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Bodily self-identity and the performativity of peripersonal space in schizotypy and schizophrenia

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Abstract

Anomalies of self-experiences have been associated with schizophrenia spectrum disorders. It has been proposed that the weak basic sense of self ('minimal self'), the disturbed implicit bodily functioning and the disruption of intercorporeal attunement with others are manifestations of a disturbed bodily self in schizophrenia (Sz). This altered basic sense of self, strictly related to self-recognition and self-other discrimination impairments, have been linked to deficits in multisensory integration mechanisms. One of the basic experiences of self concerns the sense of body-ownership (BO) which is not only associated with body parts but also with the face, a crucial cue for self-identity allowing to distinguish the self from the others and in differentiating others. Sz is characterized by deficits in one's own and others' face recognition, as well as by a disturbed BO. Thus, the aim of the first study here presented was to integrate these lines of research investigating the Enfacement Illusion (EI) proneness in Sz. Results showed how EI induced the expected malleability of Self-Other boundary among both controls and patients; interestingly, it also demonstrated how Other-Other boundary is influenced by EI, suggesting how EI is not only confined to self-sphere but it also affects the way we discriminate others.

The second study adds important new evidence in the context of the bodily self in Sz, focusing on the implicit bodily self processing, operationalized in the so-called self advantage effect (SA_{eff}, a faster sensory motor mental rotation with self than others' body-parts in a laterality judgment task). Results showed the absence of the SA_{eff} in Sz revealing a specific alteration in the sensorimotor processes of self body parts, suggesting a potential distorted motor nature of the minimal self.

Another crucial aspect shaping our sense of self is bodily self-awareness, the feeling of being a bodily self in space (spatial self). This experience depends on multisensory integration occurring within the portion of space surrounding our body, Peripersonal Space (PPS). PPS is not fixed, rather it dynamically shapes through motor experiences (e.g. after a tool-use). Moreover, the size of PPS largely varies across people depending on several individual characteristics, including schizotypy (St). However, little is still known about the relationship between PPS plasticity and personality traits. To this aim, we investigated PPS plasticity after two different motor trainings (i.e. after using a tool and after observing someone else using the tool), in participants along the St continuum. Results showed PPS expansion after tool-use, whereas absence of PPS expansion emerged after the observation task. Moreover, we found greater PPS expansion in the relatively-low St group than in the relatively-high one, regardless of the type of motor training performed. These results underline a potential general functional alteration of PPS with the increase of St level.

Taking into account the idea of a dynamic continuum ranging from St to full-blown psychosis, it is reasonable to hypothesize a lesser malleability of PPS boundaries in Sz. No studies until now have

investigated this functional aspect of PPS in Sz. Hence, this represents the focus of the last study that illustrates the preliminary results on Sz patients, constituting another relevant contribution to our understanding of the spatial self in psychopathology.

Taken together, all this evidence enriches the current state of the art of the minimal self disorder in Sz, empirically supporting the idea of a fragile self, which shatters into a variety of small pieces that enclose multiple interrelated bodily aspects.

Riassunto

Esperienze anomale del sé sono state associate ai disturbi dello spettro schizofrenico. Si ritiene che un debole senso del sé (sé minimale), un disturbato funzionamento corporeo implicito e della sintonizzazione intercorporea con gli altri siano manifestazioni di un sé corporeo disturbato nella schizofrenia (Sz). L'alterazione del sé minimale, correlata ai disturbi del riconoscimento di sé e della discriminazione sé-altro, dipende da deficit nell' integrazione multisensoriale. Una delle esperienze di base del sé riguarda il senso di appartenenza del corpo (BO) che è legato sia alle parti corporee che al volto, un segno cruciale per la propria identità che consente di distinguerci dagli altri e di differenziarci dagli altri. La Sz è caratterizzata da deficit nel riconoscimento del proprio volto e di quello altrui, nonché da un BO alterato. Pertanto, lo scopo del primo studio è stato quello di integrare queste linee di ricerca indagando la propensione all'Enfacement Illusion (EI) nella Sz. I risultati hanno mostrato come l'EI abbia indotto la malleabilità del confine Sé-Altro sia nei controlli che nei pazienti; l'EI ha influenzato inoltre il confine Altro-Altro, suggerendo come l'EI non sia solo confinato alla sfera del sé, ma influenzi anche il modo in cui discriminiamo gli altri.

Il secondo studio aggiunge nuove importanti evidenze nel contesto del sé corporeo nella Sz, focalizzandosi sul processamento implicito del sé corporeo, operazionalizzato nel cosiddetto effetto del vantaggio del sé (SAeff, rotazione mentale motoria più veloce con proprie parti corporee rispetto a quelle altrui in un giudizio di lateralità). I risultati hanno mostrato l'assenza del SAeff nella Sz rivelando un'alterazione nei processi sensorimotori delle proprie parti corporee, suggerendo una potenziale natura motoria distorta del sé minimale.

Un altro aspetto cruciale che influenza tale senso del sé è la consapevolezza corporea, la sensazione di essere un sé corporeo nello spazio (sé spaziale), che dipende dall'integrazione di segnali multisensoriali che si verificano all'interno di una porzione di spazio circostante il corpo, lo Spazio Peripersonale (PPS). Il PPS non è fisso, ma si modella dinamicamente attraverso le esperienze motorie, come dopo l'uso di strumenti. Inoltre, l'estensione del PPS varia tra le persone al variare di diverse caratteristiche individuali, come la schizotipia (St). Tuttavia, ancora poco si conosce sulla relazione tra la plasticità del PPS e i tratti di personalità. A questo scopo, abbiamo studiato la plasticità

del PPS dopo due diversi allenamenti motori (dopo l'utilizzo di uno strumento e dopo l'osservazione dell'utilizzo di quello strumento), lungo il continuum St. I risultati hanno mostrato l'espansione del PPS dopo l'uso dello strumento, mentre in seguito all'osservazione non è emersa alcuna espansione. Abbiamo riscontrato inoltre una maggiore espansione nel gruppo St relativamente basso rispetto a quello relativamente alto, indipendentemente dal tipo di allenamento motorio eseguito. Questi risultati sottolineano una potenziale alterazione funzionale del PPS all'aumentare del livello St.

Tenendo conto dell'idea di un continuum che va dalla St alla psicosi conclamata, è ragionevole ipotizzare una minore malleabilità del PPS nella Sz. Nessuno studio ha fino ad ora indagato tale aspetto nella Sz; pertanto, questo rappresenta il focus dell'ultimo studio, che illustra i risultati preliminari sui pazienti Sz, rappresentando un altro importante contributo alla conoscenza del sé spaziale nella psicopatologia.

Tutte queste evidenze arricchiscono l'attuale stato dell'arte dei disordini del sé minimale nella Sz, supportando l'idea di un sé fragile che si rompe in piccoli pezzi che includono molteplici aspetti corporei interrelati.

INDEX

1. General Introduction

1.1 The Bodily and Spatial Self

According to the phenomenological approach, selfhood is a multi-layered concept (Parnas 2000, 2003). First, there is the implicit awareness that this is my experience, commonly referred as *Minimal Self* or *Ipseity*. Second, there is a more explicit awareness of being the subject of experience. Such reflective level of self-awareness presupposes the minimal self. Finally, the third level of selfhood is the *Social* or *Narrative Self*, which encompasses the "complex" characteristics such as personality, temperament and social identity. In cognitive neuroscience, the concept of minimal self is currently being debated since it is not clear which experience concurs in shaping this implicit sense of self. Specifically, one of the central issues is the contribution of bodily experience to its composition. Coherently, Merleau-Ponty (1962, pp.77-94) has argued how the corporeity and the potential for action represent crucial factors in shaping the self: *"Through the world, I am aware of my body (…) through my body, I am aware of the world".* Thus, the acknowledgement of action as a fundamental element for the minimal self led to the concept of the bodily self as a possible substrate for self-awareness. Embracing this perspective, Legrand stated that the body and the self cannot be considered as two separate identities, rather we need to consider the existence of a *bodily self* as a self identical to its body, rooted in sensory-motricity (Legrand 2006). Thus, in this way we can define the bodily self as a "*pre-reflective basic sense of one's own body as power for action"*(Gallese and Sinigaglia, 2010).

The sense of bodily self is built upon the neural mapping of both facial (e.g., Devue and Brédart 2011; Platek et al., 2008) and non-facial body parts (e.g., Ionta et al. 2011). In particular, the face is crucial for our sense of identity. A coherent representation of one's own face is formed and continuously updated, based on the congruent multisensory signals that are constantly experienced and integrated. Given that one's own face constantly changes throughout life, our brain should allow a plastic self-face representation. The relevant role of the multisensory integration processes underlying the plasticity of the bodily self have been extensively demonstrated by the bodily illusions paradigms which are able to temporary change our body experience (e.g., Botvinick and Cohen, 1998; Lenggenhager et al., 2007) or face representation (Sforza et al., 2010; Tsakiris, 2008). Indeed, in the well-known rubber hand illusion (RHI) paradigm (Botvinick and Cohen, 1998) synchronous tactile stimulation applied to the participants' own unseen hand and visible fake rubber hand induces an illusory ownership over the rubber hand. Moreover, in a similar procedure, named *Enfacement Illusion* (EI) (Sforza et al., 2010), participants are synchronously touched on the same part of the face as another person standing in front of them, and have the impression of seeing themselves in the mirror and feeling the tactile stimuli observed on the other person's face. These sensations are accompanied by a misattribution of the others' facial features to the self-face (i.e., the so-called *self-face attribution bias*) in self-other discrimination and recognition tasks (Sforza et al., 2010; Tsakiris, 2008). Several studies have replicated the EI phenomenon showing how the synchronous multisensory stimulation over self-face produces both implicit and explicit changes in the bodily self. Thus, not only the body but also face representation is malleable.

As previously stated, the bodily self is based on the neural mapping of self-body parts. Thus, another crucial component in defining our bodily identity is the recognition of self-body parts. The recognition of our body implies a distinction between one's own body and others' body (Devue et al., 2007; Sugiura et al., 2006). Indeed, when submitted to a matching-to-sample visual task where they were required to decide which of two images matched the central stimulus, healthy participants responded faster and more accurately when the visual matching involved their own body parts (Frassinetti et al., 2008). This effect has been named *'self advantage'*. Further studies have deeply investigated this effect, showing that in a laterality judgment task of depicted self or others' hands, presented in different orientations, participants showed the self-advantage for their own right hand, but only during an implicit task where self-recognition was not required (Ferri et al., 2011). A subsequent fMRI study (Ferri et al., 2012), adopting the same paradigm, revealed a neural network for the mapping of the bodily self, including motor areas like the supplementary and the pre-supplementary motor areas, and the anterior insula and the occipital cortex, bilaterally. Crucially, the representation of one's own dominant hand seems to be primarily confined to the left premotor cortex. This evidence strongly suggests the existence of a sensorimotor representation of the bodily self that could allow the distinction of our own body from the body of others.

"Our bodily experience represents the implicit background of our day-to-day experiences against which we develop a coherent sense of self as a unified, bounded entity, naturally immersed in a social world of meaningful others" (Stanghellini et al., 2014, p. 1703; see also Damasio, 1999; Gallese, 2005; Gallese and Goldman, 1998;).

Thus, a fundamental question comes to light: *Where does 'my body' act?*

Our bodily awareness is one of the crucial aspects of our sense of self, defined as the feeling of being located within a body we own and that is located in a specific space position (Noel et al. 2015). The experience of being a bodily self in space (the so-called 'spatial self') depends on the multisensory signals integration occurring within the peripersonal space (PPS) which represents a limited sector of the space immediately surrounding our body (Rizzolatti et al., 1981). PPS has been described in different ways, as a reaching, defensive or social space (di Pellegrino and Làdavas, 2015; Rizzolatti et al., 1997; De vignemont and Iannetti, 2015). The neural basis of PPS mapping has been originally demonstrated by neurophysiological data on monkey's brain that relies on the activity of bimodal and trimodal neurons in the ventral premotor cortex and in the posterior parietal cortex, with tactile receptive fields (RFs) centred on specific body parts and visual and or auditory RFs anchored to the tactile ones (Rizzolatti et al., 1997). Neuroimaging studies (Brozzoli et al., 2011, 2013; Brozzoli, Gentile, & Ehrsson, 2012; Ferri et al., 2015; Makin, Holmes, and Zohary, 2007; Sereno and Huang, 2006) have shown the existence of a similar PPS mapping in humans, relying on the activity of multisensory parietal and premotor regions. From what stated above, it follows that PPS is a multisensory space where tactile and proprioceptive information concerning specific body parts, and visual inputs related to the environment are efficiently integrated (Gross and Graziano, 1995; Rizzolatti et al., 1997; for a review see Serino, 2019).

Usually, all the physical interactions between our body and the environment occur within the PPS. However, we can use tools to reach targets beyond the limits of our body. Indeed, a seminal study by Iriki et al. (1996) has shown how, after a period of tool-use, the visual RFs of intraparietal sulcus neurons extended to include the space where the tool was operating. The plasticity of PPS was also demonstrated in humans. Indeed, important evidence has been reported both in neuropsychological patients (Berti and Frassinetti 2000; Farnè, Iriki, and Làadavas 2005; Farnè and Làdavas 2000; Maravita et al. 2001) and in healthy participants, after short (Serino et al. 2007) and long motor training with a tool (Bassolino et al. 2010; Canzoneri et al. 2013; Serino et al. 2007). Moreover, it has been found that the boundaries of PPS expanded not only after actively using a tool to reach objects in far space but also after the mere observation of the tool use (Costantini et al. 2011). This effect seems to occur only if the observer shares the same action potentialities with the observed agent (i.e., while passively holding a tool compatible with the observed action). It should be added that it has been found that tool-use observation influences the visual distance judgements, as the ones measured in the Costantini and colleagues' paradigm (2011). To date, however, there is no study investigating whether the observation of tools action might also affect multisensory PPS tasks. This represents one of the main aims of the study illustrated in Chapter 4. Moreover, a recent study (Serino et al., 2015) has provided new evidence in this context showing how the synchronicity between the tactile stimulation and auditory or visual stimulation from the far space is sufficient to trigger PPS expansion, suggesting that tool action may be not necessary to extend PPS representation. Thus, taking into account all these findings, it emerges that little is still known about the mechanisms underlying tool-use observation.

1.2 The disruption of the Bodily Self in Schizophrenia

The disruption of the basic sense of self has been recognized as a fundamental feature in schizophrenia psychopathology (Parnas 2000; Parnas and Handest 2003). Indeed, according to the phenomenological perspective (Parnas, 2000; Parnas and Handest 2003; Stanghellini, 2009), the main self-disturbance in patients with schizophrenia occurs at the most basic level, the minimal self (Sass and Parnas, 2003). Disturbances of the mineness of experience or sense of presence, disturbed corporeality, stream of consciousness and existential reorientation represent some critical features affecting the minimal self. Recently, it has been suggested that a fragile bodily self may represent a core component of the psychiatric condition of schizophrenia, potentially caused by an inefficient body-related multisensory integration processes (Postmes et al. 2014) which entails a loss of the implicit self-knowledge and self-other differentiation (Gallese and Ferri, 2014). For all these reasons, schizophrenia has been identified as a disorder characterized by a *disembodiment of the self* (Fuchs, 2005; Stanghellini 2009; Zahavi, 2005).

The impairment in multisensory integration processes has been called 'perceptual incoherence' (Postmes et al. 2014). This status can be induced by a contradictory sensory input or an imbalance between various types of sensory input that results from local or generalized decreased somatosensory feedback or sensory-motor contradictions. Thus, depending on which somatosensory feedback is impaired, the perceptual incoherence might lead to depersonalization, blurred boundaries, cenesthopathies and/or diminished sense of ownership and agency. It has been proposed that *"the loosening of the sensory contextual goes with changes in the perceptual composition in which hyperawareness to some background processes is coexistent with a decline of the usual clearness in the field of awareness"* (Postmes et al., 2014, p. 45).

