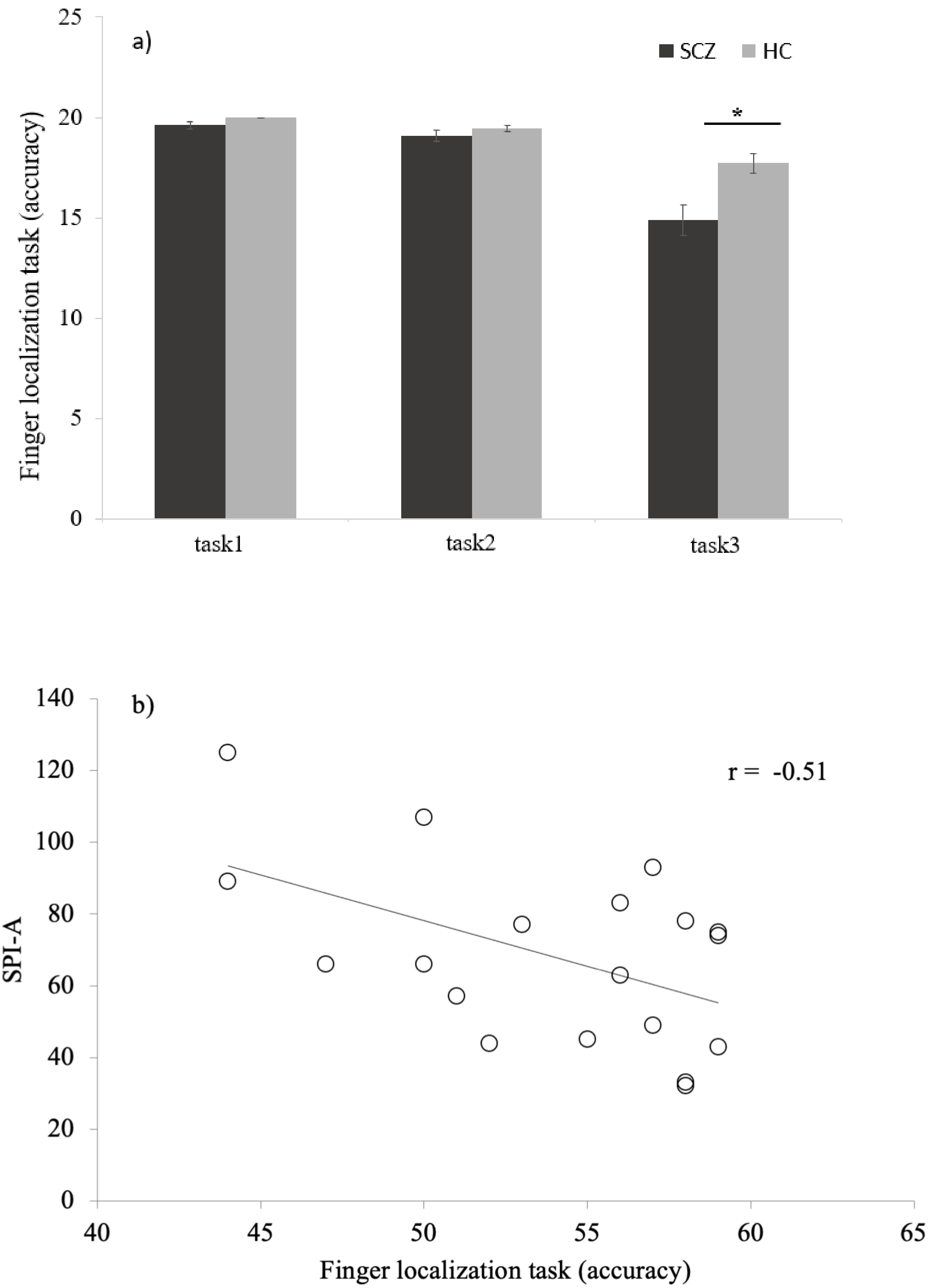
a)
SCZ
HC
*
Finger localization task (accuracy)
25
20
15
10
5
0
task1
task2
task3
b)
r = -0.51
SPI-A
140
120
100
80
60
40
20
0
40
45
50
55
60
65
Finger localization task (accuracy)

Fig. 5.2. Panel a) Mean accuracy in the Finger Localization Tasks in both healthy controls and SCZ patients. The maximum score for accuracy (i.e. summation of scores between right and left hand) is 20. **Panel b)** Correlation between SPI-A and accuracy in the Finger Localization Task in SCZ patients.

Importantly, for the SCZ group, we found a statistically significant negative association between the performance at the Finger Localization Task and the basic symptoms: the higher the SPI-A total score, the worse the individual accuracy when localizing the touched fingers ($r = -0.51$, $p = .026$; Fig. 5.2b).

5.6.2. Rubber Hand Illusion Task

An analysis of variance showed that factor “mode of RHI induction” was significant ($F(2,42) = 4.41$, $p = .02$, $\eta p2 = 0.173$). Post-hoc analyses (Newman-Keuls) revealed that the proprioceptive drift was significantly larger for the CS condition ($M = 1.93$, $SE = 0.71$) than both the control conditions, IS ($M = 0.18$, $SE = 0.03$; $p = .03$) and CA ($M = -0.27$, $SE = 0.66$; $p = .02$), which instead did not differ from each other ($p = .56$) (Fig. 5.3a).

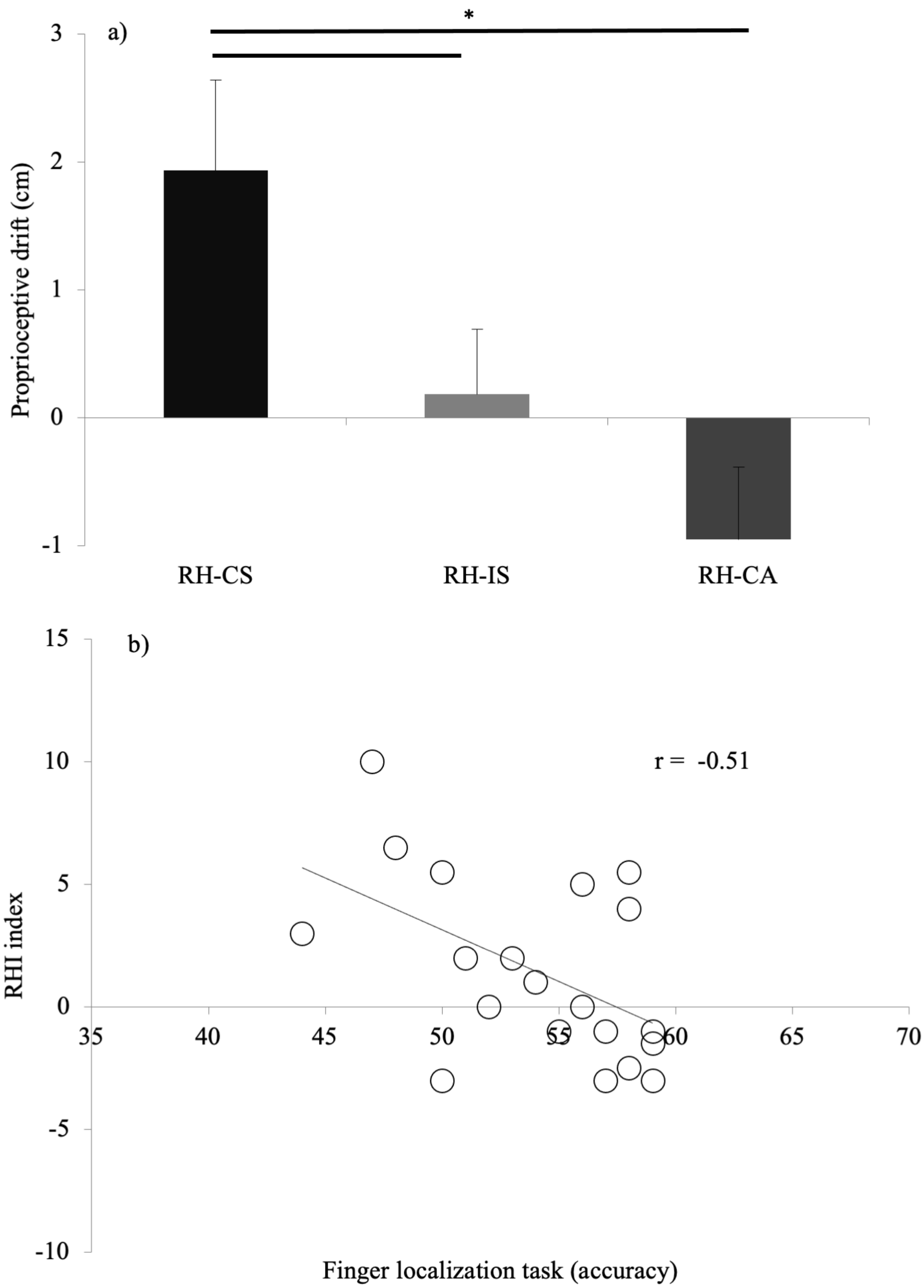

Fig. 5.3. Panel a) Mean proprioceptive drifts toward the rubber hand. Error bars indicate standard errors. Asterisk indicates significant differences between conditions.

Zero represents the felt position of the participant's hand in the pre-induction judgment. **Panel b)** Linear correlation between the RHI index and the accuracy in the Finger Localization Task.

5.6.3. Correlation between Rubber Hand Illusion and Finger Localization

As they did not differ significantly, we averaged the proprioceptive drift induced by the control conditions (IS and CA) for each participant and computed the individual RHI index as the difference between the proprioceptive drift induced by the CS condition and M(IS, CA). The test for the effect of hand representation on the sense of body ownership in patients showed a negative relationship ($r = -0.51$, $p = .02$). Thus, the lower the accuracy in the Finger Localization Task, the larger the RHI index. (Fig. 5.3b).

5.6.4 Correlation between Rubber Hand Illusion and basic symptoms

We found a non-significant correlation between the RHI index and the basic symptoms (as assessed by the SPI-A total score) ($r = 0.08$, $p = 0.725$).

5.7. Discussion

Disturbances in bodily self-awareness are considered to be hallmark signs for schizophrenia proneness (Magini & Raballo). This is supported by the basic symptom model of schizophrenia. Basic symptoms are considered as the most immediate expression of the neurobiological correlates of the illness (Klosterkotter et al., 1992; Nelson et al., 2019). The present study investigated the body structural representation (BSR), a specific type of body representation, and its association to basic symptoms in patients with schizophrenia. To this purpose, schizophrenic patients performed a Finger Localization Task. Results show that patients are significantly less precise than healthy controls when asked to identify pairs of fingers touched by the experimenter (when the hand is hidden from view). Furthermore, patients' performance at the Finger Localization Task was negatively correlated with basic symptoms: the worse the individual performance at the task, the higher the SPI-A total score. Also, performance at the Finger Localization Task was negatively correlated with the malleability of the sense of embodiment: the less the individual ability to localize fingers, the stronger the rubber hand illusion. These results suggest that a reduced body structural representation might stem from more malleable models of the body in schizophrenia, thus promoting an excessive incorporation of objects in the external space. Moreover, it provided evidence that body representation abnormalities are correlated with basic symptoms, which are considered the earliest subjectively experienced symptoms of schizophrenia.

In contrast to the emergent literature on body image in schizophrenia (Peled et al., 2003; Thakkar et al., 2011), the integrity of the BSR in schizophrenia has been investigated (so far) only in one study from Graham-Schmidt et al. (2016). The authors assessed the BSR by means of the In Between-Task, a task in which participants estimate the number of unstimulated fingers between two touched fingers. Moreover, the authors asked participants to perform a matching body parts by location task, a task in which participants determine which of three body parts presented on a screen is closest to the target body part. Both these tasks assess the integrity of BSR but using different stimuli, that is, tactile/proprioceptive stimuli the former task, while visual stimuli the latter. Interestingly, the authors reported that patients with schizophrenia made more errors than controls in the In Between task, while they performed no different from controls in the matching task. Thus, our results are consistent with those from Graham-Schmidt and colleagues.