From a phenomenological viewpoint, the weakening of the basic sense of self (Cutting and Dunne 1989; Fuchs and Schlimme 2009; Sass and Parnas 2003; Stanghellini et al. 2012), the disturbed implicit bodily functioning and the disruption of intercorporeality (see Gallese, 2003b) are manifestations of a fundamental disturbance of the bodily self (Stanghellini, 2009). Moreover, as argued by Stanghellini (Stanghellini, 2001), the "lack of ipseity" (the weakening of the feeling of being embedded in oneself and of distinctiveness between the self and the external world) and "hyper-reflexivity" (the monitoring of one's own life entailing the tendency to objectify parts of one's own self in an outer space, see Sass, 1992) have been considered key phenomena of schizophrenia. Thus, the analyses of self-disorders in schizophrenia caught only some dimensions of schizophrenic vulnerability, since it focused only on the subjective experience of an isolated self. However, our existence is essentially tied to the phenomenon of intersubjectivity. "*The self is not a purely personal but, rather, a social phenomenon"* (Stanghellini, 2001). One explanation of intersubjectivity refers to the relevant role of the lived body (Dillon, 1997; Merleau-Ponty, 1964): "*Intersubjectivity is based on my identification with my partner's body as like my own, through an immediate perceptual linkage with his body [...]"*. Thus, this phenomenon should be better called as 'intercorporeality' (see Gallese, 2009) and it is antecedent to the distinction between ourselves and others, as it constitutes a 'we-centric space', Gallese, 2003a).

Consistently, along with the loss of a coherent sense of self, also the distinction between self and other may blur in schizophrenia (Sass and Parnas, 2003). Indeed, anomalies in face processing, including one's own self and others' faces recognition and self-other distinction (Ameller et al. 2015; Bortolon, Capdevielle, and Raffard, 2015; Chan et al. 2010; Maher et al. 2016; Martin et al. 2005; Sachs et al. 2004; Yun et al. 2014) have been found in schizophrenia, possibly underlining a generalized mechanism of identity disruption. Moreover, an fMRI seminal study (Ebisch et al., 2013) has shown a specific impaired differentiation between self and other during the social perception of touch in schizophrenia patients. Specifically, schizophrenic patients showed a reduced activation in the ventral premotor cortex for observed bodily tactile stimulations, positively correlated with the severity of basic symptoms, and aberrant differential activation in the posterior insula for first-person tactile experience and observed affective touch. Thus, these findings have provided neural evidence of a pre-reflective social perception deficit in schizophrenia, characterized by impaired self-experience including altered multisensory representations and self-other distinction.

Hence, taking into account both the altered minimal self and deficits in the processing of one's own self and others' faces as well as the blurring of self boundaries and confused interrelationships with others (Sass and Parnas, 2003), it would be crucial to delineate both the extension of the bodily self malleability and the potential roots of the described psychopathological aspects connoting schizophrenia also at the social level. To tackle these issues, I have investigated, in the first study here presented (Chapter 2), the Enfacement Illusion (EI) proneness in schizophrenia patients and in healthy controls. In order to also test the malleability of the Other-Other boundaries after a shared multisensory experience, I decided to include also new non-self related conditions in the face recognition task, where, no EI effect was expected, considering the self-specificity of the bodily illusions. Finally, coherently with the previously described literature, I expected higher proneness to EI in patients than in controls.

The alterations of the minimal self in schizophrenia have been investigated mainly focusing on body ownership and sense of agency. Several studies have found increased malleability of the sense of ownership over body-parts (e.g., Ferri et al. 2014; Peled et al. 2000, 2003; Thakkar et al. 2011) and anomalous agency in schizophrenia (see for a review Hur et al. 2014). Recently, all these results have been questioned by a systematic review and meta-analysis revealing quite limited empirical support

(Shaqiri et al., 2018). However, despite the disputable findings reported up until now, all this evidence highlights a fragile minimal self in people suffering from schizophrenia. Nevertheless, the nature of this disruption has not been identified. Thus, the aim of the study described in Chapter 3 was to test the hypothesis of a specific alteration of the motor roots of the bodily self in schizophrenia, taking advantage of a task relying strictly on sensory-motor mental rotation of one's own and others' body-parts.

Furthermore, as described in the previous paragraph, another crucial aspect of a coherent sense of self is the experience of being a bodily self in space. The experience of being located within a specific portion of space in the world depends on the efficient multisensory inputs' integration occurring in this space. This sector of space, called PPS (Rizzolatti et al. 1981), thus can be considered as a representation of the self in space which may mediate the interactions between ourselves and the environment (Noel et al., 2015). For this reason, PPS representation recently grasped the attention of the psychopathological literature focused on self-disorders. Indeed, narrower PPS boundaries have been recently described either in people with high schizotypal traits or in schizophrenia patients, when compared with low schizotypal traits and healthy controls, respectively (Di Cosmo et al., 2018). Other studies have reported different results showing a larger extent of PPS in schizophrenia (Holt et al. 2015; Park et al. 2009), related also to positive symptoms severity (de la Asuncion et al. 2015; Schoretsanitis et al. 2016). From a clinical point of view, a recent study by Stanghellini et al. (2020) highlights the abnormal space experiences (ASE) characterizing schizophrenia. According to the authors, ASEs can be summarized by five main phenomena: a) experiences of strangeness and unfamiliarity, *b)* experiences of centrality/invasion of peripersonal space; *c)* alteration of the quality of things, *d)* alteration of the quality of the environment, and *e)* itemization and perceptive salience. As argued by Binswanger and others, in schizophrenia *"attuned space loses its homogeneity, consistency and taken for grandness, which can lead to delusional mood or to revelatory experiences"* (Binswanger 1933, pp. 123-177; see also Conrad, 1958; Silverstein, Demmin, and Skodlar, 2017).

Given all these premises, and considering also the large amount of studies focusing on PPS representation, it is crucial to first investigate the plasticity of PPS in healthy individuals with different levels of schizotypy before focusing on schizophrenia. Moreover, despite the relevance of the plasticity of PPS, due to its adaptive function (see paragraph 1.1), and the association between individuals' PPS boundary and schizotypy, no study so far has investigated the integrity of the functional properties of PPS in schizotypy, such as its plasticity after motor training. It follows that investigating the plasticity of PPS could be relevant to better delineate the altered self-boundaries in schizotypy, which represents the aim of the study presented in Chapter 4. Moreover, taking into account the idea of a dynamic continuum ranging from personality variation to psychosis (Debbané and Mohr 2015; Lenzenweger 2006; Raine 2006), it is crucial also to investigate the functional aspects of PPS in schizophrenia. Considering previous evidence reported among schizophrenic patients, characterized by bodily-self disturbances such as blurred body-boundaries, it is reasonable to hypothesize a lesser malleability of PPS boundaries among schizophrenia patients. The preliminary results of this study are presented in the Chapter 5, representing another crucial contribution to the current knowledge of the spatial self in psychopathology.

I wish to declare that the studies here presented in the Chapters 2-4 have been already published in scientific peer-reviewed journals. The results of Chapter 2 were published as Ferroni et al., 2019; the results of Chapter 3 were published as Ardizzi et al., 2020 and Chapter 4' results were published as Ferroni et al., 2020.

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Chapter 2

2. Shared multisensory experience affects Others' boundary

2.1 Introduction

Schizophrenia has been described as a psychiatric condition characterized by anomalies in self-experiences. The alterations in the minimal self, strictly related to the impaired self-recognition and self-other discrimination (Gallese and Ferri, 2014), have been associated with schizophrenia spectrum disorders. Empirical research on self-recognition impairments in schizophrenia has mainly referred to a disturbed sense of body ownership and agency of action (see for example Cermolacce et al., 2007; Jeannerod, 2009). The concept of body ownership has been investigated by studies applying the Rubber Hand Illusion protocol (Botvinick and Cohen, 1998) in which schizophrenia patients seem to show a greater malleability over body parts than healthy controls (Ferri et al., 2014; Peled et al., 2000, 2003; Thakkar et al., 2011). Despite the recent criticism concerning these results on schizophrenia (e.g., for a review sees Shaqiri et al., 2018), all these studies have demonstrated specific relations between body-ownership deficits and the psychopathology of schizophrenia. Indeed, a weak sense of ownership over body-parts has been associated with both positive and negative symptoms (Ferri et al., 2014; Peled et al., 2000; Thakkar et al., 2011).

The sense of body ownership is not only related to body parts but also to the face, which represents a crucial cue for self-identity, allowing us to distinguish not only self from the other (Self-Other boundary) (Zahavi and Roepstorff, 2011) but also in differentiating others (Other-Other boundary). A widespread literature on bodily illusions has investigated the malleability of self-face representation, extending the multisensory integration procedure adopted in the RHI protocols to self-face recognition (Paladino et al., 2010; Sforza et al., 2010; Tsakiris, 2008). This effect has been named Enfacement Illusion (EI) (Sforza et al., 2010). In this paradigm, the illusion is induced by the observation of another person's face being touched at the same time of participants' face. Synchronous, but not asynchronous, visuo-tactile stimulation between the two faces modifies the usual Self-Other boundary, shifting it toward the other's face. The EI effect is conventionally measured by performance on a self-face recognition task arranged before and after the visuo-tactile stimulation and/or by ad-hoc questionnaire (i.e., Illusion Questionnaire). Participants have the impression of seeing themselves in the mirror and feeling the tactile stimulation observed on the other person's face. These sensations are accompanied by a misattribution of the others' facial features to the self-face. However, considering the self-specificity of the bodily illusions (Tsakiris, 2008), at the moment no study has investigated the potential effect of EI on the malleability of the Other-Other boundary.

Interestingly, evidence suggests anomalies in face processing in schizophrenia, including one's own self and others' faces recognition, self-other distinction and impairments in emotional facial expressions processing (Ameller et al., 2015; Bortolon et al., 2015; Chan et al., 2010; Maher et al., 2016; Yun et al., 2014). Furthermore, a distinctive clinical sign of schizophrenia is represented by the so-called Mirror-related phenomena, (Parnas et al., 2005) that has been experimentally assessed in a study showing how, by means of mirror gazing test, apparitions of strange faces in the mirror were significantly more intense in patients with schizophrenia than in controls (Bortolon et al., 2017; Caputo et al., 2012). All these well-studied phenomena may have implications for face-to-face social interactions. Indeed, social cognition is very poor among schizophrenia patients (for a review see Gur and Gur, 2015), they underestimate the social reward of genuine others' positive facial expressions (Catalano et al., 2018) and they often show social anhedonia and/or asociality (e.g., Blanchard et al., 1998, 2001; Kalin et al., 2015; Robertson et al., 2014). Reduced social interests are evident prior to illness onset (Cannon et al., 1997; Cornblatt et al., 2011; Tarbox and Pogue-Geile, 2008) and often persist despite effective positive symptoms treatment (Blanchard et al., 2001; Horan et al., 2008).

Considering both the altered minimal sense of self and the deficit in the processing of one's own self and others' faces, this is the first study that tries to integrate these parallel lines of research with the aim of investigating EI proneness in schizophrenia. This is crucial to delineate both the extension of the malleability of the bodily self and the potential roots of the described psychopathological aspects connoting schizophrenia also at the social level. In the present study, we adopted the same EI protocol used by Tajadura-Jiménez and Tsakiris (2013) in which participants were stroked on the left side of their face while they were seeing the face of an unfamiliar person being stroked in synchrony either on the specularly congruent location or on the incongruent side of the face. The illusion effect was tested through the commonly used Illusion Questionnaire and Face Recognition Task. This protocol was chosen because it includes only synchronous visuo-tactile stimulation, ensuring comparable levels of attention between conditions (Tajadura-Jiménez and Tsakiris, 2013), and avoiding the effect of the interindividual variability in temporal binding window (TBW) extension (Costantini et al., 2016; Stevenson et al., 2012), two aspects crucial when clinical and non-clinical samples are compared.

Accordingly, an alteration in both TBW (Foucher et al., 2007; Tseng et al., 2015) and attentional abilities (Bleuler, 1958; Fioravanti et al., 2012; Fuller et al., 2006; Kraepelin, 1919; Young et al., 2017) has been demonstrated in patients with schizophrenia. In order to introduce a further control condition able to test also the malleability of the Other-Other boundary after a shared multisensory experience, we decided to include new non-self related supplemental trials in the Face Recognition Task, where, according to the self-specificity of the body-illusions, no EI effect was expected.

Coherently with the literature, we expected higher proneness to EI in patients with schizophrenia than in controls.

2.2 Methods

Participants

20 patients with schizophrenia (SCZ; mean age 37.15 years SE 3.23, 17 males) and 23 healthy control participants (HC; mean age 32 years SE 0.59, 10 males) were included in the present study (Table 1). The total sample size exceeded the minimum amount required (n. 36) estimated by means of statistical a priori sample size calculation, obtained for repeated-measures ANOVA considering both within and between interactions (1-ß = 0.95, $\alpha = 0.05$ and effect size f = 0.25). Post-hoc power estimation analysis conducted for repeated-measures ANOVA considering both within and between interactions including the actual effect size of our main interaction (f = 0.41) and the final sample size (n. = 43) confirmed the high achieved statistical power achieved (1-ß = 0.99). SCZ were recruited among patients seeking treatment at the Psychiatric Unit of the University Hospital of Parma. All patients were under medication during the period of the study, and medication was based on a low-medium dose of a single atypical antipsychotic drug. HC were recruited through fliers posted in meeting places. Inclusion criteria for SCZ were I) a diagnosis of Schizophrenia according to DSM-IV-TR criteria (First et al., 2002) and II) stable phase of recovery (i.e., with no acute symptoms for at least 6 months post morbid). SCZ patients were evaluated and recruited for the study after a clinical stabilisation to assure that they were able to participate in the study. Inclusion criterion for HC was the absence of current or past psychiatric or neurological illnesses as determined by their clinical history, and assessed by means of a general psychopathology questionnaire. Exclusion criteria for all participants were I) substance abuse or dependence; II) pathological conditions likely affecting cognition or interfering with participation in the study (i.e., presence of neurological and vascular disorders, dysmetabolic syndrome and mental retardation) and III) face-recognition deficits like prosopagnosia disorder, possibly affecting participants' performance. Written informed consent was obtained from all participants after full explanation of the procedure of the study. The study was approved by Ethics Committee of the University Hospital of Parma and was in line with the ethical standards of the 2013 Declaration of Helsinki.

Clinical scales and control measures

SCZ were evaluated by means of the structured clinical interview for DSM-IV Axis I disorders (SCID-I) to establish Axis I diagnoses (First et al., 2002). Patients were evaluated with the

Assessment of Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) that measures symptoms severity in schizophrenia. Disturbances of subjective experience were investigated through the Examination of Anomalous Self-experience scale (EASE; Parnas et al., 2005). Furthermore, patients carried out the backward Digit Span (Wechsler, 1997) in order to control for executive deficits potentially affecting task performance. All the equivalent scores were greater or equal to 1. HC completed the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) to evaluate the individual schizotypal traits in the healthy population. Both groups completed the Coloured Progressive Matrices (CPM; Raven et al., 1998), to assure that cognitive functionality was preserved. All the equivalent scores were greater or equal to 1, with no significant difference in the mean equivalent scores between the two groups. We also evaluated participants' reaction times (RT) to gradually changing visual stimuli in order to assess the motor reactivity of the two groups. Participants were asked to press the space bar as soon as they perceived a change in the colour of an oval shape. The oval shape matched the dimension of the faces in the face-morphing movies (see below) and the progressive change in colour (e.g., from blue to yellow) simulated the dynamic transition of the same morphing movies. No significant difference was found between the two groups. For participants' clinical scale and control measure, Table 1 shows groups' mean scores and the results of the statistical comparisons between the two groups.

Scales	**Subscales**	**SCZ**	**HC**	**Between-groups differences**
Age (years)		37.15; SE 3.23	32; SE 0.59	$t_{(41)} = -1.57$; $p = 0.13$
Education (years)*		11.30; SE 0.58	14.91; SE 0.48	$t_{(41)} = 4.80$; $p < 0.001$
CPM (ES)		3.37; SE 0.22	3.78; SE 0.12	$t_{(40)} = 1.64$; $p = 0.11$
Digit Span (ES)		3.2; SE 0.26	n.a	
Reaction Time (msec)		5999.27; SE 2064.27	3849.22; SE 159.42	$t_{(41)} = -1.11$; $p = 0.27$
Rate of adapted digital photos	Self images	8.60; SE 0.14	8.74; SE 0.13	Interaction Identity by Group: $F_{(1,41)} = 0.207$; $p = 0.65$
	Other images	0.45; SE 0.33	0.80; SE 0.31	
SPQ_TOT		n.a.	18.13; SE 2.26	
	Positive Factor		6.78; SE 1.23	
	Negative Factor		8.96; SE 0.99	
	Disorganized Factor		5.30; SE 0.92	
PANSS_TOT		79.30; SE 3.84	n.a.	
	PANSS positive	16.60; SE 1.41		
	PANSS negative	22.20; SE 1.48		
	PANSS general	40.50; SE 2.07		
EASE_TOT		18.80; SE 1.72	n.a.	
	EASE 1	5.80; SE 0.74		
	EASE 2	7.33; SE 0.65		
	EASE 3	1.73; SE 0.55		
	EASE 4	0.67; SE 0.25		
	EASE 5	3.27; SE 0.48		

Table 1. Demographic information and clinical scales of SCZ and HC groups. Significant between-groups differences were estimated. *= $p < 0.05$. SCZ = schizophrenia patients group; HC = healthy controls group; CPM = Coloured Progressive Matrices; STAI= State-Trait Anxiety Inventory; SPQ = Schizotypal Personality Questionnaire; PANSS = Assessment of Positive and Negative Syndrome Scale; EASE = Examination of Anomalous Self-experience; EASE1 = Cognition and Stream of Consciousness domain; EASE2 =Self-awareness and presence domain; EASE3 = Bodily experiences domain; EASE4 = Demarcation/Transitivism domain; EASE5 = Existential Reorientation domain; ES = Equivalent Score; n.a.= not applicable.

Procedure

Induction movies

In order to induce the Enfacement Illusion, induction movies were created displaying an unfamiliar face (Other) - matching the participant's sex, age (±5 years) and ethnic group - being stroked on the cheek with a cotton-bud at 0.33 Hz. Each stroke covered a distance of 2 cm from the zygomatic bone downwards. The side of the stroking (i.e., right cheek or left cheek) was balanced (i.e., Congruent or Incongruent stimulations, see below). For each participant, 2 different unfamiliar faces (Other) were used in the induction movies, one for the Congruent and one for the Incongruent stimulation. Each induction movie lasted 120 s.

Face-morphing movies

A digital photograph of each participant with a neutral facial expression was taken before the beginning of the experimental session (max. 1 week before). The participant's face in the photograph was converted to greyscale, and all non-facial attributes were removed (e.g. background, hair, ears) with Adobe Photoshop software. Abrasoft Fantamorph (www.fantamorph.com) was used to merge participant's face with Other's face (i.e., the unfamiliar face displayed in the induction movie) in proportional steps. Each movie, lasting 10 s, displayed the graded blending of the two faces in 150 frames (0.67% steps). The same procedure was followed to merge the Other face with a Stranger face. The Stranger was an unfamiliar individual - matching the participant's sex, age (±5 years) and ethnic group – not displayed in any induction movie. For each participant, 2 different Strangers' faces were used to create the face-morphing movies, one for the Congruent and one for the Incongruent stimulation. For each participant, four morphing movies were created for each stimulation. In two cases, Other was morphed into the participant's face, either from Other to Self (i.e., from 100% Other to 100% Self; Other-Self morph) or from Self to Other (i.e., from 100% Self to 100% Other; Self-Other morph) directions. In the other two cases, the Other's face was morphed into the face of the Stranger, either from Other to Stranger (i.e., from 100% Other to 100% Stranger; Other-Stranger morph) or from Stranger to Other (i.e., from 100% Stranger to 100% Other; Stranger-Other morph) directions. Please see **Fig. 1** for an exemplificative representation of the four face-morphing movies.

The adapted digital photographs used to create the Self-Other and the Other-Self morphs were previously rated by participants to make sure that they recognized their faces as belonging to the Self and that they distinguished their faces from those of unfamiliar Others. The adapted digital photographs of Self and Others were rated one at a time according to the sentence “Does this face represent yourself?” using a 0–9 Likert scale (0 = “strongly disagree”; 9 = “completely agree”). Both groups were able to distinguish the images of the Self from those of the unfamiliar Others (Self: 8.67 SE 0.09, Other: 0.63 SE 0.22; $F_{(1,41)} = 1155.53$, $p < 0.001$; $\eta^2_p = 0.97$). No significant differences were estimated between the two groups (Main effect of Group: $F_{(1,41)} = 0.94$; $p = 0.34$; $\eta^2_p = 0.02$; Interaction Identity by Group: $F_{(1,41)} =0.207$; $p=0.65$; $\eta^2_p =0.005$; see Table 1 for means and SE).

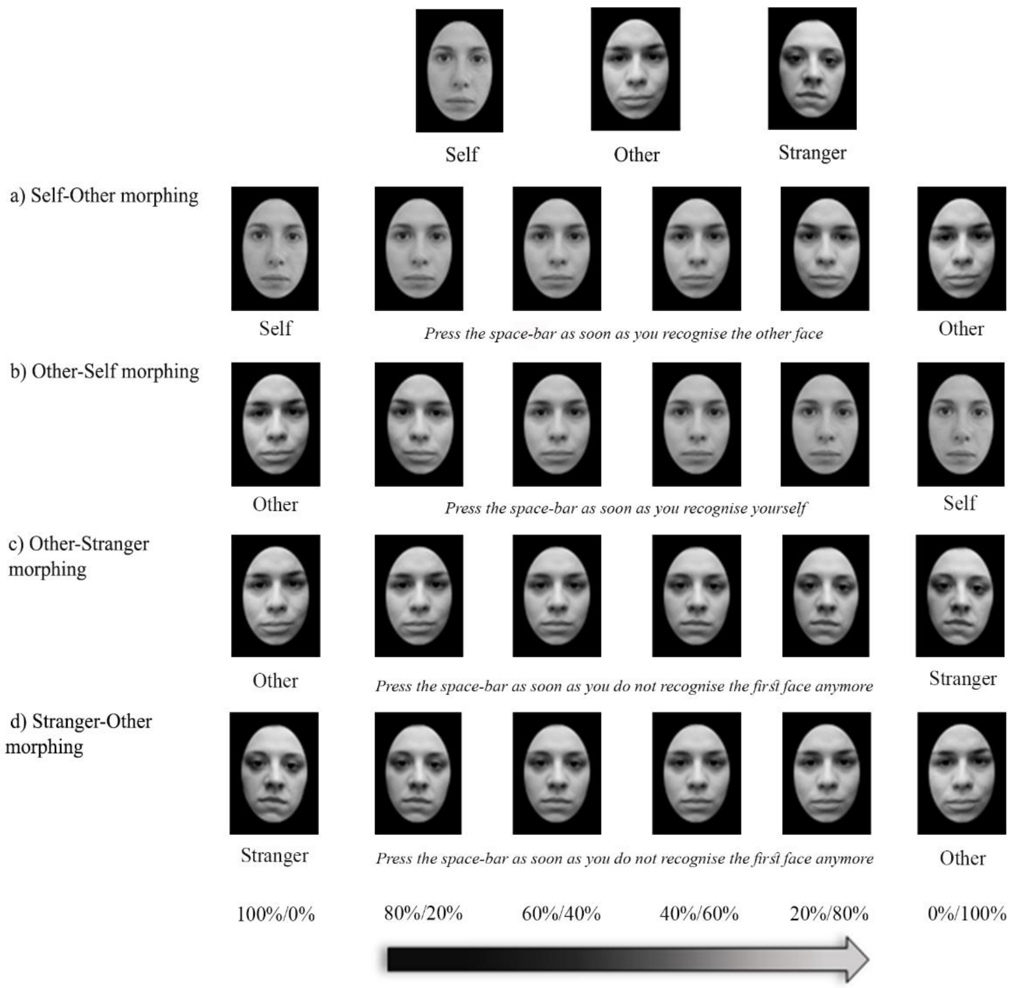

Figure 1. Face-morphing movies. A qualitative representation of the four video-morphing movies. Panels a), b), c) and d) display the direction of each morphing and the associated questions of the Face-recognition task.

Illusion Questionnaire

After each stimulation session (see the Experimental session), participants were asked to complete the Italian version of the Illusion Questionnaire (Sforza et al., 2010) in order to evaluate their subjective experience of the illusion (see Table 2 for the English translation of IQ). Specifically, item 1 and 2 describe the experience of being touched on the same side of the face of the other person touched (i.e., referred sensation); item 3 codes the feeling of identification with the other's face; while item 8 describes the feeling of similarity in visual features with the observed face (Bufalari et al., 2014). The other questions were control items. Participants indicated their response on a Visual Analogic Scale (10 cm) ranging from “completely false” to “completely true”.

Item 1	*It seemed as if I were feeling the touch of the cotton bud in the location where I saw the other’s face touched.*
Item 2	*It seemed as though the touch I felt was caused by the cotton bud touching the other’s face.*
Item 3	*I felt as if the other’s face was my face.*
Item 4	*It felt as if my face were drifting toward the other’s face.*
Item 5	*It seemed as I might have more than one face.*
Item 6	*It seemed as if the touch I was feeling came from somewhere between my own face and the other’s face.*
Item 7	*It appeared as if the other’s face were drifting toward my own face.*
Item 8	*The other’s face began to resemble my own face, in terms of shape, skin tone, or some other visual feature.*

Table 2. IQ’s items that describe the experience of the EI.

Experimental session

Participants sat comfortably, approximately at 50 cm from a screen. E-Prime 2.0 software (Psychology Software Tools, Inc.) was used for stimuli presentation. A training session consisting of a series of face morphing movies with famous faces was administered before the first stimulation to assure that participants understood the instructions. The experimental protocol consisted of two sessions: Congruent stimulation and Incongruent stimulation. The order of sessions was balanced between participants and there was a 15 min break between them. Each session contained three phases: the Pre-IMS Face Recognition Task (Pre-Test), the interpersonal multisensory stimulation (IMS) phase, and the Post-IMS Face Recognition Task (Post-Test). In the Pre- Test, the 4 face-morphing movies were presented in random order. For the Other-Self morph, participants were asked to press the spacebar as soon as they perceived the face to look more like Self than Other. For the Self-Other morph, participants were asked to press the same key when they perceived the face to look more like Other than Self. As soon as the participants pressed the key, the movie stopped and the number of frames at which the movie was stopped was recorded each time. For Other-Stranger and

Stranger-Other morphs, participants had to stop the movie as soon as they perceived that the identity of the first face was not detectable anymore (see **Fig. 1**). The Other-Stranger and Stranger-Other morphs were used as control condition to test the Other-Other boundary malleability in which no EI effect was expected, since EI challenges specifically the self-face recognition (Porciello et al., 2018). In the IMS phase, participants were stroked, synchronously, on the left side of their face with a cotton bud while they saw, in the induction movie, the face of the Other being stroked either in a specularly congruent location (i.e. Congruent stimulation), or in the incongruent side of the face (i.e. Incongruent stimulation) (see **Fig. 2**). After IMS phase, participants performed the Post-Test consisting in the same procedure of the Pre-Test. At the end of each block, participants completed the IQ. Lastly, a subjective rating of the perceived physical similarity between the Other and the Self, as well as, the trustworthiness and attractiveness attributed to the Other were measured along a 0–7 Likert scale (0 = “not at all”; 7= “a lot”).

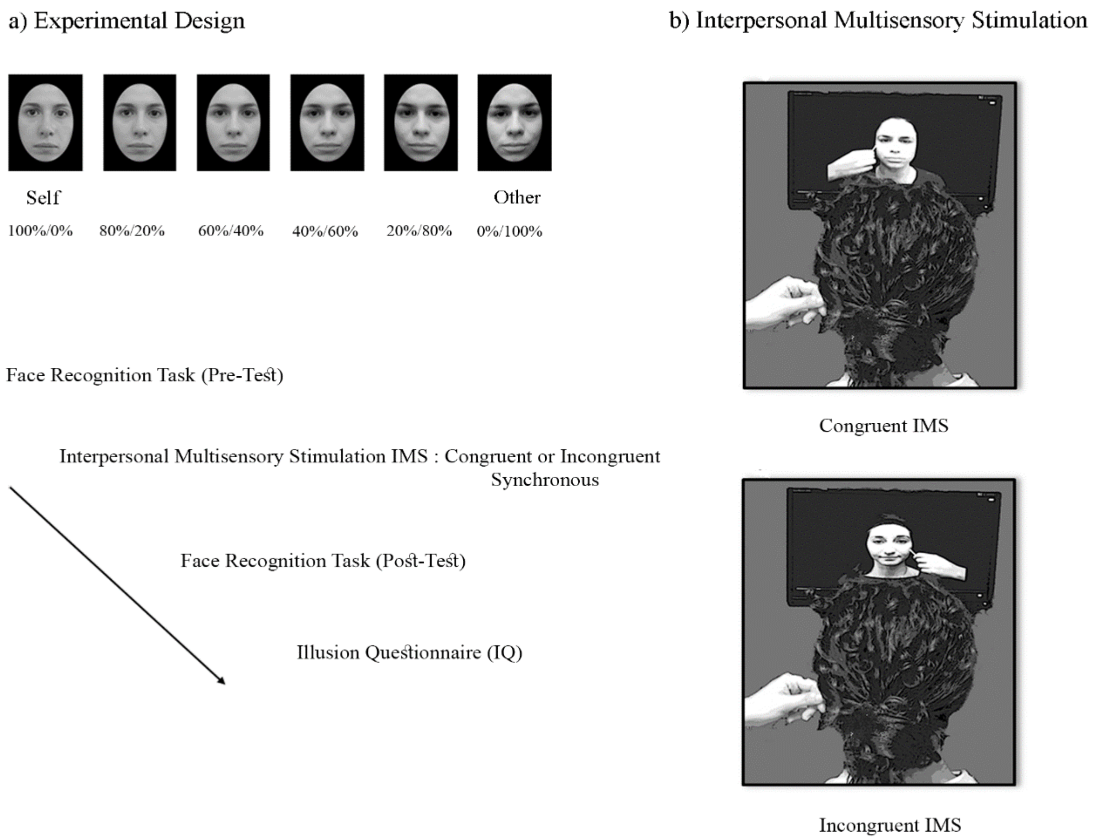

Figure 2. Experimental protocol and visuo-tactile stimulation. a) (top panel): Exemplificative frames taken from Self-Other morphing. The percentage of Self and Other of each frame are reported below the image. **a) (bottom panel)**: Design of the experimental phases: Pre-Test, Interpersonal Multisensory Stimulation phase (IMS), Post-Test and Illusion Questionnaire. **b)**: Experimental set-up during IMS phase, for Congruent and Incongruent stimulation, respectively.