It could be that the body structural representation is influenced by tactile acuity. This is also suggested by recent empirical evidence. Indeed, Peviani et al. (Sci Rep. 2019), using a Line Length Judgment task, showed that the estimation error relative to the length, but not the width, of most body parts, is predicted by the individual tactile acuity. Thus, it could be that the reduction in tactile acuity, already observed in schizophrenia, may at least contribute to some aspect of their body structural representation. Somatosensory disorders have been observed among individuals at higher risk for schizophrenia (Postmes et al., 2014). For instance, Chang and Lenzeweger (2001; 2005), found abnormal somatosensory processing in first-degree biological relatives of schizophrenia patients, such as a poor performance in the two-point discrimination task. Moreover, Ferri et al. (2016) found that individuals with high schizotypy were characterized by poor touch remapping abilities. When asked to perform a temporal order judgment of tactile stimuli delivered on their hands, high schizotypy individuals performed worse than individuals with low schizotypy, in both uncrossed- and crossed-hand conditions. It could be then, that the worse performance in the Finger Localization Task in patients compared to healthy controls, is caused by a reduced tactile acuity in schizophrenia. However, we observed a significant difference between patients and controls only for the third task of the Finger Localization Task -i.e. identification of pairs of fingers hidden from view (task C), but not in the first two tasks, i.e., identification of a single touched finger, with the hand visible (task A), or hidden from view (task C). If the within difference were entirely due to the possibly reduced tactile acuity in patients with schizophrenia, then it should impact upon all the three tasks constituting the Finger Localization Task. The fact that patients and controls differed only on the third task, the most difficult one, suggests that such difference was mainly due to the higher complexity of the body structural representation tested.

Previous accounts on the sense of embodiment, often inspired by studies on the Rubber Hand Illusion, have suggested that feelings of ownership result from both bottom-up processes (i.e. involving the multisensory integration of visual, tactile and proprioceptive information) and top-down processes (i.e. involving an internal representation of the body) (Tsakiris, 2010). Indeed, the illusion is usually not experienced when the rubber hand is spatially incongruent with the participant's real hand, or when non-corporeal objects are used, suggesting that a prior structural-spatial representation of one's body has a key role in constructing the experience of mineness. On this line of reasoning, it could be that the higher proneness to the Rubber Hand Illusion reported in schizophrenia (Peled et al., 2003; Peled et al., 2000; Thakkar et al., 2011), stems from more complex disturbances in, and higher malleability of, body representation. Unsurprisingly, body representations issues have been well-documented among schizophrenia spectrum disorders (Klosterkötter et al., 2001; Maggini & Raballo; Peled et al., 2003; Peled et al., 2000; Priebe & Rohricht, 2001; Rohricht & Priebe, 2002; Thakkar et al., 2011; Tordjman et al., 2019; Graham-Schmit, 2016). The results observed in the present study provides evidence in this direction. Indeed, reduced acuity in the BSR - as indicated by less accuracy at the Finger Localization Task - was negatively correlated with the Rubber Hand Illusion in patients with schizophrenia, indicating that individuals with less stable body representation are more susceptible to incorporate external objects.

Research has suggested that disturbances in the minimal self are a trait marker of schizophrenic vulnerability. Possessing a pre-reflective and implicit sense of self entails that there is a sense of embodiment; thus, the constitution of the minimal self has a bodily basis (de Haan & Fuchs, 2010). Disturbances in the sense of the embodiment occur many years before first frank symptoms appear (Parnas, 2000, 2003; Stanghellini, 2012). Pre-onset and onset phases are characterized by the presence of body abnormalities such as subtle transitivistic phenomena and disruption of bodily boundaries. The former refers to the inability to distinguish the self from the not-self; the latter refers to the externalization of parts of the body that are normally within the bodily boundaries, as well as the internalization of objects that normally occupy the external space (Mancini et al., 2015). Thus, the disruption of the ego boundaries assumes a particular relevance as a psychopathological phenomenon insofar as it is useful for describing and understanding the schizophrenic prodrome.

This inability to inhabit one's body implies that the body has lost its 'taken for granted', implicit quality of a medium for relating to the world (Sass, 2000). For instance, parts of the body that are normally tacitly and implicitly present in the background of experience must be recovered from time to time, controlled and reasserted. This excessive form of reflectivity (see hyperreflexivity, section 1.2.1) leads the subject to assume a third-person perspective towards their body (Nelson et al., 2009; Parnas 2003; Mancini et al., 2014). Typically, this sensation is accompanied with an experience of devitalization and diminished self-presence. Interestingly, this persistent feeling that one is observing oneself from an outside perspective is typically observed in depersonalization-derealization disorder and in dissociative identity disorder (Grauz et al., 2011; Salami, Andreu-Perez & Gillmesteir, 2020).

To conclude, the results suggest that abnormalities in the body structural representation in schizophrenia i) are linked to core symptoms that are commonly taken as phenomenological markers of schizophrenia risk; ii) may contribute to a more malleable body representation, reduced sense of body ownership and more “permeable and blurred boundaries of the body” (Postmes et al., 2014). In this context, the subject may progressively experience a dissociation between their lived body (i.e. the body that ‘I’ am) and the objective body (i.e. the body that ‘I’ have), with the third-person perspective becoming more salient than the first-person perspective. This hypothesis needs to be tested in future investigations in order to shed new light on the interaction between different body abnormalities in schizophrenia spectrum disorders and, more broadly, in dissociative experiences generally.

Chapter Six

Body Structural Representation in schizotypy

6.1. Abstract

A deficient sense of self, typically observed in schizophrenia spectrum disorders, is often accompanied by abnormalities in bodily perception and awareness. These abnormalities are seemingly among the most powerful predictive factors for the onset of schizophrenic illnesses. According to the hypothesis of the schizophrenia continuum, high schizotypal traits in the general population may be characterised by a progressive sense of detachment from one's lived body. Building upon previous research that found an abnormal Body Structural Representation (BSR) in individuals with schizophrenia, this study aims to extend these findings to schizotypy. To do so, we utilised the Finger Localization Task (FLT), in which participants must identify the finger touched by the experimenter, and the In Between Task (IBT), in which two fingers are touched, and participants must specify the number of fingers in between the two stimulated fingers. We found that individuals with high schizotypy were significantly less accurate than individuals with low schizotypy in determining the spatial configuration of their own fingers relative to each other. Most significantly, performances on both tasks were negatively correlated with the score on the Dissociative Experiences Scale (DES). These findings support the hypothesis that the progressive loss of one's sense of self is associated with abnormal bodily experiences and dissociative symptomatology which may represent a potential marker for schizophrenia proneness.

6.2. Introduction

Schizophrenia spectrum disorders are characterised by a complex profile of symptomatology. The core feature of the spectrum appears to be characterised by abnormalities of fundamental selfhood, sometimes termed 'ipseity' or the 'minimal self' (Nordgaard & Parnas, 2014; Gallagher 2004). The minimal self could be described as a pre-reflective sense of awareness that one is an autonomous agent who 'owns' their experiences. The minimal self can be contrasted with the narrative or descriptive self, which involves autobiographical information or an explicit concept about one's individual identity. Thus, even if the narrative or descriptive self is impaired (as may occur in amnesia), the minimal self will remain intact provided that the individual retains a pre-reflective sense of agency and body ownership. Phenomenologically oriented neuroscientists have posited that one's body provides a tacit, "background" sense of one's first-person presence and relationship to the environment. Thus, pre-reflective forms of selfhood are likely rooted in a bodily context as the body represents a "minimal threshold" component of selfhood, which does not need to be explicitly conceptualised to profoundly influence the agent's cognition (de Haan & Fuchs 2010). Research has afforded significant attention to clinical manifestations of embodiment and selfhood, particularly insofar as such body perception related measures improve the early detection of, and provide preventive measures for, schizophrenia. Indeed, several studies have found that an anomalous sense of body ownership (Peled, 2000, 2003, Thakkar et al., 2011, Ferri et al., 2014; Ferri et al., 2020), aberration in body image (Priebe & Rohricht, 2001; Ferri et al., 2012), disintegration of bodily boundaries (Parnas et al., 2003; Noel., 2016; Di Cosmo, 2018), abnormal sensorimotor representation (Ardizzi, 2020) and perceived changes in the shape and location of body parts (Priebe & Röhricht, 2001) are common features to schizophrenia spectrum disorders. In particular, it has been observed that abnormalities in the sense of embodiment, such as loss of contact with one's own body and disintegration of bodily boundaries, actually manifest prior to the first symptoms typically used to establish a diagnosis (Szczotka & Majchrowicz, 2018; Maggini & Raballo, 2004; de Haan & Fuchs, 2010) and persist during the course of the disorder (Nelson et al., 2012). Thus, these abnormalities in embodiment and corporeality are observable in those who merely carry liability for schizophrenia (e.g., schizotypes), significantly before the onset of the first schizophrenia symptoms occur (Handest & Parnas, 2005). Correspondingly, the symptomatology observed in schizophrenia spectrum disorders may be a consequence of more malleable models of body representation (Graham-Schmidt et al., 2016) and of an earlier loss of contact with one's own body (Huber, 1957; Stanghellini et al., 2012)

The development of a coherent sense of self can be considered as a process that requires the retention of various body representations. Most prominent of these include 'body schema' and 'body image'. However, there has been confusion surrounding the distinction between these two concepts (Gallagher & Zahavi 2012). To clarify, body *image* is an explicit attitude or perception directed towards one's own body, whereas the body *schema* constitutes a set of largely automatic task-related, bodily-motor orientations. While my body itself is the intentional-object in the body image (how my body looks or feels *to* me), the environment is the intentional-object in the body schema (how I use my body to engage in various actions) (Merleau-Ponty, 1945; Gallagher & Zahavi 2012). This distinction echoes the phenomenological division between the body-as-object or *"Körper"* (i.e., the physical body "I" that is observable both by myself and by others), and the body-as-subject or "*Leib*" (i.e. the body "I" pre-reflectively experience as a subject) (Merleau-Ponty, 1945).

One emerging yet understudied example of a body representation is the Bodily Structural Representation (BSR). BSR denotes the agent's topological model of how their various body parts relate to one another in a spatial configuration (Longo, 2016). A functional bodily structural representation likely allows the individual to properly explore their own body (body image) and to use their body as an interface for engaging with the world (body schema) in a properly co-ordinated fashion. Impairments in the BSR are often localised to the fingers, such as in finger agnosia (patients who are unable to identify their digits) (Kinsbourne & Warrington, 1962). Those with severe BSR impairments cannot point to their body parts on command nor judge the spatial relationships between body parts, such as in the condition of autotopagnosia (Longo, 2016).

In Chapter Five, we found that schizophrenic patients show impairments in the Finger Localization Task, a task designed to detect abnormalities in the BSR (Costantini et al., 2020). Our findings show that BSR abnormalities were correlated with deficits in body ownership, as indicated by higher susceptibility to the Rubber Hand Illusion, and to basic symptoms (i.e. a set of mild self-experienced subclinical disturbances that are present since the prodromal phase; Schultze-Lutter, 2009). These findings support previous evidence which found that the somatotopic map of the hand and fingers in the primary somatosensory cortex (SI) is altered in patients with schizophrenia (Geyer et al., 1999). Moreover, evidence supporting a deficient BSR in schizophrenia has recently been observed by Graham-Smith et al. (2016). The authors found that patients with schizophrenia performed poorly in the In Between Task, a task in which a correct performance relies on an intact BSR of the hand and more particularly the fingers. This deficit in body structural representation could be conceptualised in terms of a weakened internal modelling of the self or an excessive plasticity of its boundaries and spatial configuration. This is consistent with observations that the sense of self generally is either deteriorated or more malleable in people with schizophrenia spectrum disorders (Thakkar et al., 2011) and that this deterioration or malleability includes pre-reflective experiences of embodiment (Parnas, 2013; Fuchs, 2005; Ferri et al., 2012).

The aim of the present study was to broaden previous findings by investigating the Body Structural Representation in individuals with high and low schizotypy. For this purpose, we utilised the Finger Localization Task (FLT) (Benton et al., 1994), in which participants have to identify which of their fingers is being touched by the experimenter, and the In Between Task (IBT) (Kinsbourne & Warrington, 1962), in which two fingers of the same hand are touched, and the participants must count the number of fingers in between the two stimulated ones. Both tasks assess fine-grained acuity in body mapping (Kinsbourn & Warrington, 1962; Benton et al., 1994; Graham-Smith et al., 2016) and have been utilised to investigate Body Structural Representation in schizophrenic individuals (Graham-Smith et al., 2016; Costantini et al., 2020).

Our hypothesis was that individuals with high schizotypy, as assessed by the Schizotypal Personality Questionnaire (SPQ), would display less accuracy in BSR-related tasks than people with low schizotypy. This hypothesis is in keeping with the continuum hypothesis which posits that characteristic symptoms of schizophrenia are present in less severe forms in individuals with high schizotypy (DeRosse & Karlsgodt, 2015; Kwapil & Barrantes-Vidal, 2015; Nelson et al., 2013). Moreover, grounding on prior research that observed an overlap between dissociation and schizophrenia (Ross, 1997; 2009), we asked participants to complete a questionnaire designed to measure dissociative experiences: the Dissociative Experiences Scale (DES). We predicted that reduced performance accuracy in the tasks would be associated with higher scores in the SPQ and the DES.

6.3. Materials and Methods

6.3.1. Participants

Two hundred sixty-eight students, recruited via mailing lists at the University of Essex, were screened with respect to schizotypal personality traits using the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). The distribution of scores was divided into quintiles, with the first quintile representing the participants rated as low schizotypes and the fifth quintile representing the participants rated as high schiotypes. Based on their scores, 55 participants in total were called to complete the full study. The study was approved by the University of Essex Ethics Committee. All participants read and signed a consent form prior to their participation. None of the participants reported any history of substance abuse or other neuropsychiatric disorders.

6.3.2. Questionnaires

6.3.2.1. *Schizotypal Personality Questionnaire (SPQ)*

Schizotypal personality traits were assessed using the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991). The SPQ is a 74-item questionnaire that has been modelled after the DSM-III-R schizotypal personality disorder diagnostic criteria

(Venables and Raine, 2015). The questionnaire assesses three well-replicated factors of schizotypy: cognitive-perceptual deficits, interpersonal deficits, and disorganisation. This factor structure of the SPQ corresponds to the three cluster symptoms observed in people with schizophrenia (DSM-V, 2014): positive symptoms (i.e., cognitive-perceptual symptoms such as hallucinations and delusions), negative symptoms (i.e., interpersonal symptoms such as apathy and social avoidance) and disorganised symptoms (i.e., disorganisation symptoms such as abnormal speech and behaviour).

6.3.2.2. *Dissociative Experiences Scale (DES*)

On the day of the experiment, participants were asked to complete the Dissociative Experiences Scale (DES) (Bernstein and Putnam, 1986). The Dissociative Experiences Scale (DES) is a widely used instrument in both clinical and nonclinical samples. The scale consists of 28 items assessing the frequency and the severity of a series of dissociative experiences. Participants were asked to determine to what extent the experiences described would apply to them by using an eleven-point visual analog scale (0%–100%) (Mazzotti et al., 2016). The DES assesses different aspects of dissociation: absorption (e.g. experiences of detachment with the immediate surroundings and with the present moment); depersonalisation (e.g. feelings of disconnection from one's identity and body, such as out-of-body experiences); derealisation (e.g. feelings of alienation from the outside world which is perceived as unreal and not recognizable – i.e. objects perceived as altered, individuals perceived as inanimate); dissociative amnesia (i.e. failure into retrieving personal information that would normally be accessible) (Waller et al., 1998). Factor analyses has showed that a three-factor model best account for clinical samples (Ross et al., 1995), whereas one-factor best account for nonclinical samples (Holtgraves & Stockdale, 1997), indicating that overall score is the most reliable measure for the purpose of the current study where we investigated sub-clinical samples. Research has suggested that scores above 30 are highly indicative of severe dissociative pathology and scores above 40 are highly indicative of dissociative personality disorders (Carlson & Putnam, 1993).

6.4. Behavioural tasks/Procedure

6.4.1. Finger Localization Task

Participants sat in front of a table with a box, which served to hide the participant's hands, and a drawing (outline) of a human hand. In the outline drawing, the fingers of each hand were given a number (see Fig. 6.1) that participants could use to identify the corresponding finger on their own hand. Participants were asked to put their hands on the table, with their palms facing upwards and their fingers stretched and slightly separated. Participants provided their responses by naming the fingers that were stroked referring to the outline drawing of a hand with numbered fingers. Correct responses were recorded with pen and paper. The test consisted of three tasks (ten trials on each hand per task). The first task required participants to identify the finger of the left or the right hand touched by the experimenter (Fig. 6.1a). The second task required participants to identify the finger of the left or the right hand touched by the experimenter, with the hands hidden from view (Fig. 6.1b). Finally, the third task required participants to identify pairs of fingers of the left or the right hand touched by the experimenter with the hand hidden from view (Fig. 6.1c). In the third task, responses were counted as correct when both fingers were accurately identified. The maximum total score was 60 across tasks A, B and C (20 for each task).

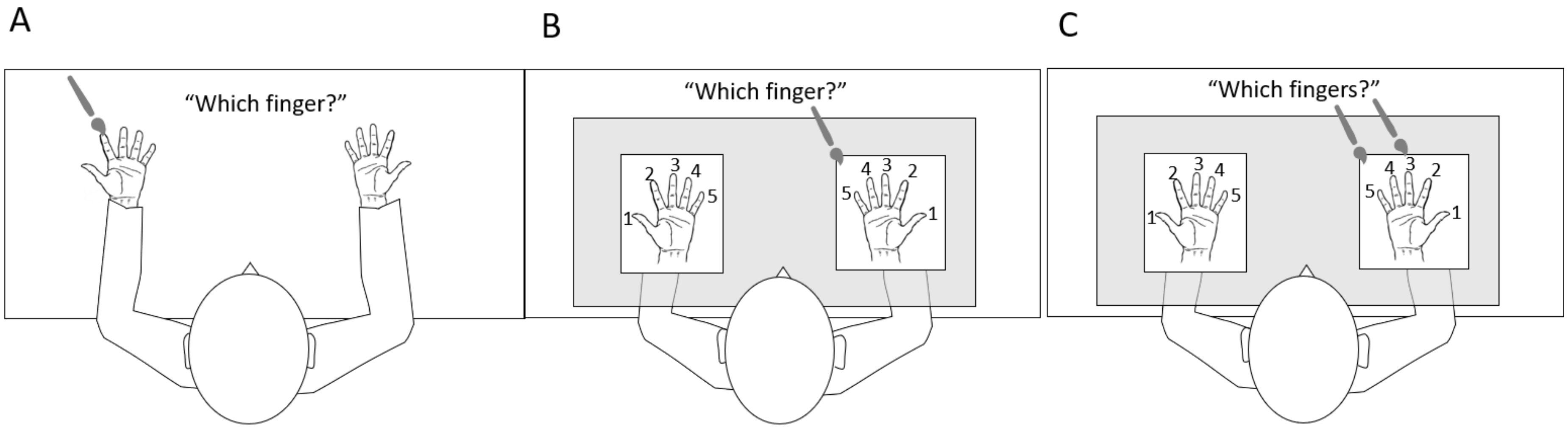

Fig. 6.1. (a, b, c) Experimental conditions of the Finger Localization Task. Participants had to identify the finger touched by the experimenter, with the hands visible **(a)** or hidden **(b)** from view. In a third condition, they had to identify pairs of fingers touched by the experimenter, with the hand hidden from view **(c).**

6.4.2. In Between Task

The In Between Task has been widely used in research to investigate body structural representation of the hand in neurological patients (Kinsbourne & Warrington, 1962). The task has had various adaptations in different research assessing body structural representation also in healthy participants, and the cortical areas involved (Rusconi et al., 2014). Here, we utilised a variation of the original task by Kinsbourne & Warrington (1962).

Participants sat in front of a table with their hands resting on the table and their palms up, finger slightly spread, eyes closed. The experimenter simultaneously stroked two fingers on the participant's hand, making sure to apply the same pressure for approximately one second (Graham-Smith et al., 2014). Participants were asked to make unspeeded verbal responses as to how many fingers they felt were between the fingers that were touched (See Fig. 6.2). Responses were manually documented by the experimenter. The procedure was repeated ten times for each hand. The order of the trials was established in a pseudo-random manner before the test began, following a pre-established combination. The combination in which no fingers was in between on either hand ("0" answer) was presented twice; one finger in between ("1" answer) was presented three times; two fingers in between ("2" answer) was presented twice and three fingers in between ("3" answer) was presented three times. This particular adaptation was adopted as a variation of the original task (Kinsbourn and Warrington, 1962), which was considered too simplistic to assess performance in healthy individuals without any known neurological condition.

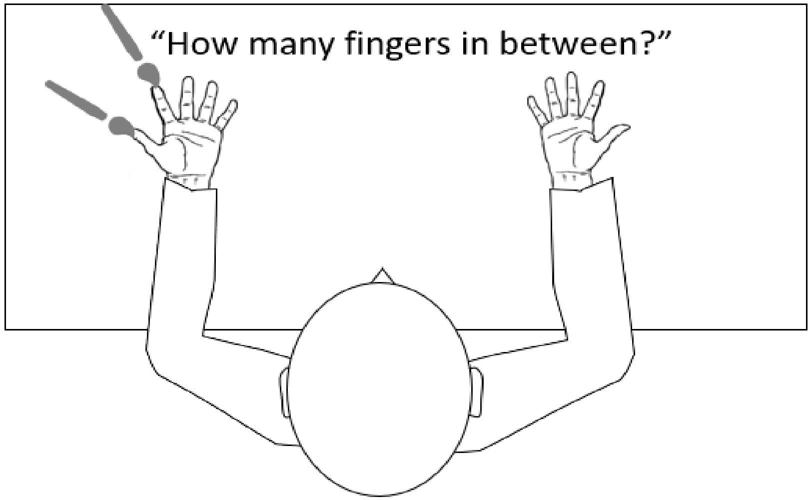

Figure 6.2. In Between Task. Participants kept their eyes closed. Experimenter stroked two fingers of the same hand. Participants had to verbally report how many fingers they felt were between the fingers that were stroked. There was one block of 20 trials per hand (40 trials in total). The combination in which there were no fingers in between on either hand (answer "0") was presented twice; one finger in between (answer "1") was presented three times; two fingers in between (answer "2") was presented twice and three fingers in between (answer "3") was presented three times.

6.5. Results

6.5.1. Self-report measures

6.5.1.1. Schizotypal Personality Questionnaire

From 268 participants who initially completed the SPQ questionnaire, 55 participants in total were called to complete the full study. Based on their scores, a total of 28 participants were selected from the uppermost 20% of the scores (score range: 35-60), representing participants rated as high schizotypes, and 27 from the lowermost 20% of the scores (score range: 2 -16), representing participants rated as low schizotypes. This sample consisted of 14 male and 41 female participants.