Statistical analyses

Studies demonstrated that Self-Other discrimination is not influenced by the direction of face-morphing movies (Heinisch et al., 2011; Payne and Tsakiris, 2017). In order to assure that also in our dataset the direction of movies did not affect the results, we performed two independent repeated-measures ANOVAs, one for each group, which showed neither a main effect of Direction nor any significant interaction between Direction and the experimental manipulations (see results section 2.3.3 of the control analyses for a detailed description). For these reasons, similarly to the procedure followed by previous studies (Panagiotopoulou et al., 2017; Tajadura-Jiménez et al., 2012), the analyses were conducted on the global number of frames attributed to the Self by considering Self-Other and Other-Self morphs altogether (Self-frames). The same procedure was followed to calculate the global number of frames attributed to the Other by considering Other-Stranger and Stranger-Other morphs altogether (Other-frames). EI effect on Self-Other boundary was estimated calculating the changing score for Self-frames in the Post-Test relative to the Pre-Test (Δ Self frames). The potential EI effect on Other-Other boundary was assessed by calculating the changing score for Other-frames in the Post-Test relative to the Pre-Test (Δ Other frames). To clarify, the Other's face was present in all morphs. The name attributed to the Δ frames (and to the Morphing factor in the subsequent statistical analyses), was chosen to stress the different measures obtained from the morphs (i.e., the number of frames attributed to the Self or the number of frames attributed to the Other). If EI occurred, we expected a higher number of frames attributed to the Self in the Post-Test than in the Pre-Test (positive Δ Self frames significantly higher than zero) in the Congruent stimulation. No difference was expected for the Incongruent stimulation (no changes in the Δ Self frames resulting not significantly different from zero). Differently, regardless of the inter-individual susceptibility to the illusion, no difference between the number of frames attributed to the Other in the Post-Test with respect to the Pre-Test, both in Congruent and Incongruent stimulations, were expected (no changes in the Δ Other frames resulting not significantly different from zero). Lastly, we expected an increment of the score of the IQ selected items, with a significant increment different from 50 (i.e., neutral evaluation), only after Congruent stimulation. Due to the new conditions added to the standard EI protocol, we run a series of analyses only on the control group to verify the effectiveness of the procedure followed. First, the performance at Face Recognition Task was investigated. Controls' Δ frames were submitted to a repeated measures ANOVA. In this case, Morphing (i.e., Self and Other) and Stimulation (i.e., Congruent and Incongruent) were entered as within subjects factors. Secondly, based on the significant interaction Morphing by Stimulation, the expected significant and not-significant differences from 0 of both Δ Self and Δ Other frames after the two stimulations were tested by 4 independent one sample t-tests against 0. Regarding the scores at the Illusion Questionnaire, we run a repeated-measures ANOVA with Statement (1–3, 8) and Stimulation (i.e., Congruent and

Incongruent) entered as within-subjects factors. Lastly, to test if among controls, the selected statements of Illusion Questionnaire differs from a rating of 50 (indicating a consistent deviation from a neutral explicit evaluation of EI), one sample t-tests against 50 were conducted on the scores of Statements 1–3 and 8 for both Congruent and Incongruent stimulations. After the assessment of the EI protocol among controls, the same statistical analyses were run again comparing the performance of the two groups. All participants' Δ frames were submitted to a repeated measures ANOVA with Morphing (i.e., Self and Other) and Stimulation (i.e., Congruent and Incongruent) as within-subjects factors, whereas Group (i.e., SCZ and HC) was entered as between-subjects factor. Again, the significant interaction Morphing by Stimulation was further investigated throughout 4 independent one sample t-tests against 0 performed on the whole sample (due to the absence of the significant three-ways interaction Morphing by Stimulation by Group). The Illusion Questionnaire scores were again submitted to a repeated-measures ANOVA with Statement (1–3, 8) and Stimulation (i.e., Congruent and Incongruent) included as within-subjects factors, whereas Group (SCZ and HC) was entered as between-subjects factor. Lastly, one sample t-tests against 50 were conducted on the scores of the entire sample (due to an absence of a Group main effect) of Statements 1–3 and 8 for both Congruent and Incongruent stimulations. Whenever appropriate, significant within- and between-group differences were explored performing Tukey HSD post-hoc comparison. Partial eta square (η^2_p) was calculated as effect size measure. Additional control analyses were performed on the ratings of Attractiveness, Similarity and Trustworthiness, please refer to results section 2.3.3. Moreover, Pearson's correlations analyses were performed on SCZ group between the psychopathological measures and the performance at the EI paradigm; please refer to results section 2.3.3. A qualitative graphical representation of Δ Self frames and Δ Other frames displayed group by group are showed for each stimulation (i.e., Congruent and Incongruent) in **Fig. 3**. For sake of clarity, in the graph Δ frames are expressed in percentage values calculated on the total number of frames (300).

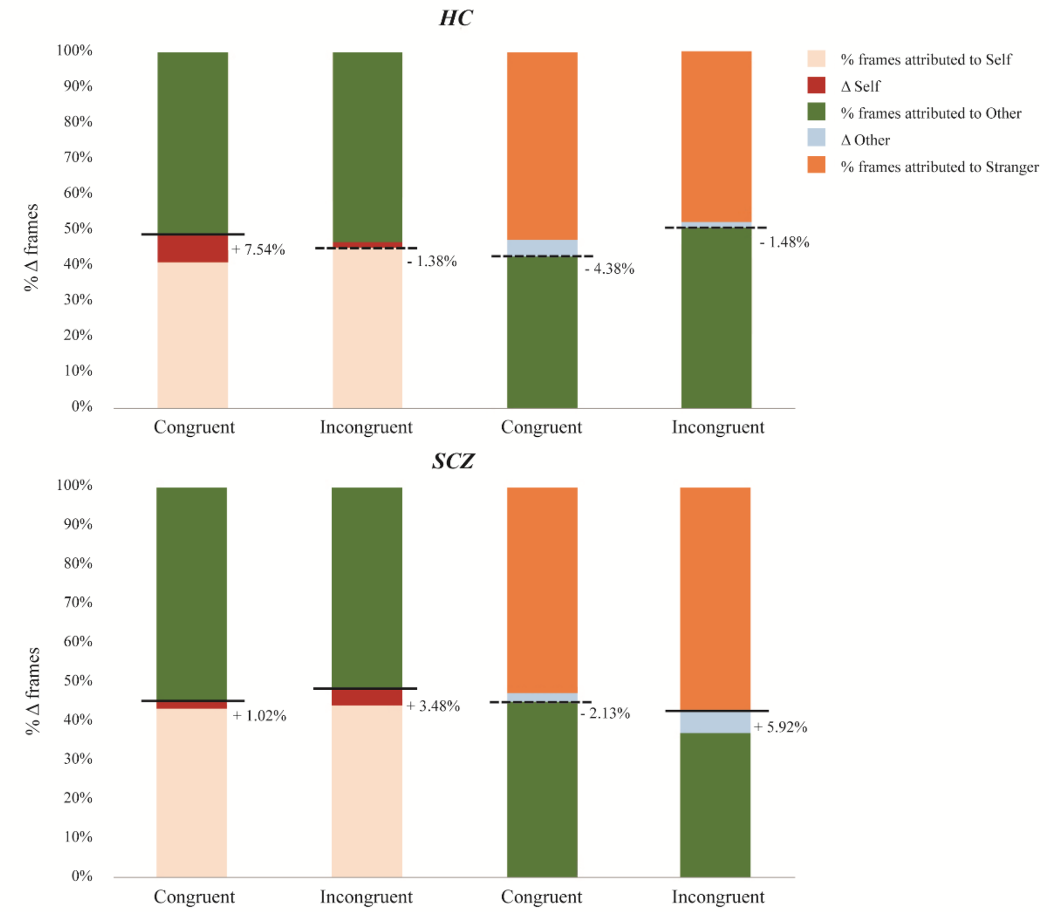

Figure 3. Qualitative graphical representation of Δ Self frames and Δ Other frames of HC and SCZ groups. Percentage of Δ Self frames and Δ Other frames of SCZ and HC groups displayed for Congruent and Incongruent stimulations. Black continuous lines represent a higher number of frames measured in the Post-Test relative to the Pre-Test (positive Δ frames). Black dashed lines represent a lower number of frames measured in the Post-Test relative to the Pre-Test (negative Δ frames). Positive Δ Self frames denote an Enfacement Illusion effect.

2.3 Results

2.3.1. Enfacement Illusion in Controls

Face recognition task

Repeated-measures ANOVA, performed only among controls on Δ frames, revealed a main effect of Morphing ($F_{(1,21)} = 35.74$, $p < 0.001$, $\eta^2_p = 0.63$) as well as a significant interaction Morphing by Stimulation ($F_{(1,21)} = 22.32$, $p < 0.001$, $\eta^2_p = 0.51$). Tukey HSD post-hoc comparison conducted on the significant main effect of Morphing revealed a significantly higher number of Self frames than Other frames, regardless of Stimulation (Δ Self frames = 9.29 SE 3.13; Δ Other frames = -8.36 SE 3.02 $p < 0.001$). Crucially, post-hoc comparisons conducted on the significant interaction Morphing by Stimulation (see **Fig. 4**) revealed the expected EI effect for the Self and not for Other only in the

Congruent stimulation. Indeed, the number of frames was significantly higher after the Congruent than after the Incongruent stimulation only for the Self (Δ Self Congruent = 22.73; SE 4.54; Δ Self Incongruent = -4.14; SE 3.92; $p < 0.001$) and not for the Other (Δ Other Congruent = -13.82; SE 3.49; Δ Other Incongruent = -2.91; SE 5.93; $p = 0.25$). Moreover, the number of frames attributed to the Self were significantly higher than the number of frames attributed to the Other after Congruent stimulation ($p < 0.001$).

Results of one sample t-tests against 0 revealed that the Δ Self frames measured after the Congruent stimulation were significantly higher than 0 ($t_{(23)} = 5.20$, $p < 0.001$). On the contrary, the Δ Other frames measured after the Congruent stimulation were significantly lower than 0 ($t_{(23)} = -3.85$, $p < 0.001$) (see **Fig.4**, purple stars). No significant differences were estimated against zero considering both Δ Self ($t_{(22)} = -1.05$, $p = 0.30$) and Δ Other frames ($t_{(23)} = -0.75$, $p = 0.46$) measured after Incongruent stimulation.

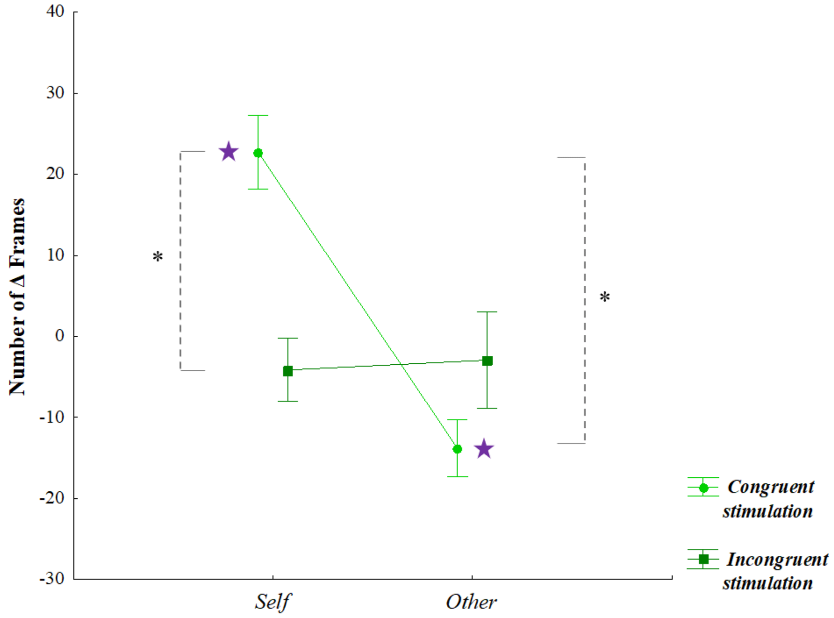

Figure 4. Enfacement Illusion in controls. Number of Δ Self frames and Δ Other frames of Healthy Controls for Congruent (light green/circle) and Incongruent (dark green/square) stimulations. * = $p < 0.05$ of Repeated-measures ANOVA, Purple stars = $p < 0.05$ of one sample T-tests against zero; error bars depicted SE.

Illusion Questionnaire

The repeated-measured ANOVA showed a significant main effect of Statement ($F_{(3,66)} = 23.25$, $p < 0.01$, $\eta^2_p = 0.51$). Tukey post-hoc comparisons showed that the score of the Statement 1 differed from all the other scores (Statement 1 = 61.02 SE 5.41; Statement 2 = 29.37 SE 6.77; Statement 3 = 24.74 SE 5.93; Statement 8 = 19.85 SE 4.92; all $p_s < 0.00011$). All other interactions were non-significant (all $p_s > 0.14$).

Results of t-tests against 50 showed that the only Illusion Questionnaire statement that was rated significantly higher than 50 was the statement 1 when referring to the experience of EI after Congruent stimulation (66.96 SE 6.73, $t_{(22)} = 2.52$ $p = 0.019$). This was also the only statement that discriminated between Congruent and Incongruent stimulations. Indeed, no significant difference from 50 was found for statement 1 referring to the experience of EI after Incongruent stimulation (55.09 SE 7.12, $t_{(22)} = 0.71$ $p = 0.48$). All the other comparisons were significantly lower than 50 (all $p_s < 0.008$).

2.3.2. Between-groups differences in Enfacement Illusion

Face recognition task

The repeated measures ANOVA showed a significant main effect of Morphing ($F_{(1,35)} = 7.50$, $p = 0.01$ $\eta^2_p = 0.18$). Moreover, the interactions Morphing by Group ($F_{(1,35)} = 5.1$, $p = 0.03$, $\eta^2_p = 0.13$), Stimulation by Group ($F_{(1,35)} = 12.58$, $p = 0.01$, $\eta^2_p = 0.26$) and Morphing by Stimulation were significant ($F_{(1,35)} = 10.07$, $p = 0.01$, $\eta^2_p = 0.22$). Tukey HSD post-hoc comparison conducted on the main effect Morphing revealed a significantly higher number of frames attributed to the Self than to Other, regardless of Stimulation (Δ Self frames = 9.51; SE 2.64; Δ Other frames = - 0.16 SE 3.05; $p = 0.01$). Post-hoc comparisons performed on the interaction Morphing by Group (see **Fig. 5**) revealed that both groups showed an equal number of frames attributed to the Self after the stimulation irrespective of the side (HC: Δ Self frames = 9.29 SE 3.37, SCZ: Δ Self frames = 9.73 SE 4.08; $p = 0.99$). Differently, only controls showed the expected EI Self specificity as demonstrated by a higher number of frames attributed to the Self than to the Other (Δ Other frames = - 8.36 SE 3.88; $p = 0.002$). No significant difference was found in the same comparison for SCZ group (Δ Other frames = 8.03 SE 4.70; $p = 0.98$). Consequently, the number of frames attributed to the Other was significantly different between the two groups ($p = 0.027$). Tukey HSD post-hoc comparisons conducted on the interaction Stimulation by Group revealed a significant higher number of frames measured after the Incongruent stimulation than after the Congruent stimulation only for SCZ group (Congruent stimulation: - 1.37; SE 4.00; Incongruent stimulation: 19.13 SE 5.20; $p = 0.011$). Moreover, the number of frames measured after the Incongruent stimulation for SCZ group was also significantly higher than the number of frames measured in the same condition for HC (HC: Incongruent stimulation = - 3.52 SE 4.29; $p = 0.002$). Post-hoc comparisons performed on the significant interaction Morphing by Stimulation revealed a significantly higher number of frames attributed to the Self than to the Other after the Congruent stimulation (Self: 12.63 SE 3.21, Other: -9.54 SE 3.52; $p > 0.001$). This effect was not found after the Incongruent stimulation (Self: 6.40 SE 3.67, Other:

9.21 SE 5.29; $p = 0.97$). Comparing the two stimulations, only the number of frames attributed to the Other were significantly different ($p = 0.016$).

Results of one sample t-tests against 0, performed on the whole sample, revealed that the Δ Self frames measured after the Congruent stimulation were significantly higher than 0 ($t_{(37)} = 4.28$, $p < 0.001$). Differently, the Δ Other frames measured after the Congruent stimulation were significantly lower than 0 ($t_{(37)} = -2.95$, $p = 0.005$). No significant differences were estimated against zero considering both Δ Self ($t_{(36)} = 1.11$ $p = 0.27$) and Δ Other frames ($t_{(37)} = 1.04$, $p = 0.30$) measured after Incongruent stimulation.

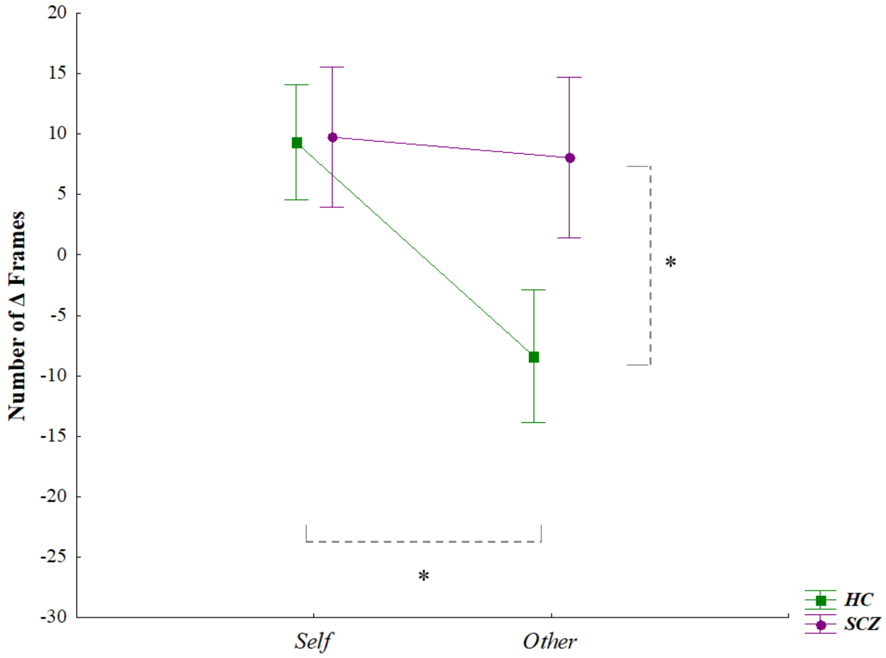

Figure 5. Enfacement Illusion comparing Schizophrenia patients and controls. Number of Δ Self frames and Δ Other frames of Healthy Controls (green/square) and Schizophrenia patients (purple/circle). * = $p < 0.05$, error bars depicted SE.