6.5.1.2. Dissociative Experiences Scale

The 28 items of the questionnaire were assessed using an eleven-point scale (0%-100%). The scores were calculated by totalling the percentage indicated by each participant for each question (from 0% to 100%) and then dividing it by 28. The scores ranged from 0 to 100 (score range: 6.4-74). Those who scored above 30 (24 participants out of 55), were considered to have high dissociative traits. A t-test was performed to check whether the DES scores differed between participants who scored high and low in the SPQ. Mean score on the DES for participants with low SPQ scores ($M = 17.4$, $SD = 10.8$), significantly differed from mean score on the for participants with high SPQ scores ($M = 39$, $SD = 17$), demonstrating that individuals with higher schizotypal traits on average scored higher on the DES ($t(54) = 2.009$, $p =.00$).

6.6. Behavioural Tasks

6.6.1. Finger Localisation Task and SPQ

As in Chapter Five (Costantini et al., 2020), performance in tasks A and B was at ceiling, with 96.4% of participants obtaining the maximum score in task A and 80% obtaining the maximum score in task B. Correct responses from the Finger Localisation task C (i.e. hands hidden condition) were analysed using 2 by 2 ANOVA with laterality (left hand vs right hand) as within-subject factors, and group (high vs low schizotypy) as between-subject factor. Post-hoc analyses (Newman-Keuls) tested for between-group differences. An analysis of variance showed that the factor group was significant ($F(1,53) = 9.301$, $p < 0.001$, $\eta^2 = 0.15$) as the low schizotypy group ($M = 17.9$, $SE = .44$) showed higher accuracy than the high schizotypty group ($M = 15.64$, $SE = .59$) in task performance (Fig. 6.3.). No effect was found for hand laterality ($F(1,53) = .399$, $p = 0.53$).

6.6.2. Finger Localization Task and DES

The effect of dissociative symptomatology on the structural representation of the hand was analysed using the Spearman correlation analysis. A statistically significant negative correlation was found ($rs(53) = -.32$, $p = .01$) indicating that the higher the DES total score, the worse the individual accuracy when localising the touched fingers (Fig.6.3.).

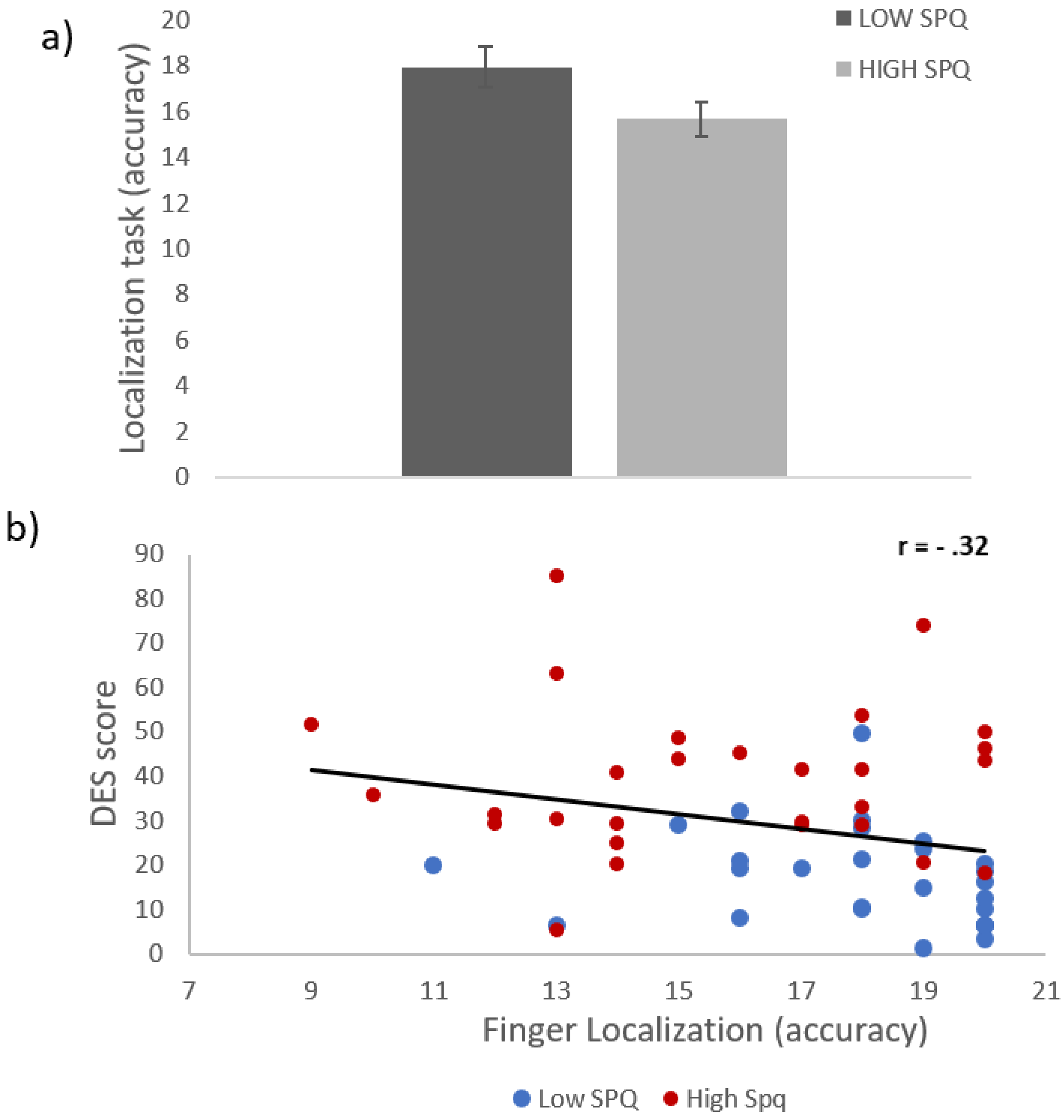

Figure 6.3.

Panel A. Mean accuracy in the Finger Localization Task in both high and low schizotypes. Values correspond to task condition "c" ("hands hidden"). **Panel B.** Correlation between DES total score and accuracy in the in the Finger Localization Task for all participants. Participants are colour-coded according to whether they were from the low or high schizotypy group.

6.6.3. In Between Task and SPQ

Correct responses from the In Between Task were analysed using 2 by 2 ANOVA with laterality (left hand vs right hand) as within-subject factors, and group (high vs low schizotypy) as between-subject factor. Post-hoc analyses (Newman-Keuls) tested for between-group differences. Analysis of variance showed that the factor group was significant ($F(1,53) = 7.900$, $p < 0.001$ $\eta^2 = 0.13$) as the low schizotypy group ($M = 19.33$, $SE = .25$) showed higher accuracy than the high schizotypty group ($M = 17.71$ $SE = .51$) in task performance (Fig.6.4.). No effect was found for hand laterality ($F(1,53) = 1.276$, $p = 0.26$).

6.6.4. In Between Task and DES

To test for the effect of dissociative symptomatology on the structural representation of the hand (in absence of multisensory stimulation), we ran a correlation (Spearman) between the individual accuracy at the In Between Task and the DES total score. A significant negative correlation was found ($r_s(53) = -.35$, $p < .001$) indicating that individuals with high dissociative traits are less accurate when asked to identify how many fingers are in between the stroked fingers (Fig.6.4.).

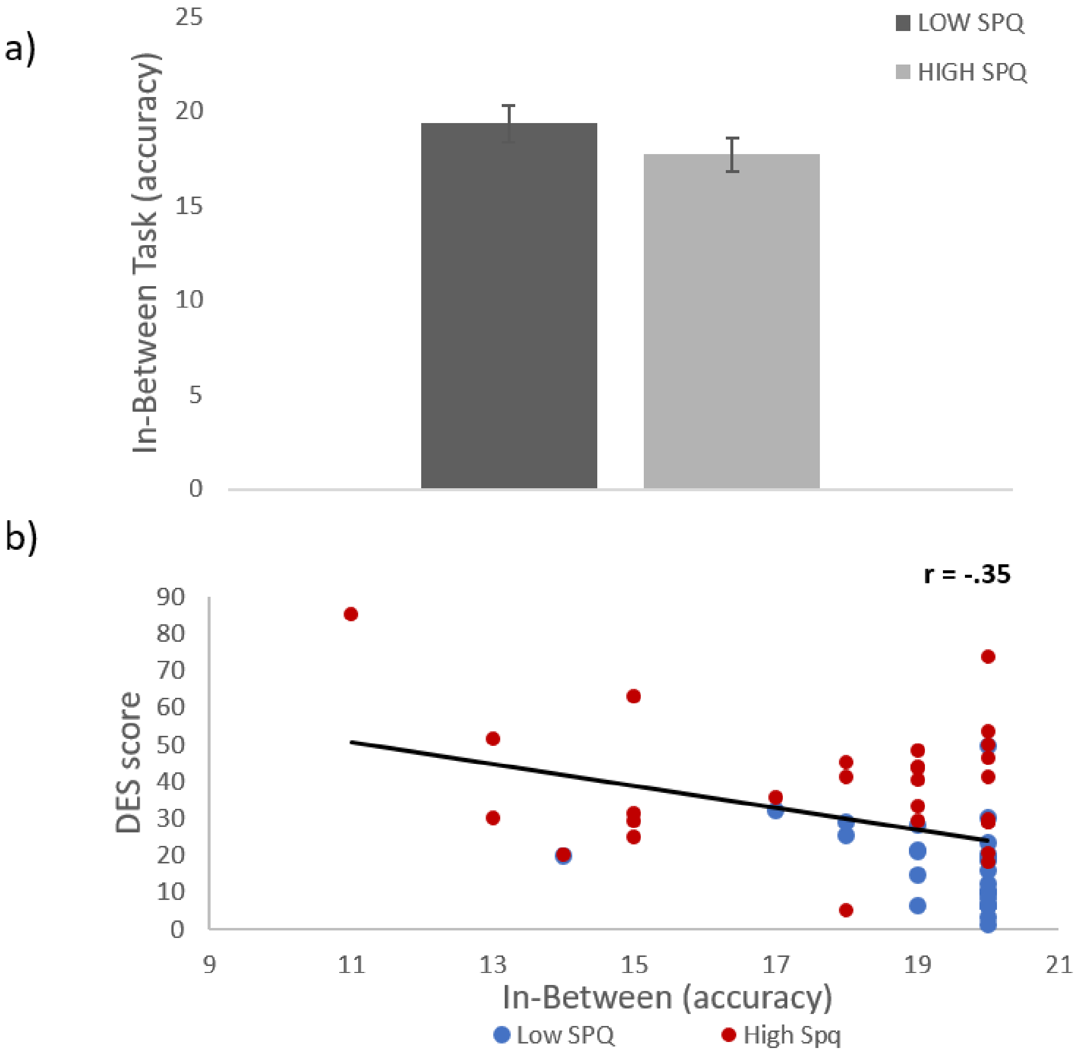

Figure 6.4. Panel A. Mean accuracy in the In Between Task in both high and low schizotypes. **Panel B.** Correlation between DES total score and accuracy in the In Between task for all participants. Participants are colour-coded according to whether they were from the low or high schizotypy group.

6.7. Discussion

This study aimed to investigate the body structural representation in individuals with high and low schizotypy. To this purpose, we used two tasks: the FLT and the IBT. Both tasks have recently been employed for assessing BSR in individuals with schizophrenia (Costantini et al., 2020; Graham-Smith, 2014). In accordance with the idea of schizophrenia as a continuum (DeRosse & Karlsgodt, 2015; Kwapil & Barrantes-Vidal, 2015; Nelson et al., 2013), our findings suggest that individuals with high schizotypy, similar to schizophrenic patients, display a reduced accuracy in BSR-related tasks. More specifically, our results show that individuals with high schizotypy are significantly less accurate than individuals with low schizotypy in identifying the stimulated fingers and situating them to an outline of the hand (FLT), or in determining the spatial relationship between the stimulated fingers when their eyes are closed (IBT). Moreover, our findings show that performances in both tasks were negatively correlated with scores in the DES: the worse the individual accuracy, the higher the DES score.

Taken together, these results contribute to the mounting evidence that suggests that abnormalities in various dimensions of corporeality and self-awareness are common, unifying features in schizophrenic-like condition, including the sub-clinical types. In line with this hypothesis, we propose that aetiological features of schizophrenia spectrum disorders might be better understood by further explicating their shared bodily roots. In the case of Bodily Structural Representation, a functional BSR implies an understanding of the objective spatial configuration of one’s body and of its place in the environment. Consequently, agents with an impaired understanding of the structure of their bodies and its specific spatial configuration may be more malleable to adopting faulty models of their body’s spatial mapping and location. The lack of a coherent understanding of oneself as a structural entity in the world may be associated with deficits in the minimal self that are typically observed in the schizophrenic spectrum. As the minimal self is mediated through the body, disruptions in BSR may constitute one of several embodiment-related factors that contribute to well-documented disturbances in minimal selfhood and the confusion between first and third-person perspectives present in schizophrenia spectrum disorders.

Interestingly, research observed that schizophrenic patients display a tendency to disengage from normal forms of involvement with the external world, particularly with such acts that would normally be tacit ("in the background") and transparent. For instance, some patients report becoming excessively aware of the act of breathing or the movements of their arms while walking (Nelson & Sass, 2016). These sensations often concern the domain of pre-reflective bodily experience, whereby the body is no longer experienced as tacitly given in the first-person perspective, but it rather loses its transparent quality and becomes an overt object of observation and concern (Irrazàval, 2015). This loss of the transparent, pre-reflective sense of one's embodiment ultimately affects the capacity to switch between the body-as-subject (body schema) and the body-as-object (body image) dimensions of embodied experience, producing a fracture between the observing and the observed self (Sass, 2003). Consequently, one could feel as if they are observing their own experiences in third-person, rather than from a first-person perspective. This tendency has also been referred to as "hyperreflexivity", i.e. where bodily processes that are otherwise typically unnoticed instead become intensified in reflective consciousness. It has been hypothesised elsewhere that hyperreflective dimensions of self-consciousness might stem from disturbances in the minimal self (Sass 2013; Fuchs, 2005).

Interestingly, similar experiences of self-detachment (i.e., a fracture between the observing and the observed self) are predominant characteristics of dissociative disorders (Sass, 1992; Bob et al., 2013; Ciaunica, 2020). Research has found that dissociative symptoms often overlap with schizophrenic symptoms (Haugen and Castillo, 1999; Putnam et al., 1986) and with schizotypal personality traits (Pope & Kwapil, 2000; Merckelbach et al., 2000; Watson, 2001). In particular, a study by Watson (2001), found that the features that contribute most strongly to this relationship pertain to symptomatology concerning detachment and depersonalisation constructs that are deeply related with changes in the quality of embodied, pre-reflective experiences. These experiences include sensations of estrangements from one's self, body, body parts, or one's surroundings (Ciaunica et al., 2020). However, individuals with dissociative disorders are usually aware that these are subjective and temporary phenomena, rather than an 'objective' reality (Ciaunica et al., 2020). It could be hypothesised then, that their 'minimal selfhood' is preserved. On this basis, future research could investigate which processes could represent distinguishing clinical factors between dissociative disorders and schizophrenia spectrum disorders. We propose that greater focus on the early detection of minimal selfhood disruptions and body abnormalities in dissociative symptomatology and schizophrenic spectrum conditions could provide useful insights in regard to this facet.

In conclusion, our results suggest that an abnormal BSR represents a potential early marker of schizophrenia. Indeed, abnormalities in BSR contribute toward observed anomalies in related body representations (e.g. body schema) which, collectively, may contribute to the development of a deficient sense of self. Evidence of a deficient BSR in both clinical and sub-clinical populations may further illuminate the nature of disordered self-experiences that are predictive of schizophrenia onset. Further research could investigate to what extent deficits in the BSR extend to other parts of the body. Furthermore, it may also be productive to investigate the difference between deficits in body structural representation and other deficits in spatial processing and representation. In addition, the results from the present paper provide further insights regarding the relationship between schizophrenia spectrum conditions and dissociation. Interestingly, prior research found that both dissociation and schizophrenia spectrum disorders are often associated with a history of trauma (Allen & Coyne, 1995; Salami, Andreu-Perez & Gillmesteir, 2020). This relationship might be linked to the fact that post-traumatic intrusions foster abnormal perception, temporality deformation, dysfunctional reality testing abilities and bodily sensations, and may ultimately induce changes in the overall texture and quality of experience and contribute to the development of dissociative experiences (Morrison et al., 2003). Subsequent research might focus on the interrelationship between body abnormalities in schizophrenia spectrum disorders, the history of trauma and dissociation. This may further clarify the link between self-disturbances and schizophrenic spectrum conditions and help to identify suitable strategies for early intervention.

7. Chapter Seven

7.1. General Discussion

The goal of this doctoral research project was to investigate the mechanisms underlying the development of schizophrenia spectrum disorders. Although there have been many attempts to explain the processes involved in the emergence of the disorder, there is still the need to extract from these processes a cohesive theory. The necessity of understanding the subjective dimension of schizophrenia has led researchers to make use of the contribution of phenomenology, which provides an adequate conceptual framework for describing the experiential aspects of the disorder. For this reason, this project revolved around past and recent theories, both from phenomenology, psychology and neuroscience, which have attempted to create a comprehensive account of the disorder. Most prominent theories have conceptualised schizophrenia spectrum disorders as disorders of the most basic sense of self-awareness: the minimal self. Minimal selfhood entails that a subject has an implicit, pre-reflective, non- objectifying and non-observational sense of existing as a subject of awareness. This basic form of self-awareness is rooted in the bodily experience, is based on the integration of multisensory information, and carries the potential for action (i.e. it is understood as a “predisposition” towards objects in the environment or an “immersion” in a world of affordances). The disruption of aspects such as multisensory integration, ego-boundaries and agency, have been well documented in schizophrenia. On this line of evidence, I aimed to investigate how abnormalities in multisensory temporal integration (Chapter Three), its underlying patterns of neuro-oscillatory activity in the brain (Chapter Four) and body representation (Chapters Five and Six) deficits may account for self-disorders and could be predictive of schizophrenia onset.

Linking the evidence that has emerged from the studies presented in this thesis to disturbances in the minimal self can be problematic, as most of the concepts relating to the “self”, are largely descriptive concepts. In general, phenomenological oriented researchers argue that self-disturbances are strictly related to abnormal perceptual organization and multimodal integration, and to fundamental anomalies in the experienced sense of existing as a subject of awareness (e.g., body ownership) or agent of action (e.g., sense of agency) (Borda & Sass 2015). The studies presented in this thesis have attempted, at least indirectly, to address the aforementioned components (i.e., multisensory integration and bodily self-awareness).

7.2. Summary of findings

7.2.1. Multisensory Integration

A background composition of multisensory information is always present in everyday experience and is responsible for shaping and maintaining the implicit awareness of ourselves, i.e., minimal self. In this sense, the minimal self could be thought of as analogous to a “sensory self” (Postmes et al., 2014). Therefore, it has been assumed that a disruption in multisensory processing might reflect a general decline of the common clearness in the field of awareness, which indicates a more fundamental decline in normal self-experience. As already observed in research, specific degrees of temporal tolerance for multisensory stimuli asynchronies are fundamental to integrate different inputs into a singular holistic Gestalt, or a coherent percept. The version of Double Flash Illusion utilised in Chapters Three and Four has allowed us to specifically manipulate the time window wherein multisensory stimuli were presented and to investigate the difference in multisensory temporal acuity of low-level information (e.g., a simple tactile and a simple visual stimulus) in individuals with high and low schizotypal traits. Both studies revealed an increased amount of illusions for temporally distant auditory (Chapter Three) and tactile (Chapter Four) stimuli (i.e. enlarged temporal window of integration), in line with research on schizophrenic patients. These results might suggest that a reduction in multisensory temporal acuity could indicate of a more general disruption of the 'grip' or 'hold' on the perceptual world and ultimately be responsible for a decline in normal self-experience.

With this in mind, the work in **Chapter Three** (Ferri et al., 2018) was based on the initial observation that integration of simple audio-visual sensory stimuli in healthy individuals seems to happen within a temporal window of around 100ms (Shams et al., 2012; Cecere et al.,2015), and that such window of audio-visual integration is larger in individuals with schizophrenia spectrum disorders (Haß et al., 2017). For this purpose, we utilised the auditory-induced Double Flash Illusion to investigate whether individuals with high schizotypy exhibited reduced temporal sensitivity, indexed by an enlarged temporal window within which the illusion is maximally perceived (i.e. the Temporal Window of Illusion, TWI). Results showed that individuals with high schizotypy integrate audio-visual information over longer periods of time (i.e. they have reduced temporal sensitivity) compared to individuals with low schizotypy. Moreover, we observed a higher proneness to the illusion in individuals with high vs low schizotypal traits.

In order to test whether such enhanced proneness to the illusion was a direct consequence of a larger TWI and not, instead, a consequence of a more general noise in sensory processing, we normalised the measure of proneness to the DFI to each individual TWI by calculating the percentage of perceived illusion falling in the 3 SOAs preceding the inflection point (i.e. the point in which the illusion starts to decay). In this way, the absolute number of SOAs sensitive to the illusion was kept constant across participants and any differential effect of proneness was now controlled for by any individual difference in TWI. Results show that the between-group differences in the proneness to perceive the illusion were abolished when correcting for the individual TWI. Therefore, we have discarded, at least indirectly, the alternative hypothesis that our results reflect a general problem in sensory processing per se that is independent of the individual TWI. Instead, our novel findings point to the idea that a reduced temporal sensitivity, as indexed by an enlarged TWI, fully mediates the proneness effects of the crossmodal induced illusion observed in the high- (vs low-) schizotypy group.

Here, a possible limitation is that even if the TWI represents an implicit measure of multisensory binding, it is derived from the same data as the mean rate of double-flash illusions. Indeed, the TWI has been inferred from the rate of illusion itself. In future research, it will be convenient to utilise additional unimodal or multisensory control conditions to test for alternative interpretations of our data, notably response bias toward saying “2” (i.e., reporting seeing two flashes) against sensory temporal resolution. A similar approach has been utilised by Stevenson et al. (2014). The researchers measured the TWI by manipulating the stimulus onset asynchronies between visual and auditory information (i.e., simultaneity judgment task). Subjects had to evaluate whether auditory and visual information was simultaneous or asynchronous. Afterwards, the researchers examined whether the individual TWI, i.e., the audio-visual discrimination abilities, correlated with the McGurk or sound-induced flash illusion, which were evaluated in a separate experimental session.