Illusion Questionnaire

The repeated-measured ANOVA showed a significant main effect of Statement ($F_{(3,123)} = 37.98$, $p < 0.01$, $\eta^2_p = 0.48$). Tukey post-hoc comparisons showed that the score of the Statement 1 differed from the other scores (Statement 1 = 60.92 SE 4.42; Statement 2 = 28.27 SE 4.82; Statement 3 = 26.66 SE 4.47; Statement 8 = 20.90 SE 3.31; all $p_s < 0.01$). All other interactions were non-significant (all $p_s > 0.26$).

Results of t-tests against 50 showed that the only Illusion Questionnaire statement that was rated significantly higher than 50 was statement 1 when referring to the experience of EI after Congruent stimulation (64.93 SE 5.35, $t_{(42)} = 2.79$, $p = 0.008$). Similarly to what happened among controls, this was also the only statement that discriminated between Congruent and Incongruent stimulations. Indeed, no significant difference from 50 was found for statement 1 referring to the experience of EI after Incongruent stimulation (56.93 SE 5.70, $t_{(42)} = 1.21$, $p = 0.23$). All the other comparisons were significantly lower than 50 (all $p_s < 0.001$).

2.3.3. Control results

Absence of direction influence on movies

In order to confirm that the direction of the movies did not affect our results in both group, we submitted to two repeated measures ANOVAs, one for each group, the Δ Self frames (calculated as the number of frames attributed to Self in the Post-Test respect to Pre-Test for Self-Other and Other-Self morphing movies) and the Δ Other frames (calculated as the number of frames attributed to Other in the Post-Test respect to Pre-Test for Other-Stranger and Stranger-Other movies). Morphing (i.e., Self-Other morphing and Other-Stranger morphing, in both directions), Stimulation (i.e., Congruent and Incongruent) and the Direction of morphing (i.e., Direction1: from Self to Other or from Other to Stranger; Direction2: from Other to Self or from Stranger to Other) were included as within-subjects factors. The repeated-measures ANOVA conducted on controls showed the significant main effect of Morphing ($F_{(1,20)} = 36.56$, $p < 0.001$, $\eta^2_p = 0.65$) and a significant interaction Morphing by Stimulation ($F_{(1,20)} = 22.15$, $p < 0.001$, $\eta^2_p = 0.52$). Relevant for the point under the focus here, neither the main effect of Direction ($F_{(1,20)} = 0.50$, $p = 0.49$, $\eta^2_p = 0.02$) nor the interaction Morphing by Direction ($F_{(1,20)} = 0.48$, $p = 0.50$, $\eta^2_p = 0.02$), Stimulation by Direction ($F_{(1,20)} = 0.11$, $p = 0.75$, $\eta^2_p = 0.005$) and Morphing by Stimulation by Direction ($F_{(1,20)} = 1.74$, $p = 0.20$, $\eta^2_p = 0.008$) were significant. The same analyses conducted on schizophrenia patients revealed a significant main effect of Stimulation ($F_{(1,6)} = 6.60$, $p = 0.04$, $\eta^2_p = 0.52$). Again, neither the main effect of Direction ($F_{(1,6)} = 3.81$, $p = 0.09$, $\eta^2_p = 0.39$) nor the interaction Morphing by Direction ($F_{(1,6)} = 0.37$, $p = 0.57$, $\eta^2_p = 0.006$), Stimulation by Direction ($F_{(1,6)} = 0.11$, $p = 0.75$, $\eta^2_p = 0.02$) and Morphing by Stimulation by Direction ($F_{(1,6)} = 0.37$, $p = 0.56$, $\eta^2_p = 0.006$) were significant.

Rating of Attractiveness, Similarity and Trustworthiness

Ratings of the perceived physical similarity between the Other and the Self, as well as, the trustworthiness and attractiveness attributed to the Other, were submitted to a repeated-measures ANOVA. Question (i.e., Attractiveness, Similarity and Trustworthiness) and Stimulation (i.e., Congruent and Incongruent) were entered as within-participants factors, whereas Group (SCZ and HC) was included as between-participants factor. The interaction Question by Group resulted significant ($F_{(2,82)} = 10.47$, $p < 0.001$ $\eta^2_p = 0.20$). Tukey HSD post-hoc comparisons conducted on the significant interaction revealed that in the HC group, trustworthiness ratings were significantly higher than the ones of attractiveness and similarity (Trustworthiness = 4.00 SE 0.25; Attractiveness = 2.96 SE 0.27; Similarity = 2.74 SE 0.23; all $p_s < 0.01$). The ratings of the perceived trustworthiness attributed to the Other in the HC group was also significantly higher than the ones of SCZ group (Trustworthiness SCZ = 2.55 SE 0.26; $p = 0.002$).

Correlations analyses between clinical data and patients' measurements of EI

Correlations between clinical data (i.e., PANSS and EASE scale and subscale scores) and illusion measurements (Δ Self frames and Δ Other frames in both Congruent and Incongruent stimulations, IQ scores after both Congruent and Incongruent stimulations) were estimated by Pearson's correlation analyses. No significant correlations were found (all Bonferroni corrected for multiple comparisons $p_s > 0.1$). These negative results could be due to our selection criteria. Indeed, we enrolled only patients in stable phase of recovery, which can reduce the interaction between psychopathology and the tested effects.

2.4 Discussion

The present study investigated, for the first time, EI proneness in schizophrenia. To accomplish this goal, the classical EI protocol was adapted to test the potential plasticity of both Self-Other and Other-Other boundaries. The results obtained considering only healthy participants showed that controls manifested the expected Enfacement Illusion effect. Indeed, only after Congruent stimulation, the number of frames attributed to the Self increased significantly from zero and were significantly different from the number of frames attributed to the Self after the Incongruent stimulation. At an explicit level, the IQ questionnaire revealed an increment of the sensation of being touched at the same location where participants saw the Other being touched (i.e., Statement 1 of Illusion Questionnaire), especially after the Congruent stimulation.

Overall, these results confirm that, at least among controls, the sharing of a synchronous and congruent multisensory experience modifies the usual Self-Other boundary, shifting it towards the Other's face. Even if bodily illusions have been considered self-specific, the inclusion in the present study of a new control condition to test the malleability of the Other-Other boundary demonstrated unexpected significant results. Among controls, besides the expected increment of the number of frames attributed to the Self after the Congruent stimulation, there was also a significant decrement of the number of frames attributed to the Other. This decrement was significantly less than zero only after the Congruent stimulation, and not after the Incongruent one. Besides the plethora of studies focused on Self-Other boundary, little is known about how the Other-Other boundary could be modified by bodily illusions protocols. On the basis of the current state of the art, we can only speculate that the reduction of the number of frames attributed to the Other, visible among controls, may represent a functional adjustment, probably relevant in the context of social domains. According to this view, Zahavi (2014) claimed that *"…as existing-in-the-world, we are constantly dependent upon others, and their coexistence is co-implied in our daily activities."* The phenomenal experience we entertain when relating to others is possible by our bodily nature, which shapes our perception and pre-reflective conception of others as other selves incarnated in a motoric capable physical body with capacities and experiences similar to ours (Gallese, 2014). This intriguing new finding may suggest that congruent visual-tactile stimulation is one of the potential mechanisms influencing both Self-Other and Other-Other boundaries, soliciting also a better investigation of the mechanisms underlying the bodily illusions (or at least the EI), which might be not purely self-related. However, considering that this is the first study addressing this topic, in order to generalize our results, additional research is needed.

Comparing the two groups, results showed common and distinct effects of EI on controls and schizophrenia patients. On the one side, both groups showed an equal malleability of the Self-Other boundary after EI. Indeed, both groups increased the number of frames attributed to the Self in the Post-Test. Furthermore, they both rated similarly the experience of the illusion at an explicit level. Specifically, only after Congruent visuo-tactile stimulation, participants reported a significant sensation of being touched by the cotton bud in the same location where they saw the Other's face being touched (i.e., scores significantly greater than 50 in Statement 1 of Illusion Questionnaire). These results do not confirm schizophrenia patients' higher tendency to be affected by bodily illusions (Ferri et al., 2014; Peled et al., 2003, 2000; Thakkar et al., 2011). It is possible that body parts ownership (i.e., the hand tested by RHI) is more malleable than face ownership in schizophrenia, probably because of the particular distinctiveness of the face and the specific procedure followed by EI that anchors patients more explicitly to their self-identity than other bodily illusions paradigms (i.e., RHI and full-body illusion). It is important to outline that, according to a recent meta-analysis (Shaqiri et al., 2018), the sense of ownership over body parts or over the full body seems to be unaffected by the illness. Consequently, the present negative result could support and extend this conclusion to the sense of ownership of the face.

In spite of the above-mentioned similarity in the Self-Other boundary, the two groups differed in the malleability of the Other-Other boundary. After visuo-tactile stimulation, controls decreased the number of frames attributed to the Other when it was paired with the Stranger. Oppositely, schizophrenia patients increased the number of frames attributed to the Other in the same condition. In other words, after the visuo-tactile stimulation, controls increased the number of frames attributed to the Stranger and decreased the number of frames attributed to the Other. Conversely, schizophrenia patients increased the number of frames attributed to the Other and decreased the number of frames attributed to the Stranger. This opposite performance led to a significantly greater number of frames attributed to the Other after the multisensory procedure among schizophrenia patients than controls. Interestingly, in schizophrenia patients the number of frames attributed to the Other and to the Self were not significantly different. These results suggest that instead of a greater EI proneness, a qualitative difference is visible among patients in the malleability of the Other-Other boundary. Indeed, in controls, EI differentially affects the malleability of the Self-Other and Other-Other boundaries, as they increased the number of frames attributed to the Self and decreased the number of frames attributed to the Other. Differently, patients extended in the same way both the Self and the Other toward their respective different poles, as they showed an equal increment in the number of frames attributed both to the Self and to the Other after EI. Indeed, schizophrenia patients often reportedly show a disordered sense of uniqueness, assigned not only to the self but also to surrounding people (Cutting, 1991; Margariti and Kontaxakis, 2006). Coherently, at a psychopathological level delusional, misidentification syndromes (i.e., Capgras and Frégoli syndromes), which represent this blurred sense of uniqueness, occur primarily in schizophrenia.

We demonstrated that in all participants, both Self-Other and Other-Other boundaries malleability was a specific effect of the Congruent stimulation (i.e., significant interaction Morphing by Stimulation). However, the absence of a three ways interaction between Group, Morphing and Stimulation prevents us to fully ascribe to the multisensory stimulation the specific effect found in the malleability of Other-Other boundary in patients. This was mainly due to the high sensitivity of the patients to the Incongruent stimulation, as revealed by the significant interaction Group by Stimulation. This greater sensitivity could be due to impaired self-processing in the tactile domain demonstrated in schizophrenia (Allen et al., 2004; Blakemore et al., 2000; Chang et al., 2005; Johns et al., 2001; Lenzenweger et al., 2000). Moreover, specific touch side remapping was found in the high schizotypes when compared to low and moderate schizotypes (Ferri et al., 2016). Accordingly, other studies performed on schizophrenia patients failed to find a significant difference even between synchronous and asynchronous stimulation (e.g., Kaplan et al., 2014). Coherently, Sandsten and colleagues (2020) have recently investigated the temporal contribution to the multisensory integration in EI in schizophrenia, showing how the EI was induced after both synchronous and asynchronous stimulations in patients. Thus, these findings suggest that patients may have an atypical spatiotemporal tactile experience. Besides the described potential explanations, according to the present results it is possible that even the mere exposure to the Other's face induced the patients' specific malleability of the Other-Other boundary. This consideration acquires a crucial importance to better delineate the psychopathological side of this effect, also considering the well-demonstrated familiarity alteration among schizophrenia patients (Ameller et al., 2015, 2017; Horn et al., 2015).

In conclusion, the present study confirms the plasticity of Self face representation to temporarily include another person's facial features following a multisensory procedure, as it has already been demonstrated by previous studies on the EI (Sforza et al., 2010; Tsakiris, 2008). Noteworthy, we also demonstrated, for the first time, that after the Enfacement Illusion protocols, the Other-Other boundary of the healthy controls is affected in a specific direction, as showed by the decrement of the number of frames attributed to the Other only after a congruent and simultaneous visuo-tactile stimulation. This result suggests that the Enfacement Illusion effect is not only related and confined to self-sphere, but it extends to the way we distinguish others, representing a potential crucial aspect in the social domain. Secondly, the present study demonstrates that schizophrenic patients' Self-Other boundary is not more flexible than in controls. Instead, schizophrenia patients show an opposite malleability of the Other-Other boundary as revealed by an increment, and not a decrement, of the number of frames attributed to the Other after a visuo-tactile synchronous stimulation. In the light of these new findings, further studies should investigate the role of multisensory integration in the perception of the boundary between others as a potential crucial link between the phenomenology of self-experience and social cognition.

Some limitations of the present study should be highlighted. First of all, even though the decision to exclude a control asynchronous condition was due to specific reasons (see introduction section), the lack of the asynchronous condition could represent a potential intrinsic limit of the present study. However, recent studies have shown how asynchrony, commonly used as control condition in multisensory integration paradigms, may not be an actual sensitive measure (Longo et al., 2008; Rohde et al., 2011; Sandsten et al., 2020). Moreover, differences between laboratory settings and daily life in self-face recognition should be considered. Specifically, it is unusual to observe our own face displayed in a neutral expression or without the characteristic facial features (such as hair or ears). Lastly, the protocol only involved patients in stable phase of recovery. This selection criterion may reduce the sensibility to EI illusion as well as the potential psychopathological interaction with the tested effects.

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Chapter 3

3. The motor roots of minimal self disorders in schizophrenia

3.1 Introduction

A fragile minimal sense of self has been considered to be at the core of schizophrenia spectrum disorders (Sass and Parnas, 2003), but the nature and the extent of this disruption has not been precisely identified, mainly due to the inconsistency and the large variety of the results (Shaqiri et al., 2018). An implicit and pre-reflective sense of self mapped in sensory-motor terms has been named bodily self (Gallese and Ferri, 2014). The bodily self has been operationalized in the so-called self-advantage effect (SA_{eff}). The SA_{eff} is a faster performance with self than others' right hands, displayed at different orientation angles, in a laterality judgment task requiring sensory-motor mental rotation (Ferri et al., 2011, 2012a). As any other mental motor rotation process applied to lateralized objects, to mentally rotate self and others' body-parts, the same temporal and kinematic properties of actual body transformations in space are applied (Decety et al., 1991; Decety, Jeannerod and Prablanc, 1989; Parsons, 1994; Porro et al., 1996; Shepard and Metzler, 1971). Indeed, the involvement of sensory-motor mental rotation processes is demonstrated by the classical bell-shaped function of participants' reaction times (RTs) for clockwise orientation degrees of the presented stimuli and, by the consequently high slope values of the curve fitting the RTs in function of increasing orientation degrees (β_{eff}) (Ionta et al., 2007; Parsons, 1994; Petit et al., 2003). The SA_{eff} and the β_{eff} demonstrate that the motor experience of one's own body-parts, even at a covert level, allows the implicit and pre-reflective bodily self-experience to emerge, leading to an implicit self-other effective differentiation.

The implicit experience of the bodily self seems to be mapped in motor terms. This claim has been supported by several neuroimaging studies demonstrating the activation of somatosensory and motor cortices during tasks entailing an implicit processing of self body-parts (Devue et al. 2007; Ferri et al., 2012; Sugiura et al., 2006; Uddin et al., 2005). Further evidence derives from a study that applied single-pulse TMS to the right motor cortex showing a concomitant increase in cortical excitability for self-related stimuli when compared to non-self-related stimuli (Salerno et al., 2012). Lastly, a clinical neuropsychological study showed that lesions in subcortical structures implicated in motor functions (i.e., basal ganglia and internal capsule) specifically impaired patients' implicit self body-parts processing (Candini et al., 2016).