With the purpose of understanding which processes underlie such difference in the width of the TWI between individuals with high and low schizotypy, in **Chapter Four**, we went a step forward and investigated the neural processes underlying multisensory integration. Successful multisensory processing requires the coordination of information across widespread brain areas (Stekelenburg et al., 2013). Research has recently started to focus on the neuro-oscillatory processes that facilitate the coordination and integration of sensory information across modalities. Unsurprisingly, evidence is now emerging linking abnormal oscillatory activity in different frequency bands and impaired multisensory integration in schizophrenia spectrum disorders (for a review, see Uhlhaas et al., 2011). Thus, our research grounded on previous evidence which found that the temporal window of integration for the auditory-induced DFI in healthy individuals (100 ms), corresponds to the duration of an alpha cycle (Cecere et al., 2015). Cecere et al. (2015) provided causal evidence for a link between oscillatory alpha activity and temporal resolution of the TWI by stimulating the occipital pole via transcranial alternating current stimulation (tACS) at slower vs faster oscillatory alpha frequencies. Cecere et al. (2015) showed that stimulation set at slower alpha frequency induced larger TWI, while stimulation set at faster alpha frequency induced shorter TWI.

More recently, Cooke et al. (2019), extended this observation to tactile-to-visual crossmodal interactions (i.e. the tactile-induced DFI). The authors found a dissociation between auditory and tactile induced flash illusion with respect to the oscillatory peak accounting for this effect. Indeed, while alpha peak could account for the auditory induced flash illusion (replicating previous findings, i.e. Cecere et al., 2015; Keil et al., 2017), this same frequency does not account for the tactile-induced flash illusion. Interestingly, the authors looked into the beta frequency band (which is functionally relevant in the sensory-motor domain) and found a correlation between individual beta peak and the TWI for the tactile induced DFI.

With this in mind, in **Chapter Four** (Fotia et al., 2021), we utilised the tactile-induced Double-Flash-Illusion (tDFI) to investigate the tactile-to-visual temporal sensitivity in schizotypy, as indexed by the temporal window of illusion (TWI), and its neural underpinnings. First, we aimed to replicate the behavioural findings from Chapter Three (Ferri et al., 2018) to the tactile-induced Double Flash Illusion. Second, we aimed to replicate the findings from Cooke et al. (2019) who showed that the individual TWI for the tDFI positively correlates with the individual beta frequency (IBF) in the occipital cortex. Moreover, we wanted to investigate the potential association between schizoptypy and IBF.

Results confirmed that there is a temporal sensitivity reduction in people with high schizotypy vs low schizotypy. Indeed, we found a positive correlation between the TWI, as measured with the tDFI, and the SPQ scores. Here, it has to be noted that we could not find any significant difference in the overall proneness to perceive the illusion. This could be dependent on many factors: in this study, our participants were not clustered into extreme scores (high vs low), but rather were distributed across a continuum of the SPQ score. Also, along with evidence which observed high inter-individual variability in the susceptibility to the illusion (de Haas et al., 2012), previous research noted that susceptibility to the illusion is higher for the auditory induced illusion compared to the tactile-induced illusion (Cooke et al., 2019). A possible explanation for this discrepancy is that the tactile-induced DFI appears to be noisier than the auditory-induced DFI, possibly due to the fact that auditory information tends to be more precise in the temporal domain when compared to tactile information. Hence, auditory stimuli are more likely to influence other sensory modalities when compared to tactile stimuli (Bresciani et al., 2008; Plaisier, Van Dam, Glowania & Ernst, 2014).

Also, in Chapter Four, we expected to reproduce the relationship between beta – but not alpha – frequency and TWI. To this aim, individual oscillatory frequencies were converted from cycle units (Hz) into millisecond units (period=1000/frequency) so as to correlate TWI and oscillatory activity on the same measure scale (of time) and the same unit (ms). Our findings show a significant positive correlation between the TWI and the duration of an individual beta frequency, suggesting that participants with wider TWIs have also a slower beta cycle. In line with our expectations, we found no association between the TWI and the peak alpha frequency. supporting the notion that oscillatory activity in the visual cortex relate to the illusion in a frequency and network-specific manner (i.e. depending on the neural network involved). As discussed in Cooke et al. (2019), a possible mechanism linking temporal integration across the senses with specific cross-sensory oscillatory patterns is that communication between sensory areas follows a cyclical gating allowing for efficient cross-sensory coordination at the specific temporal loop of the cross-sensory feedback network.

Most notably, we found an association between the IBF and the SPQ scores. Again, as we expected, there was no relationship between the IAF and the SPQ scores. Specifically, individuals with higher schizotypal traits exhibit wider TWI and slower beta waves accounting for the temporal window within which they perceive the illusion. This observation is in line with extensive research reporting slower oscillatory activity (Fuggetta et al., 2014; Nagase et al., 1996; Omori et al., 1995) as well as larger period of integration of information across the senses in schizophrenia spectrum disorder (Stevenson et al., 2017; Haß et al., 2017).

Finally, we performed a mediation analysis to better understand the relationship between SPQ, TWI and IBF, and to examine a possible mediation role of the TWI for the effect of IBF on SPQ. We found no residual correlation between IBF and SPQ that is not mediated by TWI (i.e. the relationship between IBF and schizotypy disappear when TWI is introduced as a mediator). Indeed, the model suggests that the relationship between IBF and SPQ is fully mediated by the TWI.

A possible limitation for both Chapters Three and Four is that the illusion differences observed between the groups, rather than being a consequence of reduced temporal sensitivity in multisensory integration, could be explained by other types of information processing abnormalities. For instance, a reduced ability to concentrate on relevant stimuli while simultaneously ignoring the irrelevant ones is a central feature of acute schizophrenia and has been observed in schizotypal conditions as well.

Research has demonstrated that patients with schizophrenia (Perry et al., 1999; Parwani et al., 2000) and schizotypal personality traits (Wan et al.,2017) exhibit sensory gating deficits compared to the healthy population, meaning that they have more difficulties to “gate” or screen out irrelevant stimulus and to attend to salient features of the environment (McGhie & Chapman, 1961). Deficits in central gating or inhibitory functions have been investigated via the use of prepulse inhibition of the startle response (Braff et al. 1978). Prepulse inhibition is an operational measure of sensorimotor gating that is present when a weak pre-stimulus precedes a more intense one (typically by 30 to 500 milliseconds). Normally, when the intense stimulus is preceded by a similar one of weaker magnitude, the startle response is inhibited. Schizophrenic patients, however, exhibit a loss of inhibitory function as reflected by deficient prepulse inhibition, meaning that they exhibit strong startle responses despite the pre-stimulus. Most of the studies investigating prepulse inhibition in schizophrenia and in healthy individuals have used acoustic stimuli, but tactile stimuli (Braff et al., 1992; Kumari et al., 2008) have also been used. Thus, in the case of the DFI, it is possible that the second beep (in Chapter Three) and the second tap (in Chapter Four) could be louder in individuals with high schizotypal traits, and this could drive the illusion differences. With this in mind, it is crucial that future research implements control conditions, such as the simultaneity judgment task, as previously mentioned.

7.2.2. Body representation

As the background composition of multisensory stimuli shape our sense of self, our body is always present in the field of awareness. Indeed, in order to recognize and differentiate oneself from the others, a subject must coordinate inputs from various senses with the ongoing modification of the internal models of the body and of the bodily self in action (Tsakiris & Haggard, 2005). Thus, self-awareness is strictly dependent on the proper integration of multisensory inputs that arise from the body, such as proprioceptive, spatial and temporal sensorimotor ones, and by stable internal body representations: both these aspects relate to the construction of the bodily self. An intact bodily self is a prerequisite for generating a normal sense of body ownership and agency, which in turn allow the individual to experience subjective involvement in practical tasks of everyday life (i.e., self-presence) (Tsakiris et al., 2007; Gallese & Sinigaglia 2010).

By focusing more directly on the sense of embodiment, Chapter Five and Six have investigated fundamental aspects of coherent self-experience, namely the stability of body representations (top-down and bottom-up) in individuals with schizophrenia and with high schizotypal traits. More specifically, building on the hypothesis that multisensory abnormalities in the schizophrenic spectrum are linked to deeper aberrancies in the structure of the self, Chapters Five and Six have utilised knowledge from neuropsychology, neuroscience and phenomenology to investigate the bodily roots of self-awareness and bodily-self abnormalities in schizophrenia. Coherently with the clinical reports that have observed abnormal body ownership in schizophrenia, research has shown that patients with schizophrenia are more susceptible to the Rubber Hand Illusion,and exhibit a more rapid onset of the illusion (Peled et al., 2000; Peled et al., 2003; Thakkar et al., 2011; for a review see Klaver & Dijkerman, 2016). Body ownership is believed to be dependent on the successful integration of multimodal information and on pre-existing body representations which possess their own frame of reference and are distinct from external spatial representation (Blanke et al., 2002; Ehrsson, 2007). Thus, the representation of one's body, and the feeling of one's body as "mine" is multidimensional as it involves both "bottom-up" (multisensory integration) and "top-down" (internal representations of the body) processes (Tsakiris & Haggard, 2005). These "a priori" structural-spatial body representation have a key role in elaborating multimodal stimuli and creating the experience of what is "mine". Results emerging from Chapter Five and Chapter Six have suggested that more flexible bodily boundaries and bodily representation are likely to indicate a weaker sense of self. This in turn can represent an indirect measure of minimal self-disorders and can offer important insights into the disturbances of self-awareness that may contribute to the development of schizophrenia.

In **Chapter Five** (Costantini et al., 2020), we investigated body representation in relation to basic symptoms in patients with schizophrenia. Basic symptoms define a set of mild self-experienced subclinical disturbances that are present since the prodromal phase and that involve different areas of psychic functioning. Most importantly, basic symptoms are thought of as *arising from the self*, rather than *happening to the self* without its participation (see Mishara et al., 2016). Therefore, the basic symptoms approach is close to phenomenological models of self-disorders (e.g. the model proposed by Sass & Parnas, 2003, which emphasize that the symptoms are pre-psychotic 'as if' phenomena"). Thus, we utilised both the Rubber Hand Illusion and the Finger Localization Task to investigate body ownership and the body structural representation, respectively. Moreover, we investigated whether abnormalities in body representation would correlate with basic symptoms.

Results show that patients were significantly less accurate than healthy controls when asked to identify pairs of fingers touched by the experimenter (when the hand was hidden from view). Interestingly, we observed a significant difference between patients and controls only for the third task of the Finger Localization Task, i.e., identification of pairs of fingers with hand hidden from view. The fact that patients and controls differed only on the third task, the most difficult one, suggests that such difference was mainly due to the higher complexity of the body structural representation tested, and not simply to a reduced tactile acuity. Most importantly, patients' performance at the Finger Localization Task was negatively associated with basic symptoms, as measured by the SPI-A. Also, we found that performance at the task was negatively correlated with the malleability of the sense of body ownership: the less the individual ability to localize fingers, the stronger the rubber hand illusion. This evidence points towards misrepresentation of the self being core to schizophrenia and being present since the earlier stages of the disorder.

Thus, in Chapter Five we have provided important insights on the relationship between body representation and self-disorders in patients with schizophrenia. Thus, we have showcased that patients with schizophrenia possess more malleable body representations and can, therefore, more easily adopt faulty models of their own body’s spatial mapping and location. This, in result, can make them more susceptible to external, transitory influences (e.g. an external visual rubber hand). Also, we have provided evidence that these abnormalities are linked to early markers of vulnerability to the disorder (i.e. basic symptoms). As basic symptoms represent real markers of vulnerability (Magini & Raballo, 2004), the study of these represents a valid point of reference for evaluating the subjective disorders present in the prodromal phases of the schizophrenic syndrome.