Alterations of the minimal self have been suggested as a common backbone for the heterogeneous clinical manifestations of schizophrenia (Nelson, Parnas, & Sass, 2014; Parnas & Handest, 2003; Parnas et al., 2011; Parnas, Handest, Jansson, & Saebye, 2005). In this field, research mainly focused on body ownership and sense of agency. Besides the amount of studies focusing on these two aspects in schizophrenia, very little is known about the preserved or altered condition of the motor nature of the minimal self (bodily self). At a psychopathological level, bodily dysfunctions have been documented across all stages of schizophrenia and have also been considered as possible predictors of psychosis (Cannon et al., 1999). A first attempt to investigate the implicit bodily self in schizophrenia showed the absence of the self-advantage effect (Ferri et al., 2012). However, the experimental task adopted in that study (i.e., visual matching to sample task) did not require a sensory-motor mental rotation strategy to be completed. Consequently, the absence of the self-advantage could not be directly related to deficits in the motor representation of patients' bodily self. Studies focused on patients' mental rotation abilities showed that they were slower and less accurate than controls even if they retained the reaction times pattern suggesting the actual occurrence of a sensory-motor mental rotation strategy (Mazhari and Moghadas Tabrizi, 2014; Mazhari, Tabrizi, and Nejad 2015; de Vignemont et al., 2006). Dissimilarly, motor imagery tasks requiring patients to imagine simple motor sequences executed with their own body were found significantly impaired (Danckert et al., 2002; Lallart et al., 2012; Maruff, Wilson and Currie, 2003).

Taking into account all these results, it is reasonable to hypothesize specific alterations of the motor roots of the bodily self without a larger impairment of patients' sensory-motor mental rotation strategy when applied to non-self-related stimuli in schizophrenia patients.

The aim of the present study was to extend the current knowledge about minimal self-disorders in schizophrenia investigating two main hypotheses: I) to verify whether schizophrenia patients showed deficit in the implicit bodily-self processing (i.e., absence of SA_{eff}), and II) to prove whether the potential deficit in the implicit bodily self processing could be associated to a specific alteration of its motor nature (i.e., lower patients' β_{eff} for self-stimuli than controls).

3.2 Methods

Participants

The Bioethics Committee of Perugia University approved this study, written informed consent was obtained from all participants after a full explanation of the study procedure, in line with the 2013 Declaration of Helsinki. The total sample size exceeded the minimum amount required estimated by means of statistical a priori sample size calculation. It was obtained for repeated-measures ANOVA considering both within and between interactions (G*Power 3.1.9.4: 1-ß=0.95, α=0.05, number of measurements = 10, number of groups = 2 and effect size f=0.25; total sample size = 20). All participants were naive to the purposes of the experiment, right-handed and with normal or corrected-to-normal visual acuity. The mean age of the two groups was not different ($t_{(39)} = 0.36$, $p = 0.72$) as well as gender distribution ($X^2_{(1, N = 41)} = 2.11$, $p = 0.15$). SCZ were recruited among patients seeking treatment at regional mental health centers. During the period of the study, all patients, except one, were under medication with a low-medium dose of a single atypical antipsychotic drug. HC were recruited through fliers posted in meeting places.

Inclusion criteria for SCZ were a diagnosis within the schizophrenia spectrum according to the DSM-IV (American Psychiatric Association, 1994) and being in a stable phase of recovery (i.e., with no full-blown symptoms and at least 6 months post morbid). Exclusively for HC participants, either a personal history of Axis I/II disorders or a history of psychosis in first-degree relatives were considered as exclusion criteria. Exclusion criteria for all participants included physical health problems and neurological hard signs, a history of severe head trauma, loss of consciousness and IQ < 70. All participants filled an anamnestic questionnaire through which their demographic and medical information was obtained. SCZ participants were further evaluated by the Structured Clinical Interviews for DSM-IV Axis I (SCID-I) and Axis II (SCID-II) disorders (First et al., 2002). They were rated for positive and negative symptoms severity using the Positive and Negative Schizophrenic Symptom scale (PANSS) (Kay, Flszbein, and Opfer, 1987) and for their social, occupational, and psychological functioning through the Global Assessment of Functioning scale (GAF) (Hall, 1995). Patients' IQ was evaluated by means of the Raven Standard Progressive Matrices (SPM) (Raven, Raven, and Court, 1998). For a detailed description of SCZ and HC participants see **Table 1**.

		SCZ	**HC**
n.		20	21
Male, n.		14	10
Age, years		37.05; SE 1.29	36.05; SE 2.40
Scales	**Subscales**		
DSM-IV classification, n. (%)	Schizophrenia paranoid subtype	15 (75%)	n.a.
	Schizoaffective disorder	5 (25%)	n.a.
Structured Clinical Interview for DSM-IV Axis II disorders (SCID-II)	Cluster A (n. – %)	2 (10%)	n.a.
	Cluster B (n. – %)	2 (10%)	n.a.
	Cluster C (n. – %)	2 (10%)	n.a.
Illness duration (mean; SE)		10.33 years; SE 0.89	n.a.
Chlorpromazine Equivalent Dose (mean; SE)*		120.75 mg/die; SE 70.91	n.a.
PANSS (mean; SE)	Total	101.4; SE 5.39	n.a.
	Positive Scale	22.55; SE 1.92	n.a.
	Negative Scale	25.3; SE 1.88	n.a.
	General Psychopathology Scale	53.55; SE 2.80	n.a.
GAF (mean; SE)		42.75; SE 2.25	n.a.

Table 1. * Chlorpromazine equivalents were calculated following standard practices for antipsychotics (Woods, 2003). PANSS = Positive and Negative Schizophrenic Symptom scale; GAF = Global Assessment of Functioning scale; n.a. = not applicable.

Stimuli and procedure

A digital photograph of each participants' back of the hands was taken with a digital camera in a session prior to the experiment (1 week before), in order to obtain the images of the "Self" trials. This session took place in a controlled environment with constant artificial light and a fixed distance between the camera lens and the hands (40 cm), which were always photographed in the same position. Subsequently, photographs by means of Adobe Photoshop software (CS6), were converted to greyscale, cut from the original picture, pasted on a white background, and reoriented into different rotated positions. The same procedure was adopted for the Other trials. For each participant, pictures of "Other" trials were selected as the best match for size, skin colour and age (Self/other difference= from 0 to 3 years) of "Self" trials. Self and Other images were presented one at a time at the center of the computer screen in six different clockwise orientations from the upright (0°, 60°, 120°, 180°, 240°, and 300°). The upright orientation was defined as fingers pointing upwards. See **Figure 1, Panel b** for a graphical representation of the stimuli adopted.

During the experimental phase, participants were seated in front of a PC screen, at a distance of about 30 cm. Stimuli presentation was controlled by E-Prime (Psychology Software Tools Inc.). Each trial started with a central fixation cross (500 msec duration), followed by stimulus presentation. The trial was timed-out as soon as participants responded (up to a maximum of 4000 msec). The experiment consisted of 288 trials, 72 for each of the four conditions: self-right, self-left, other-right, other-left. Each orientation was randomly showed 12 times per condition. The task was always preceded by a practice block. See **Figure 1, Panel b** for a graphical representation of the followed experimental procedure.

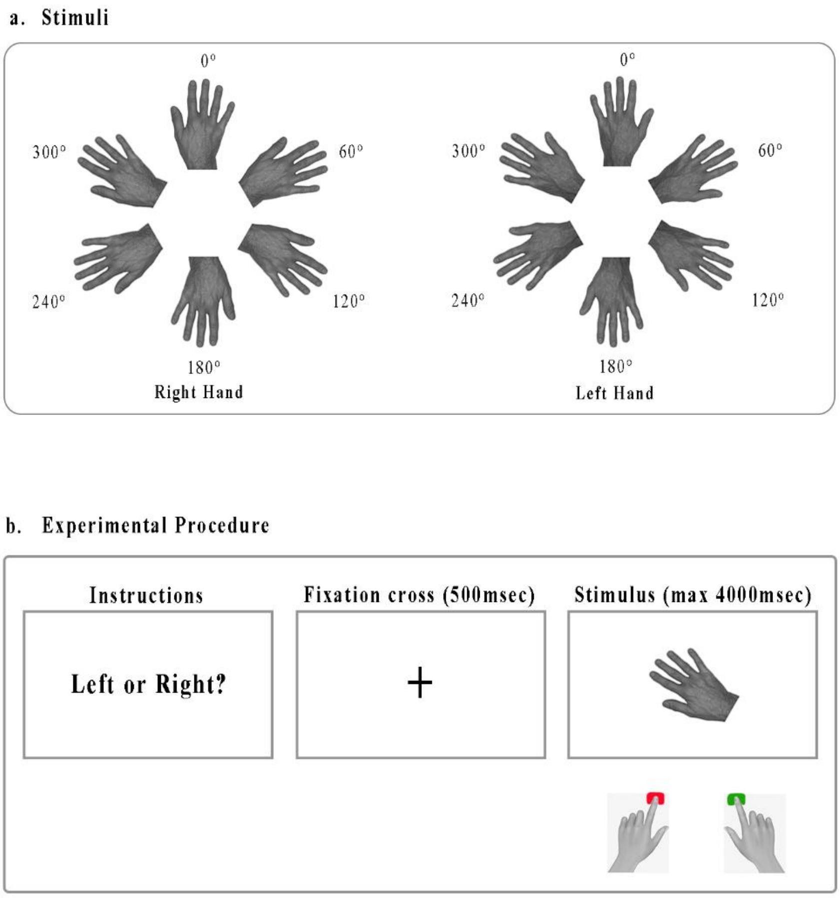

Figure 1. **Panel a: Stimuli**. Experimental stimuli consisted of pictures depicting the dorsal view of right and left hands in six different clockwise orientations. Images of participant's hands or of three other people's hands were presented one at a time in 'self' trials and 'other' trials, respectively. **Panel b: Experimental procedure.** red key = left answer, green key = right answer.

Statistical analyses

To evaluate the presence of the self-advantage effect, a repeated-measures ANOVA was performed on participants' reaction times (RTs) with Laterality (Right and Left), Owner (Self and Other) and Orientation (0°, 60°, 120°, 180°, 240° and 300°) as within-subject factors, and Group (HC and SCZ) as between-subjects factor. To answer our second hypothesis, a linear function from 0° to 180° was computed after combining data equidistant from 180° (i.e., 60° with 300°, and 120° with 240°). For each participant, slopes were derived from the linear functions obtained as a measure of changes associated with motor mental rotation (Ionta et al., 2007). Repeated-measures ANOVA was performed on participants' slopes, with Owner (Self and Other) as within-subjects factor, and Group (HC and SCZ) as between-subjects factor.

For all the performed repeated-measures ANOVAs, when the assumption of sphericity was violated, degrees of freedom (df) were corrected using Greenhouse-Geisser method. Whenever appropriate, significant differences within- and between-group were explored performing Newman-Keuls post-hoc comparison. Partial eta square (η^2_p) was calculated as effect size measure.

3.3 Results

3.3.1 Self-advantage effect (SA_{eff})

The repeated-measures ANOVA conducted on the RTs revealed a significant main effect of the factor Laterality ($F_{(1,39)} = 11.05$; $p = 0.002$; $\eta^2_p = 0.22$), showing faster RTs for the right hand stimuli (1163.16 ms, SE 74.45) than for left stimuli (1226.68 ms, SE 79.01). Indeed, right-handers take advantage from a pragmatic motor hand representation when making laterality judgements on right hands but not on left hands (Ferri et al., 2011). Relevantly to the purpose of the present study, also the three-way interaction Laterality by Owner by Group ($F_{(1,39)} = 4.94$; $p = 0.03$; $\eta^2_p = 0.11$) was significant. Post-hoc analysis conducted on the significant interaction Laterality by Owner by Group (**Fig.2, Panel a**) revealed that, in HC, RTs for right self stimuli were significantly faster than right other stimuli (right self: 1031.75, SE 102.40; right other: 1082.25, SE 106.9; $p = 0.035$). No significant difference was estimated between RTs for left self stimuli compared to left other stimuli (left self: 1145.85, SE 110.28; left other: 1110.06, SE 111.91; $p = 0.13$). On the other hand, in SCZ no significant differences were estimated neither for right self stimuli when compared to right other stimuli (right self: 1278.42, SE 104.93; right other: 1260.23, SE 109.54; $p = 0.43$), nor for left self stimuli compared to left other stimuli (left self: 1326.17, SE 113; left other: 1324.65, SE 114.68; $p = 0.94$). The same ANOVA revealed also a significant main effect of Orientation ($F_{(1.84, 71.81)} = 60.71$; $p < 0.001$; $\eta^2_p = 0.61$) and significant interactions Laterality by Orientation ($F_{(2.83,110.49)} = 7.12$; $p < 0.001$; $\eta^2_p = 0.15$) and Owner by Orientation ($F_{(4.01,156.55)} = 2.94$; $p = 0.02$; $\eta^2_p = 0.07$). Post-hoc analysis conducted on the significant main effect of Orientation revealed the expected faster RTs at 0°, 60° and 300° (972.14 ms, SE 59.69; 121.29 ms, SE 62.83; 1034.41 ms, SE 66.57; respectively) compared to RTs at 120°, 180°, 240° (1276.56 ms, SE 85.28; 1609.22 ms, SE 113.26; 1255.92 ms, SE 86.63; respectively; $p < 0.001$ in all cases). Post-hoc analysis conducted on the significant interaction Laterality by Orientation revealed faster performance with right hand stimuli than left hand stimuli at 0° (right: 922.46, SE 57.28; left: 1021.81, SE 65.52), 180° (right: 1569.81, SE 110.44; left: 1648.63, SE 118.74), 240° (right: 1179.32, SE 82.79; left: 1332.51, SE 94.38) and 300° (right: 963.95, SE 58.49; left: 1104.86, SE 78.57) (all $p_s < 0.02$). Differently, slower RTs were measured with right hand stimuli than left hand stimuli at 120° (right: 1319.69, SE 93.63; left: 1233.43, SE 82.41; $p = 0.01$). Post-hoc analysis, conducted on the significant interaction Owner by Orientation, showed slower performance with self stimuli than other stimuli at 0° (self: 1007.53, SE 60.66; other: 936.75, SE 60.04; $p = 0.005$).

3.3.2 *Slope Effect (β_{eff})*

The repeated-measures ANOVA conducted on slope values revealed a significant main effect of the factor Group ($F_{(1,39)} = 4.15$; $p = 0.048$; $\eta^2_p = 0.096$) showing higher slopes for HC (0.29, SE 0.04) than SCZ (0.18, SE 0.04). Furthermore, a significant interaction Owner by Group resulted significant ($F_{(1,39)} = 6.06$; $p = 0.018$; $\eta^2_p = 0.13$) (**Fig.2, Panel b**). Post-hoc analysis revealed higher slope values for self stimuli among HC than SCZ (HC: 0.33, SE 0.08; SCZ: -0.003, SE 0.08; $p < 0.001$). No significant difference was estimated between HC and SCZ in response to other stimuli (HC: 0.26, SE 0.07; SCZ: 0.37, SE 0.07; $p = 0.304$). Lastly, higher slope values were found in response to other stimuli than self stimuli, only among SCZ ($p = 0.027$).

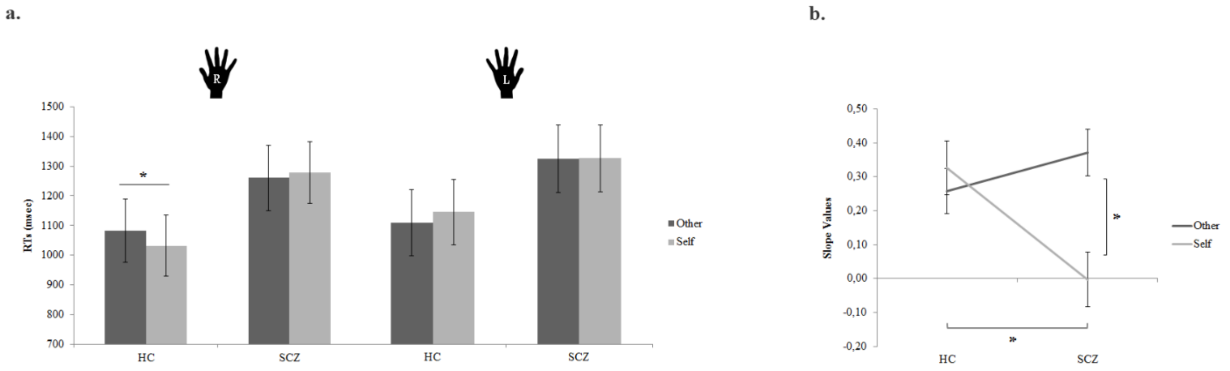

Figure 2. Panel a: Self-advantage effect for right hand stimuli, present in HC and absent in SCZ. Reaction times (RTs) measured in response to Other and Self stimuli displayed for HC and SCZ. R=right hand stimuli; L=left hand stimuli; HC=healthy controls; SCZ=schizophrenia patients. Error bars depicted SE, *=p b 0.05. **Panel b**: Higher slope in HC than SCZ for Self right hand stimuli. Slope values of Self and Other right hand stimuli displayed for the two groups. HC = healthy controls; SCZ = schizophrenia patients. Error bars depicted SE, * = p < 0.05.

3.4 Discussion

The present study integrates the current knowledge about minimal self-disorders in schizophrenia, investigating whether they could be extended to sensory-motor representation deficits of patients' bodily self. To accomplish this goal, healthy controls and schizophrenia patients were submitted to a hand laterality judgment task. Participants showed faster performance for right hands than for left hands stimuli. Indeed, right-handers take advantage from a pragmatic motor hand representation when making laterality judgements on right hands but not on left hands (Ferri et al., 2011; Gentilucci, Daprati and Gangitano, 1998). Among controls, results confirmed the presence of the self-advantage effect firmly related to effective mental motor rotation processes. Indeed, they showed faster reaction times to self right hands than to other's right hands (Ferri et al., 2011). The involvement of the motor mental rotation process for both self and other body-parts is revealed by the slope values, computed in response to self and other right stimuli that were not significantly different. In other words, although controls mentally rotated both self and other body-parts in order to answer to the laterality judgment, only when the motor body representation matched the ownership of the stimuli, the self-advantage emerged. Differently, among schizophrenia patients the absence of the self-advantage effect and the related specific deficit in the mental motor rotation of self right stimuli were demonstrated. Indeed, patients did not show faster reaction times to self than other's right stimuli indicating, as expected, the absence of the self-advantage effect. Furthermore, a significant lower slope value was found only for self right hand stimuli compared to controls, demonstrating the absence of mental rotation of self stimuli. Indeed, as already pointed out (Mazhari and Moghadas Tabrizi, 2014; Mazhari, Tabrizi and Nejad, 2015; de Vignemont et al., 2006), patients did not have a general deficit in mental motor rotation, rather, they showed a specific impairment in the sensory-motor processing of self body-parts. This result confirmed the implicit loss of self-body knowledge in schizophrenia (Ferri et al., 2012) identifying in altered sensory-motor processes one of the potential roots of other minimal self disorders.

Indeed, sensory-motor inputs shapes the widely investigated minimal self experiences (i.e., body ownership and sense of agency). Evidence collected among healthy controls suggests that the increased amount of motor-related afferent and efferent signals does affect the construction of and the consistent sense of body ownership (Pyasik, Salatino and Pia, 2019). Similarly, the susceptibility to the rubber hand illusion has been found to be affected by prolonged absence of movements (Burin et al., 2015; Scandola et al., 2014), whereas active movements increase the feeling of ownership (Dummer et al., 2009; Ma and Hommel, 2015; Tsakiris, Prabhu, and Haggard, 2006). Likewise, the sense of agency is thought to have the format of basic sensory-motor experiences (Berberian and Cleeremans, 2010; David, Newne, and Vogeley, 2008; Synofzik, Vosgerau, and Newen, 2008). Evidence for differential sensory-motor activations with respect to agency are provided by a number of consistent studies (Schütz-Bosbach et al., 2009; Schütz-Bosbach et al., 2006; Weiss, Tsakiris, Haggard, & Schütz-Bosbach, 2014), so that it has been regarded as a low-level sensory-motor proxy for feeling agency. In a similar vein, to imagine actions performed by another person or by themselves modulates participants' corticospinal excitability (Fourkas et al., 2006).

As stated before, the basic nature of a breakable minimal self experience in people suffering from schizophrenia has not yet been precisely identified and, for sure, the present study does not strive towards exhaustively solve this long-standing question. However, the collapse of the sensory-motor representation of patients' bodily self here demonstrated may suggest that before and below altered body ownership and sense of agency there could be a common distorted motor nature of the minimal self. Moreover, as recently suggested by Poletti and Raballo (2020), it could be also important to adopt a developmental perspective (Poletti et al., 2017; 2019) in studying the pathogenesis of schizophrenia spectrum vulnerability in order to address the complexity of its phenotypes and the temporal articulation of its causal mechanisms. Moreover, considering how multisensory integration processes and bodily self-consciousness develop across childhood requiring a prolonged developmental time (Cowie et al., 2018), adopting this standpoint could be also crucial to investigate the alterations of bodily self characterizing this psychiatric disorder.

In conclusion, in this study we addressed the investigation of the multi-layered concept of selfhood in schizophrenia trying to decode the nature and the extent of its disorders, identifying the potential crucial contribution of the implicit sensory-motor processes of the bodily self. Among these levels of self, the loss of the basic and implicit bodily self, anchored to sensory-motor processes, may give rise to the fragmented self-experience at the core of schizophrenia.

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Chapter 4

4. Schizotypy and individual differences in peripersonal space plasticity

4.1 Introduction

In everyday life, we regularly interact with, orient to, and reach objects. Most of these interactions occur within a limited portion of space immediately surrounding our body, defined as Peripersonal Space (PPS) (Rizzolatti et al., 1981). Neurophysiological studies on macaque monkeys have provided empirical evidence of bimodal and trimodal neurons located in the ventral premotor cortex and in the posterior parietal cortex with tactile receptive fields centred on specific body parts and visual and/or auditory receptive fields anchored to the tactile ones (Rizzolatti et al., 1997). Additionally, neuroimaging studies (Brozzoli et al., 2011; 2012b; 2013; Ferri et al., 2015a; Makin et al., 2007; Sereno & Huang, 2006) have suggested the existence of a similar PPS representation in humans, relying on the activity of multisensory parietal and premotor regions. From what stated above, it follows that PPS is a multisensory space where tactile and proprioceptive information concerning specific body parts, and visual inputs related to the environment are integrated (Gross & Graziano, 1995; Rizzolatti et al., 1997; for a review, see Serino, 2019). Nevertheless, since in our environment we interact not only with objects but also with other individuals, another specific space sector is described and mapped. This space sector, i.e. the distance between ourselves and other people, is commonly called Interpersonal Space (IPS). In this regard, it has been demonstrated that both PPS and IPS are plastic and can be modified by social and non-social interactions (e.g., Teneggi et al., 2013). Moreover, a recent study (Patané et al., 2017) has demonstrated that these two space representations can be dissociated, showing that PPS has a putative role for the guidance of interpersonal motor interactions (e.g., Ambrosini & Costantini, 2013; Brozzoli et al., 2014) while IPS is more dependent upon socio-emotional factors (e.g., Sommer, 2002; Tajadura-Jiménez et al., 2011). Crucial for the sensorimotor guidance of actions, as previously mentioned, PPS dynamically shapes through motor experience. Since seminal evidence from studies carried out on monkeys' brain (Iriki et al., 1996; Ishibashi et al., 2000), it is well known that using a tool to reach objects out of reach extends the boundaries of PPS representation. This is shown by the expansion of visual receptive fields of intraparietal sulcus neurons towards the part of space where the tool is operating. The plasticity of PPS was also demonstrated in humans. Indeed, important evidence has been reported both in neuropsychological patients (Berti & Frassinetti, 2000; Farnè et al., 2005; Farnè & Làdavas, 2000; Maravita et al., 2001) and in healthy participants, after short (Serino et al., 2007) and long motor training with a tool (Bassolino et al., 2010; Canzoneri et al., 2013; Serino et al., 2007). Overall, these findings highlight that tool use extends participants' PPS by making out-of-reach objects "reachable". The plasticity of the PPS, due to motor training, marks it as an action space (Costantini et al., 2011; Gallese, 2000; Làdavas & Serino, 2008; Maravita & Iriki, 2004; Martel et al., 2016; for a different interpretation see also Holmes et al., 2007 and Holmes, 2012). The functional malleability of this space is influenced not only by the active use of a tool to reach objects in far space, but also by the mere observation of the tool use (Costantini et al., 2011). Thus, not only after using a tool, but also after observing others using the same tool, participants become sensitive to the affording features of an object even when it is presented in far space. This effect appears only if the observer shares the same action potentialities with the observed agent, i.e. while passively holding a tool compatible with the observed action. Interestingly, a recent study by Serino and colleagues (Serino et al., 2015) provides new evidence in this context, showing that the synchronicity between tactile stimulation at the hand and auditory or visual stimulation from the far space triggers PPS expansion, suggesting that tool-action may be not necessary to extend PPS representation. Taking into account all these results, it emerges that little is still known about how tool-use observation affects PPS remapping.

The extension size of PPS largely varies across people (Ferri et al., 2015a), depending on several individual characteristics. For instance, different studies showed that PPS is affected by individual personality traits like anxiety, claustrophobia and interoceptive accuracy (Ardizzi & Ferri, 2018; Lourenco et al., 2011; Noel et al., 2018; Sambo & Iannetti, 2013). Furthermore, a recent study by Di Cosmo and colleagues (2018) has demonstrated a link between individual schizotypal traits and PPS mapping. Specifically, narrower PPS boundaries have been described either in people with high schizotypal traits or in schizophrenia patients, when compared with low schizotypal traits and healthy controls, respectively. Other studies have provided different evidence, showing larger extent of PPS in schizophrenia (Park et al., 2009; Holt et al., 2015), related also to positive symptoms severity (de la Asuncion et al., 2015; Schoretsanitis et al., 2016).

Despite the relevance of the plasticity of PPS, due to its adaptive function, and the association between individuals' PPS boundary and schizotypy, no study so far has investigated the integrity of the functional properties of PPS in schizotypy, such as its plasticity after motor training. Schizotypy is thought to reflect the subclinical expression of schizophrenia and to constitute a dynamic continuum ranging from personality variation to psychosis (Debbané & Mohr, 2015; Lenzenweger, 2006; Raine, 2006). Some shared features have been found between schizotypy and schizophrenia concerning perceptual, cognitive and motor impairments. For example, individual differences in schizotypy have been associated with motor abnormalities (e.g., anomalies in gait, reduced precision of manual motor control, impairments in oculomotor functions) and social dysfunctions, reflecting a reduced social competence (Cohen et al., 2015; Ettinger et al., 2014; Ettinger et al., 2015; Forsyth et al., 2010). Moreover, there is plenty of evidence showing that schizophrenia patients and schizotypal individuals are characterized by blurred boundaries between self-body and the environment (e.g., Peled et al., 2000, 2003; Thakkar et al., 2011), supporting the idea that the integration of body-centred and external spatial information is altered in both cohorts of individuals (for a review on spatial self representation in schizophrenia, see Noel et al., 2017). Thus, it follows that investigating the plasticity of PPS, which constitutes a multisensory interface mediating the interactions between the body and the environment (Graziano & Cooke, 2006), could be relevant to better delineate the altered self-boundaries in schizotypy. This could additionally open a so far neglected line of research on the association between the plasticity of PPS and personality traits.

In the present study we have investigated the plasticity of peripersonal space after two different trainings (motor and perceptual) along a severity continuum of schizotypal dimension. Specifically, we tested the PPS plasticity after tool use and after the mere observation of another person using the same tool. In order to assess the extension of PPS, we used an adapted version of the audio-tactile interaction task developed by Canzoneri and colleagues (2012), in accord with the idea of PPS as a multisensory interface for body-objects interactions (Brozzoli et al., 2014; Brozzoli et al., 2012a; Cléry et al., 2015). To avoid including high and low schizotypal individuals characterized by different PPS size (Di Cosmo et al., 2018), thus to better analyse PPS functional plasticity, we randomly recruited participants along the severity continuum of schizotypal traits, which is part of the low-to-medium spectrum of schizotypy (e.g., Raine, 1991), in which it is reasonable to hypothesize a similar extension size of PPS. We expected the expansion of individual multisensory PPS after both motor and perceptual trainings; however, taking into account the previously mentioned motor anomalies characterizing high schizotypal individuals, if the functional plasticity of PPS were to be different along the schizotypal continuum, we could expect a relation between the individual PPS expansion and the level of schizotypal trait. Indeed, if impaired plasticity of PPS emerged at this level of schizotypal continuum, despite not including the highest end of the distribution, we could predict a different pattern of PPS mapping (i.e., lesser expansion) with the increment of schizotypal traits.

4.2 Methods

A total of 70 participants were included in the study (35 participants were included in Experiment 1; 35 new participants were included in Experiment 2). The sampling was suspended when approximately two gender-balanced groups of enough size and with a good pre-training sigmoid fitting ($r^2 \geq 0.50$) were obtained. Moreover, we considered the sample size of previous works examining peripersonal space expansion and individual differences as reference (see Hunley et al., 2017 (n. =70); Longo & Lourenco, 2006 (n. =60); Lourenco et al., 2011 (n. =35)). Post-hoc power estimation analysis carried out for two-way ANOVA including the actual effect size of our two main effects ($f_{(Experiment)} = 0.31$; $f_{(SPQ)} = 0.25$) and the final sample size (n. = 70) confirmed the good statistical power achieved ($1\text{-}ß_{(Experiment)} = 0.95$; $1\text{-}ß_{(SPQ)} = 0.83$). Participants' handedness was assessed by the Edinburgh handedness inventory (Oldfield, 1971). All reported no abnormalities of touch or hearing. At the end of both experiments, they completed the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) to evaluate individual schizotypal traits among the healthy population. Generally, the SPQ distribution in a non-clinical sample shows a positive skew, with most scores on the lower end, thus indicating that high scores are relatively rare (e.g., Badcock & Dragović, 2006; Daneluzzo et al., 1998; Rossi & Daneluzzo, 2002). Both studies were approved by the Local Ethical Committee (AVEN) and were carried out in accordance with the Declaration of Helsinki (1964 and subsequent amendments).

Experiment 1

Participants

Thirty-five healthy volunteers (15 males, mean age 25.40 SEM 0.33, age range 21-31 years) participated in the first study and gave their written formal consent. All participants were right-handed (mean 0.74 SEM 0.03), as assessed by the Edinburgh handedness inventory (Oldfield, 1971). Participants' average SPQ score was 12.71, SEM 1.41.

Procedure

The experimental procedure consisted of three sessions. First, participants performed the Peripersonal Space task (i.e., PPS task – Session 1) in order to measure the individual PPS boundary at baseline. After this session, they took part to Session 2 (i.e., training phase, see below). Lastly, participants were submitted again to PPS task (Session 3) in order to measure PPS boundaries after actively using a tool. The total procedure was carried out on the same day. At the beginning of the experiment, participants were instructed to move two small objects in their peripersonal space with their right hand (20 cm far from participants' chest) for around 2 minutes. In a previous pilot study, we found that after performing a brief motor training, participants' sigmoidal fits improved. The likely involvement of participants in a short and easy motor activity would emphasize participants PPS boundaries, resulting in a better performance in terms of improved data fitting. For this reason, in the present study this short motor training was carried out at the beginning of the experimental procedure to better emphasize participant's peripersonal space boundaries, stressing the limit between peri- and extra-personal spaces.

a) **Session 1 and 3: PPS task**

The location of participants' PPS boundary was measured using an adapted version of the well-established PPS task procedure (Canzoneri et al., 2012; Ferri et al., 2015a; Ferri et al., 2015b; Teneggi et al., 2013). The rationale behind this task refers to the PPS mapping itself, which is allowed through the integration of somatosensory information related to body parts and visual or auditory information related to objects presented in the portion of space surrounding the same body parts (for a review, see Macaluso & Maravita, 2010). Thus, the audio-tactile interaction task used here includes a bimodal stimulation (tactile and auditory stimulations), as it has been shown that stimuli from different sensory modalities interact more effectively when presented within the same portion of space (Stein & Meredith, 1993). Tactile stimuli were delivered at different temporal delays from the onset of the sound, for the sound to be perceived at different distances from the body. Hence, the looming sounds used in this paradigm (see below) allowed for the measuring of participants' PPS boundaries, as the distance where sounds affected tactile reaction times. This distance corresponds to the inflection point of the sigmoid curve that describes the relationship between reaction times (RTs) to tactile stimuli and the perceived position of the sound in space, capturing the boundaries of PPS along a continuum, ranging from near to far space. Thus, we recorded participants' RTs to a tactile stimulus applied to the hand while dynamic or flat sounds were presented. Since it has been shown that close but not far sounds boost tactile RTs (Bassolino et al., 2010; Serino et al., 2007; Serino et al., 2011), we predicted that RTs to tactile stimuli would decrease as a function of the sound's source perceived approach, in the case of dynamic sounds. Moreover, we expected that this effect would be similarly present for distances further away from the body in both Sessions 3 (i.e., post-training phases), hence revealing an expansion of peripersonal space.