In Chapter Five, we have adopted the Rubber Hand Illusion as this task has been widely utilised to investigate multisensory mechanisms of bodily self-identification and bodily self-localisation. However, especially considering novel findings, some task limitations must be addressed. A study from Lush et al. (2020) showed that the effects reported in the Rubber Hand Illusion could be attributed to imaginative suggestion (i.e. phenomenological control). The authors found substantial correlations between response to the illusion and phenomenological control. A possible way to bypass the dangers of “demand characteristics” of the task (i.e. the fact that the subjects say what they implicitly think they ought to say) is to utilise alternative tasks to test multisensory mechanisms of self-localisation (e.g. visual-proprioceptive), such as the prism adaptation task (Luautè et al., 2009). In the prism adaptation task, participants are asked to wear goggles designed to shift the visual scene laterally and to perform a series of pointing movements to a visual target. The first pointing movements are normally deviated toward the shifted location so that the subject misses the actual object. After some trials, the participants will adapt to the visual distortion and will be able to reach the target. Once the goggles are removed, the movements remain temporally biased toward the opposite side of the prism-induced displacement. What this suggests is that the resolution of the sensorimotor discrepancy caused by the optical prisms requires a remapping of bodily and space coordinates into a new egocentric spatial frame of reference.

In **Chapter Six** (Fotia et al., submitted), in accordance with the idea of schizophrenia as a continuum, we further investigated the body structural representation in individuals with high and low schizotypy. To this purpose, we utilised two body structural representation related tasks: the Finger Localization Task and the In Between Task. Results indicated that individuals with high schizotypy performed worse in both tasks. In line with what has been observed in Chapter Five, performance at the Finger Localization Task was impaired only in the third condition (two stimulated fingers with hands hidden from view). Moreover, building on research that observed an overlap between dissociation and schizophrenia (Ross, 1997), we screened participants in regard to dissociative symptomatology by means of the Dissociative Experiences Scale. Interestingly, our findings show that performance in both the Finger Localization and the In Between Tasks was negatively correlated with dissociative symptomatology (i.e. the higher the scores in the scale, the worse the performance). By showcasing that both individuals with high schizotypy and with elevated dissociative traits display a reduced acuity in body structural representation, we have raised interesting questions on whether this may account for the confusion between first and third-person perspectives present in schizophrenia spectrum disorders and in dissociative disorders. Indeed, possessing a faulty model of one own's body might contribute to the tendency to disengage from normal forms of involvement with the external world, particularly with such acts that would normally be tacit and transparent (as in hyperreflexivity and diminished self-presence).

Most importantly, we have extended the results observed in Chapter Five - i.e. reduced accuracy to the Finger Localization Task in schizophrenia - to schizotypy. However, the task details have slightly changed between the two studies (namely, palms downward in Chapter Five and palms upward in Chapter Six). The Finger Localization Task was originally developed by Benton (1955) to measure the deficits exhibited in patients with finger agnosia; the test is described in "Contribution to Neuropsychological Assessment" (Benton et al., 1983) and in "A compendium of Neuropsychological Tests: Administration, Norms, and Commentary" (Strauss et al., 2006). In the original version of the task, participants are required to put their hands with their palms facing upward. Also, the subject is given the option of responding by naming the stimulated finger (either by naming the number on the outline or naming the finger) or pointing at it on the outline. Later, this source of variability was eliminated, and the subjects were required to give a verbal response. Subsequent studies have utilized this task but with participants' hands facing downward (Pipe, 1991, Geffen et al., 1985) and since then, the studies implementing the Finger Localization Task have utilized the palms downward and upward interchangeably. However, given the test-retest reliability of the task (larger than .70), we are inclined to believe that these parameters do not have a significant impact on the overall performance. Thus, in Chapter Five, we have decided to utilise the "palms downward" version of the task so the stimulation could be similar to the one utilised in the Rubber Hand Illusion (i.e., with palms downward). In Chapter Six, we have decided to utilize the original version of the task (palms facing upward).

7.3. Further clarification on the body schema, the body image and the body structural representation

In attempting to deliver an account of the body representation abnormalities observed in schizophrenia spectrum disorders, I have focused on concepts that derive from phenomenology and that have already been well integrated into current neuropsychological and neuroscientific research (Gallagher, 1986; 2005; Paillard, 1999; de Vignemont, 2010; Dijkerman & de Haan, 2007; Di Vita et al., 2016). The concepts I am referring to are body image and body schema. As already mentioned during the course of the thesis, there has been much conflation of these two terms, presumably because of the dual meaning of the term ‘body’ (e.g., ‘lived’ or ‘objective’), despite the fact that different kinds of intentional and neural profiles underlie each one.

The concept of body schema was originally introduced by Head and Holmes in 1911 (Head & Holmes, 1911). Based on their work with neurological patients, Head and Holmes conceptualised the body schema as an “organised model of ourselves” which coordinates (multi)sensory information arising from the body in order to produce motor control and to localise sensations on the surface of the body (Head & Holmes, 1911). More specifically, they proposed the existence of different schemata. First, a body schema which registers and updates all of the sensory information coming from the postural changes of the body. Second, a “superficial schema” which is a “central mapping of somatotopic information derived from the tactile information” (Head & Holmes, 1911, p.187). Importantly, both the body schema and the superficial schema operate below the level of consciousness. This idea was later developed into the dyadic taxonomy (Dijkerman & de Haan, 2007; Gallagher, 2005), by drawing a distinction between the body schema and the body image. The body image is generated from the contribution of all of the sensory channels and consists in the conscious representation (i.e. conceptual and perceptual) of our body in space as if it was intended by an external observer. Conversely, the body schema enables the intentional directedness to the external environment that underlies perception and action and does so automatically. Thus, the body schema does not coincide with a specific perception, with an image or with a marginal form of awareness. Rather, it utilises the body to carry out actions in compliance with pragmatic interests. It has been proposed that the inferior posterior parietal cortex is mainly involved in the body-image representation (Roux et al., 2003), whereas the body schema (i.e. sensorimotor guidance) relies on subcortical and superior parietal processing (Dijkerman & de Haan, 2007). As mentioned in section 2.4, these ideas of a body schema acting as a representation for environment-directed action, and a body image employed in the perceptual identification of body features, have been supported by a series of neuropsychological studies (Paillard, 1999; Halligan et al., 1995; Dijkerman & de Haan, 2007; Anema et al., 2008). Such studies have also hypothesised the existence of two additional subcomponents of the body image: the body structural representation and the body semantics (Schwoebel & Coslett, 2005; Sirigu et al., 1991; de Vignemont., 2009). The body semantics corresponds to a conceptual and linguistic body representation, whereas the body structural representation consists of a structural description of the relationships between body parts, including the relative positions of different body parts relative to one another in a spatial configuration (for further specification, see section 2.4).

Here, the nature of the body structural representation might sound confusing. At first glance, it could seem that the body structural representation and the body schema coincide (Sirigu et al., 1991). However, while the body schema is situational and environment-focused (i.e. the intention is directed to the environment), holistic (i.e. changes in posture involve global adjustment of body parts), and features operations carried out prior to, or outside of, conscious awareness, the body structural representation involves an abstract or partial representation of the body, as conscious awareness can attend to one part or few areas of the body at a time (Gallagher, 2005). The important thing here is that the intentional content of the body structural representation features the body as an object, which is distinct from objects of the outer environment. On the other hand, the intentional content of the body schema is never one own's body; rather, the body schema operates below the level of explicit, self-conscious awareness and is not directed at the self.

At this point, some confusion might still exist regarding whether (and to what extent) there is a consciousness of the body schema and of the body image (which includes the body structural representation). To clarify, we possess a "tacitly given" awareness of our body as a sensorimotor subject in a perceptual background – the body schema - and we have an objectifiable representation of our own body – the body image - towards which we can intentionally draw our attention (i.e. as a focal object of awareness). As pointed out by Gallagher (2005), the processes of body image and body schema are dependent upon the intentional context of the agent. As such, they need to be understood under the domain of intentionality, rather than under the framework of a conscious vs unconscious dichotomy. Thus, if "my" intentionality is directed towards my body, we are referring to body image. Conversely, in the body schema, "my" body has an extra intentional direction towards the environment, and, though it involves my body, it is not directly and explicitly focused on the (objective) body itself. I will explain this more precisely. Take, for instance, the act of pouring water. The act of pouring the water defines the intentional act (body schema). Thus, the intentionality is directed towards accomplishing the task. The act is pre-reflectively accomplished without explicit moment-to-moment awareness of each body part and body movement required for the task. Conversely, if I am asked to name a body part that has been just touched, that body part become the intentional object.

The important conceptual distinction between body schema and body image should not imply a complete behavioural separation between these two aspects, as both can interact and influence each other. In normal conditions, the boundaries between body schema and body image are not rigid, and both of these components concur to structure our mind and our actions (Gallagher, 2005). For instance, tools such as prostheses can be incorporated both into the body image (at the level of a conscious perception of it as constituting part of one's body) and in the body schema (at the level of an automatic involvement with the external world) (Gallagher & Cole, 1995). Nonetheless, there is a duplicity of the body. On the one hand, the body can be taken as an object just like any other intentional object (the objective body). Thus, the body can be represented as an image that is mediated by conscious awareness, anatomy, evaluations on the body. On the other hand, the body is *first and foremost* a lived body, a body as a subject that engages in tasks and with others. In this sense, the lived body represents the medium through which we live 'from the inside' and which constantly act behind the level of conscious awareness (the lived body).

The main point of interest here is that body schema (i.e. the lived body) and body image (i.e. the objective body) reflect two aspects of two specific forms of bodily self-awareness: the first-person perspective and the third-person perspective. The first-person perspective entails that one's living body (Leib) functions as an integrated sub-conscious system of multisensory processes and this interaction between the sensory modalities and the environment manifests in the body schema. On the other hand, the third-person perspective entails that the multisensory processes (already functioning on-line), and the conceptual and affective representation of the body, contribute to the constitution of the body image (Körper). While usually functioning together, these processes could potentially be dissociated. Interestingly, as we have already proposed, the minimal self-disorders observed in the schizophrenic spectrum might stem from a disassociation between the objective body and the lived body.

7.4. Limitations

The main limitation of the present thesis is that it has emphasised a conceptual notion of the self as a separate subject, while not considering the role of the body in action and social interaction. Indeed, an agent is not an isolated entity but rather it is deeply embedded in the world through an enactive embodied existence (i.e. its embeddedness is based upon its active engagement with the surrounding environment) (Varela, 1994; Gallese, 2003). It is noteworthy that the way we perceive things is largely in the service of how we can act upon them; thus, something that can be seen, it is seen in virtue of how it can be manipulated. For instance, when I see an apple, what I actually see is the opportunity afforded by that apple, for instance grasping it, eating it or throwing it. Thus, every perceptual capability we have is grounded in a fundamental way by the opportunities for action that that percept affords. Moreover, when we perceive the "graspability" of the apple placed in front of us, we do not simply experience it passively, but at the same time we also experience its implicit call to action via our body (i.e. as something that features motor-potentiality for our body), that is, a body that can reach and grasp the apple. Consequently, we acquire and sample our world and our bodily self through movement. Such a dynamic connection between the body and the environment modulates the patterns of our self-development and gives rise to the experience of 'minneness' (Rochat, 1998; Gallese & Sinigaglia 2010; 2011). The same applies for our being in space, as bodily space represents a horizon of motor possibilities. This type of bodily self-awareness is inherently non-conceptual and non-reflective (Gallagher, 2005).

In this regard, a notable limitation of this thesis is that it has not properly experimentally assessed the body schema, which is the pre-reflective sensorimotor representation of the body morphology used for planning and executing body movements. The body schema is strictly linked to the functional representation of the space surrounding the body, the peripersonal space. The peripersonal space refers to a spatial interface immediately surrounding the body which enables the agent to interact with their immediate surroundings (Graziano, 1994), and has been conceptualised as a multisensory-motor interface which serve to determine the location of nearby sensory stimuli to generate appropriate motor act. The peripersonal space is highly malleable; using a tool to reach objects in the far space extends the boundaries of peripersonal space representation (Serino et al., 2007). Unsurprisingly, research has suggested that modifications of peripersonal space usually co-occur with changes in the body schema. For instance, the active use of a tool to interact with objects placed in the peripersonal space, produces changes in the body schema, increasing length of the sensorimotor representation of the arm (Cardinali et al., 2009; Longo & Haggard, 2010). It could be hypothesised then, that the process of structuring space is also involved in building the intention to act, and that this, as a consequence, helps to structure the sense of self as a separate entity for the external environment. This is particularly important considering that the lack of boundaries between the self and other often reported in schizophrenia, are taken as marker of minimal self-disorders.

With this in mind, in future research, I shall adopt a more enactive approach to the body, in order to emphasize the role of action and the role of space as core components of minimal selfhood. One way to do so would be to adopt tasks which more finely assess the body schema. Being an implicit component of body representation, the body schema is resultingly less accessible to empirical investigation. However, goal-directed tasks which manipulate the sense of embodiment and self-localization can be useful in this regard. For instance, one could assess the effects of visual body manipulation (e.g. by magnifying and minifying the subject's hand in virtual reality) on an open loop target locating task. The open loop task allows the participants to see their virtual hand only prior to locating the target, while being unable to view their hand when performing the movement; thus, this approach could specifically target the body schema, as during task performance the body itself is not the direct object of intentionality (see previous section). Possibly, individuals with schizophrenia spectrum condition, given their weaker body representation, would be more prone to the effects of manipulation of body perception in goal-oriented task compared to healthy individuals, thus reporting higher sense of body ownership and agency in the manipulation conditions.

7.5. Conclusions

Disturbances of the minimal self (located in pre-reflective self-awareness) have been proposed as core features of schizophrenia spectrum disorders. Possessing minimal self-awareness entails that one possesses a first-person ownership of experience which is both automatic and transparent. In normal conditions, automatic inferential mechanisms allow the agent to discriminate between objects of the surrounding space that need to be taken into the foreground, and objects of the surrounding space that have to remain in the background, depending on their salience or relevance. Moreover, the body, being the medium through which we perceive and interact with the world, needs to be transparent. Indeed, it is normally assumed that a normal relationship between the body and the mind necessitates a state of 'quiet cooperation', whereby the bodily functioning does not preoccupy the attention of an individual (Erikson, 1956; Stanghellini et al. 2012). Thus, minimal self-consciousness is characterised by "mediated immediacy" (Plessner, 1981). However, during the schizophrenic prodrome, the tacit knowledge of an agent's body and of the surrounding reality (i.e. the "already familiar" way to experience reality) – becomes progressively lost. This loss is characterised by a breakdown of Gestalt perception, that is, a dissolution of the feelings of *rootedness* and *at-homeness*. These feelings are often accompanied with an extreme focus on objects/events of the lived space that would typically remain in the background of experience. Crucially, this tacit and "in the background" form of self-awareness (i.e. the 'mineness' of experience), appears compromised during the early stages of schizophrenia. When considering the evidence from clinical, neuropsychological and neuroscientific studies, it emerges that the disturbances in the minimal self, experienced during the schizophrenic prodrome, could be better understood as a complementary distortion of this tacit aspect of the act of awareness: hyperreflexivity and diminished self-affection (or diminished presence) (Sass & Parnas, 2003).

Diminished self-affection (or diminished presence) refers to a reduced first-person perspective on the world, with a diminished sense of inhabiting one's own actions, thoughts, perception and bodily sensations. Experientially, this can manifest with a sense of being dissociated (i.e. not related) from one's own body (e.g. blurring of bodily boundaries), and from the environment, whereby the transparent and taken-for-grandtness quality of experience is progressively lost. This means that there is a diminishment in the most basic sense of self presence: the sense of existing as a self-possessed subject of awareness (Sass & Parnas, 2003). This alteration of pre-reflective self-awareness is accompanied by compensatory hyper-reflectivity (Fuchs, 2005). Hyperreflexivity refers to the hyper-objectivization of aspects of the self, which are normally tacit and implicit. Thus, hyper-reflectivity can be considered as a paradoxical effect of reflexivity itself (Sass & Parnas, 2012; Fuchs, 2005). This tendency to objectivise one's experience and one's body is manifested through an externalisation or objectification of normally "automatic" processes.

Both the concepts of hyperreflexivity and diminished self-affection involve a disruption of the aforementioned tacit-focal structure of experience and are mutually implicative aspects of the intentional relationship between the embodied agent and the environment. This is particularly relevant when pertaining the domain of bodily self-awareness. For instance, patients become excessively aware of bodily parts or functions that are typically in the tacit background of their experience (i.e. hyperreflexivity). As a result of this, the body becomes progressively experienced as devoid of life, or as mechanical and alien, often to the point of feeling that body parts are actually in possession or under the control of some alien being or force (i.e. diminished self-affection). As Sass and Parnas have noted: "...*on our view, there is a sense in which the person with schizophrenia has both too little sense of self (diminished self-affection) and too much self-consciousness (hyperreflexivity)*" (Sass & Parnas, 2003).

In affording an excessive focus to one's objective body, an agent is no longer relating to the body in a pre-reflective way (i.e. the "subjective body"). Specifically, pre-reflectivity is lost in a condition characterised by the excessive reflection on automatic aspects of body awareness (see section 2.4.). This fracture in bodily-self experience is manifested through the agent's inability to switch between the first-person perspective (i.e. the subjective body) and the third person perspective (i.e. the objective body) (Sass, 2003; Krueger, 2018). This aspect provides a useful resource for understanding schizophrenia spectrum disorders, particularly if we assume that the fracture between the observing and the observed self represents a hallmark for the emergence of the disorder. Interestingly, a disruption in the regular ability to switch between first-person and third-person perspectives is something that has been observed in individuals with dissociative symptomatology (e.g. dissociative identity disorder, depersonalization and derealization) (Ciaunica et al., 2020; Sass, 1992; Bob et al., 2013), something which is often present in schizophrenic-like-conditions (e.g. in schizotypy) and in the earliest phases of schizophrenia (see section 1.3.1). Dissociation is characterised by a reduced sense of being in touch with the world in a "vital" and "first-person" perspective. Similarly, the schizophrenic individual experiences a disintegration of the minimal level of subjectivity, which is normally implicit in every act of awareness. In both conditions, the subject may feel detached from the medium that it would normally embody them in relation to the environment (the body), leading to feelings of alienation from the self and from the surrounding environment.

This fundamentally embodied basis of the minimal self implies that the body represents the only interface with the world. Although our body is physically demarcated from the environment, the environment still influences us in profound ways. Therefore, the body needs to integrate multisensory information emanating from the environment in order to create a proper representation of both the external environment and of our body acting in it. As mentioned in Chapters Three and Four, an important aspect that enables the brain to integrate incoming stimuli depends on the temporal structure of this information. The temporal relationships of incoming stimuli, therefore, provide information on how these signals should be integrated in order to create a coherent perceptual representation of the world.

To sum up, the experiments described in the present thesis have provided evidence for disruption in two main components in schizophrenia spectrum disorders: multisensory integration and body representation. In particular, we have provided evidence that the bodily self is majorly affected in both schizophrenia and high schizotypy (Chapters Five and Six) and that this may be due to an impaired integration process of sensory information (Chapters Three and Four). On this basis, I have attempted to integrate this evidence with a broader theoretical framework which conceptualises schizophrenia spectrum disorders as disorders of minimal self. The minimal self implies that self-experience is pre-reflective (i.e., it is a form of selfhood that is prior to any explicit thinking about oneself), meaning that it is “transparent” (Sass & Parnas, 2003).

In light of this, it could be argued that self-disorders connotate a qualitative modification of this transparent dimension experience and that this modification starts to happen since the earliest stages of the disorder (e.g. pre-morbid and prodromic). Indeed, during these phases, nuanced manifestations of bodily-self disorder can indicate a latent vulnerability trait. The body, which normally provides a synthesis between subjectivity and objectivity, begins to acquire the characteristic of an “alien” entity, in which the two poles of subject and object are not anymore integrated, but rather becomes blurred. In particular, the body appears to progressively lose its transparency, whereby sensory information arising from both the outer (environment) and the inner (body) world, are not reliable and are not properly integrated. It can be argued then, that self-disorders underlie a profound fracture of the dynamic interrelationship between the self and the environment, and more specifically between the first and third-person perspective.

All in all, the aforementioned aspects have important implications for the early detection and the early treatment of schizophrenia spectrum disorders. First, creating a unifying model of self-disorders in schizophrenia would allow researchers to identify and describe the processes involved in the emergence of minimal selfhood abnormalities. Second, intervening in a situation in which the patient still maintains a certain level of self-presence implies that he will be more receptive to treatment. Indeed, during the prodromal phase (e.g. basic symptoms), individuals are aware of the peculiarity of their symptoms which are experienced as disturbing disruptions in self-experience and which negatively impacts on their self-assessed quality of life. As schizophrenia develops and the body loses its transparency, the subject becomes less able to immerse himself in the environment and to project himself toward the future. Thus, the symptomatology becomes part of the patient' core sense of identity, meaning that the patient is no longer aware of the aberration of their experiences. As a consequence, schizophrenic individuals undergo a profound reorientation of self-identity, while building a new "philosophical schema". Often times, this schema consists of a solipsistic worldview and suspiciousness of the surrounding environment (Stangehllini & Fusar-Poli, 2012). Notably, these ideas are already present during the prodrome, although to a lesser degree. For instance, individuals often react to their feelings of disorientation by consciously choosing to oppose "common-sense rules" and taking an eccentric perspective on reality (e.g. as it is the case in individuals with high schizotypy). After the manifestation of first frank symptoms, these abnormalities consolidate to the point of giving rise to symptoms such as delusion, hallucinations, disorganised speech and behaviour (Sass & Parnas, 2003).

More intensive research in the early detection of schizophrenia spectrum disorders is necessary to detect sub-threshold symptoms and to ensure the development of appropriate multidimensional therapeutic approaches. Furthermore, more focus should be given to the subjective lived experience of the patients, their interpersonal relationships and the significant events in their environment, such as life stressors that could compromise the outcome of the treatment (e.g. trauma, substance abuse) and those that could represent protective factors to the emergence of the. In this context, the conceptualisation of schizophrenia spectrum disorders as disorders of the minimal self has provided a deeper understanding of the subjective dimension of the patient who is undergoing a profound alteration of their '*being-in-the-world*' (i.e. the totality of their subjective experience). Current research on the early identification of schizophrenia should further investigate evidence-based practices in order to detect self-abnormalities in healthy individuals which exhibit sub-psychotic symptoms. For instance, semi-structured interviews could be implemented to detect sub-threshold changes in self-experience of healthy individuals with high schizotypy, thus elucidating why some people with schizotypy would eventually develop the disorder, whereas some others would not.

Finally, further research could investigate whether and to what extent minimal self-disorders in schizophrenia could be caused by failures in pre-reflective, probabilistic inference mechanisms. Indeed, in order to maintain its organization as an adaptive living system, an organism has to minimize information-theoretic free-energy (i.e. errors) in its interactions with the environment (Free Energy Principle, Friston, 2010). This minimization can be achieved by predicting upcoming events (e.g. the sensory inputs) and/or by changing the environment to match what is anticipated. In this account, the experience of the minimal self should be interpreted as the experience of having predicted or being "already familiar" with, what one perceives, something that appears deeply impaired in schizophrenia spectrum disorder. Thus, such a framework may fruitfully contribute to neuroscientific and philosophical debates on minimal self-awareness, and possibly help to bridge the gap between the two approaches.

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