Auditory stimuli were samples of pink noise (or 1/f noise) of 3000 ms duration with flat or increasing (looming) intensity levels. The sounds were sampled at 44.1 kHz. Sound intensity was manipulated using Soundforge 4.5 software (Sonic Foundry) so that "looming sounds" had exponentially rising acoustic intensity from 55 to 70 dB, whereas "flat sounds" had constant 62.5 dB acoustic intensity. Auditory stimuli were presented by two loudspeakers (see below). The looming sounds were emitted by both near and far loudspeakers, arranged so that the far loudspeaker activated at the maximum intensity and its intensity decreased up to silence along the trial, whereas the near loudspeaker activated at the minimum intensity and its intensity increased up to the main value along the trial. In this way, the looming sounds gave the impression of a sound approaching towards the participant's body.

Tactile stimuli were delivered by means of constant-current electrical stimulators (DS7A; Digitimer) via pairs of neurological electrodes placed on the hairy surface of the participant's right index finger. The electrical stimulus was a single, constant voltage, rectangular monophasic pulse. At the beginning of each session, the intensity of the tactile stimulus was set to be clearly above the threshold of each participant (Canzoneri et al., 2012). Intensity for the tested participants ranged between 5.5 and 9.5 mA. The stimulus duration was equal to 100 μs. The presentation of auditory and tactile stimuli, as well as the recording of participants' responses, were controlled by custom software implemented in MATLAB (The MathWorks 2015).

During the experiment, participants were blindfolded and comfortably seated behind a table with their right arm resting palm down. The audio-tactile apparatus, which was mounted on the table, consisted of two loudspeakers, one placed near participants' right hand and the other at a distance of 100 cm from the near loudspeaker (i.e., far from the participant), and a constant-current electrical stimulator controlling a pair of neurological electrodes attached to the participant's right index finger (See **Fig. 1**). During each trial, either a looming or a flat sound was presented. Along with the auditory stimulation, in 60% of the trials, participants were also presented with a tactile stimulus. The tactile stimulus was delivered at varying temporal delays from the onset of the auditory stimulus. Five different temporal delays that resulted in five distances from participants' body were used: 300 ms (D1); 800 ms (D2); 1500 ms (D3); 2200 ms (D4); and 2700 ms (D5). The remaining trials (40% of total) were catch trials with auditory stimulation only (either looming or flat sounds) or unimodal tactile trials (with only vibration). Unimodal tactile stimuli served as baseline trials. In these trials, the tactile stimulation was delivered during silence periods, preceding sounds administration, namely at -700 ms (D0). These baseline trials were used to control for a potential confounding effect due to expectancy. Each trial was followed by an inter-trial interval of 1000 ms. Each participant was presented with a random combination of 18 target stimuli for each temporal delay for the looming and flat sounds, randomly intermingled with the catch trials. Following the procedure adopted by Teneggi and colleagues (2013), trials were equally divided into two blocks for a total of 120 trials, lasting about 8 minutes each. Participants were asked to respond as fast as possible to the tactile target, when present, by pressing a button on the laptop with their left index finger, trying to ignore the auditory stimulus. Each trial was repeated if participants failed to answer to the tactile target.

Participants performed this task both before and after the Session 2.

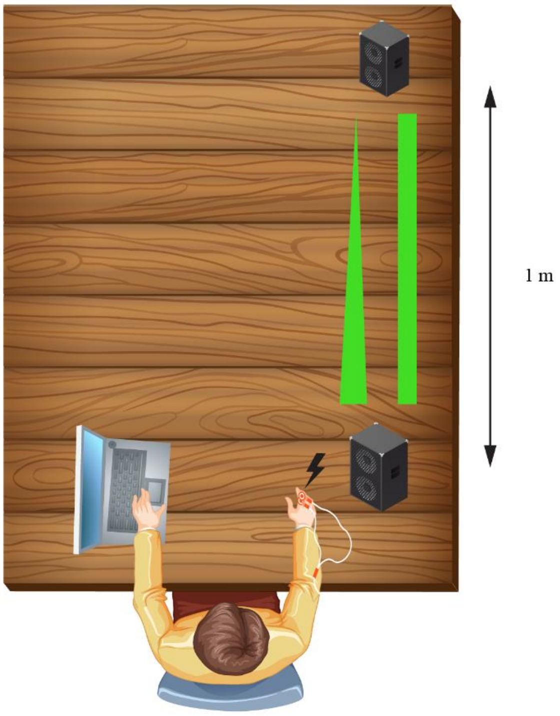

Figure 1. Experimental setting of PPS task. The green shapes represent the two adopted sounds (rectangular shape = flat sound; triangular shape = looming sound).

b) Session 2: Active tool-use

The tool used for the training session was a garbage clamp 75 cm-long composed of an ergonomic handle with a lever (12 cm), a 60 cm-long rigid aluminium shaft and an articulated 'hand', composed of two curved plastic 'fingers' (13 cm each). Participants were instructed to move 50 small coloured objects (green and red), placed on two marked areas of the table, in the far space (85 cm from participants' chest). Participants sat along the short side of the table holding the tool with their right hand and were requested to use the tool in order to grab and move one object at a time across the two areas. All objects were moved from one marked area to the other and then repositioned on the initial area for a total of 100 movements (see **Fig. 2 Panel A**). Session 2 lasted around 8 minutes.

Experiment 2

Participants

Thirty-five healthy volunteers (13 males, mean age 25.97 SEM 0.58, age range 18-34 years) were included in Experiment 2 and gave their written formal consent. All participants were right-handed (mean 0.66 SEM 0.05). None of the participants enrolled in Experiment 2 took part to the here above described Experiment 1. Participants' average SPQ score was 14.86, SEM 1.58.

Procedure

The experimental procedure followed for Experiment 2 was the same of Experiment 1 with the exception of the Session 2.

a) Session 1 and 3: PPS task

Participants underwent the same experimental task of Experiment 1 (i.e., PPS task, see above) in order to measure participants' PPS boundary. Participants performed this task both before and after the Session 2. The total procedure was carried out on the same day.

b) Session 2: Tool-use observation

Participants and a female unfamiliar confederate were seated at the short side of the table both holding in their right arm a garbage clamp (Costantini et al., 2011) (See **Fig. 2 Panel B**). A female confederate was chosen for this training phase due to recent findings that demonstrated that female confederates are generally perceived more positively and more approachable than male confederates (e.g., Holt et al., 2014; Iachini et al., 2016; Wabnegger et al., 2016). Fifty small coloured objects (green and red) were placed on two marked areas in the far space as in Experiment 1. While the confederate was instructed to use the tool to grab and move the objects in the same way as in Experiment 1, participants were requested to simply observe the movements performed by the confederate. The duration of Session 2 was similar to Experiment 1 (around 8 minutes).

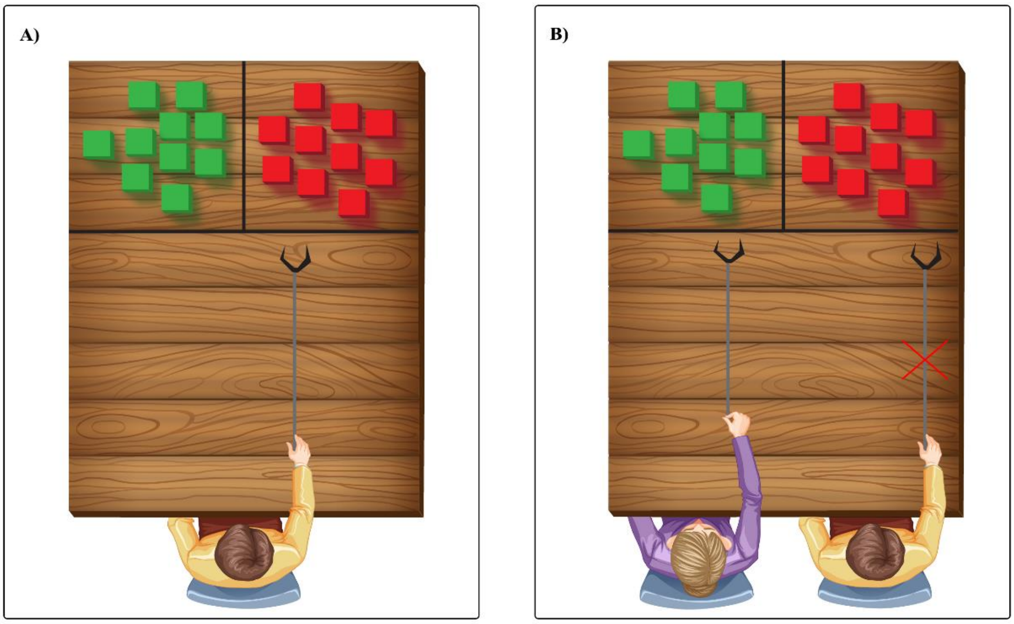

Figure 2. Qualitative representation of the training phase. This figure represents a graphical illustration of the two training sessions in which only few coloured objects are reported. Please see the main text for the complete explanation of the procedure. Panel **A)** shows the Session 2 of the Experiment 1 (Active tool-use) in which participants were instructed to move the 50 small coloured objects one at time, with the garbage clamp. Panel **B)** shows the Session 2 of the Experiment

2 (Tool-use observation) in which participants were instructed to passively observing the experimenter performing 100 movements with the garbage clamp, holding the same tool. The red cross means that participants held the garbage clamp without moving it.

4.2.1 Data analysis

To estimate the individual boundary of PPS, mean RTs to the tactile targets delivered at the different temporal delays from the onset of looming sounds – for both experiments - were fitted to a sigmoidal function (Canzoneri et al., 2012; Ferri et al., 2015a; Ferri et al., 2015b; Teneggi et al., 2013) as follows:

$$y(x) = \frac{y_{min} + y_{max} \cdot e^{(x-x_c)/b}}{1 + e^{(x-x_c)/b}}$$

where x represents the independent variable (timing of touch delivery in milliseconds); y is the dependent variable (RT); y_{min} and y_{max} are the slower and upper saturation levels of the sigmoid, respectively; xc is the value of the abscissa at the central point (CP) of the sigmoid (value of x at which y = (y_{min} + y_{max}) /2); and b establishes the slope of the sigmoid at the CP. For each participant, values of the parameters y_{min} and y_{max} were assigned a priori equal to the minimum and maximum values of individual dataset. For each participant, we then took xc, hereafter referred to as the CP of the curve, as an estimation of the individual boundary of PPS representation (Canzoneri et al., 2012; Ferri et al., 2015a; Ferri et al., 2015b; Teneggi et al., 2013). Moreover, to check the different modulation of looming compared to flat sounds on tactile RTs before performing the Sessions 2 (RTs measured at baseline – Session 1), two separate ANOVAs were carried out for each Experiment. This was considered a preliminary step in order to proceed to consider only looming stimuli as experimental variables (Results section 4.3.2). Additionally, in order to control for a potential confounding effect due to expectancy, two separate ANOVAs were carried out for each Experiment contrasting unisensory tactile trials with audio-tactile ones (Results section 4.3.3).

The difference between central points estimated in Session 3 (CP-post) relative to Session 1 (CP-pre) was calculated (Delta CP values) for both experiments. Moreover, the SPQ distribution (see **Fig. 3**) was split by median score (median score Experiment 1= 13, SEM=1.41, scores range: 3-34; median score Experiment 2: 13, SEM=1.58, scores range: 1-35) into high- and low-values representing participants rated as relatively-high schizotypes (rH) and relatively-low schizotypes (rL), respectively. This procedure was followed for both experiments. Therefore, a total of thirty-six participants in the relatively-high schizotypal group (average SPQ score rH-Experiment 1= 19.71, SEM= 1.42; rH-Experiment 2= 22.59, SEM= 1.68) and thirty-four in the relatively-low schizotypal group (average SPQ score rL-Experiment 1= 6.11, SEM= 0.78; rL-Experiment 2= 7.56, SEM= 0.84) were included in the analyses. Kolmogorov-Smirnov tests for independent samples were carried out to assure that the distributions of total SPQ scores (SPQ score Experiment 1: 12.91, SEM 1.60; SPQ score Experiment 2: 15.07, SEM 1.77) were comparable between the two experiments (SPQ scores: Kolmogorov-Smirnov Z= 0.60 p= 0.87).

Delta CP values were entered into a two-way analysis of variance (ANOVA) with Experiment (Experiment 1, Experiment 2) and SPQ group (rH, rL) as between-subjects factors. Additionally, the PPS boundaries measured at Session 1 (CP-pre) and at Session 3 (CP-post) were checked for comparison between the two experiments and secondly, related to individual schizotypal traits. Indeed, CP-pre values were entered into a two-way analysis of variance (ANOVA) with Experiment (Experiment 1, Experiment 2) and SPQ group (rH, rL) as between-subjects factor. The same analysis was carried out also for CP-post values (Results section 4.3.1).

Visual inspection of residual plots did not reveal any obvious deviations from normality. Levene's Test of equality of variances was also carried out and the assumption was met ($F_{(3,66)} = 0.50$, p= 0.684). Whenever appropriate, significant differences were explored performing Tukey post-hoc comparison. Generalized eta-squared (η^2_G) was calculated as effect size measure.

All the analyses were performed using R v.3.6.1 (R Core Team, 2019), ez (Lawrence, 2012) and emmeans (Lenth, 2019). For data visualization ggplot2 was used (Wickham, 2016).

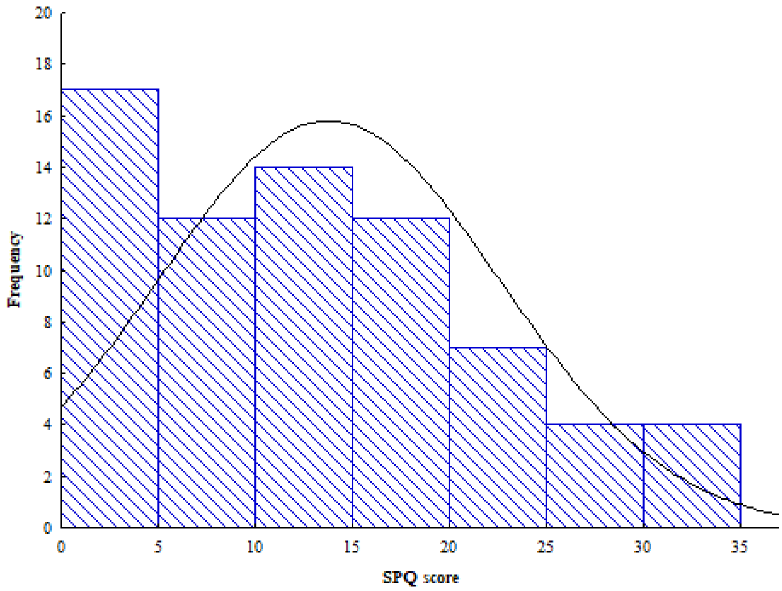

Figure 3. Distribution of SPQ scores across participants in both experiments.

4.3 Results

4.3.1 Control analyses

Peripersonal Space boundaries at baseline

The ANOVA carried out on CP-pre values revealed the absence of a significant main effect of Experiment ($F_{(1,66)} = 1.80$, $p= 0.184$, $\eta^2_G=0.03$), showing that the two experiments, at baseline, did not differ (**Fig. 4**). Moreover, the main effect of SPQ group was not significant ($F_{(1,66)} = 2.18$, $p=0.144$, $\eta^2_G=0.03$), as expected. Lastly, also the interaction Experiment by SPQ group was not significant ($F_{(1,66)} = 0.59$, $p=0.445$, $\eta^2_G=0.01$). These results showed that at Session 1, the relatively-high schizotypal group was not different from the relatively-low schizotypal one in terms of extension size of PPS.

Failure to replicate the results previously reported by Di Cosmo and colleagues (Di Cosmo et al., 2018), showing that high-schizotypes have narrower PPS boundary compared to low-schizotypes, confirms that our sampling procedure guarantees the same PPS size between our experimental groups. Specifically, whereas Di Cosmo and colleagues selected the lower and the higher tails of the larger screened sample, we included all the randomly recruited participants who generally are part of the low-to-medium spectrum of schizotypy (e.g., Raine, 1991). As a consequence, our healthy population ranged along different severity levels on schizotypal dimension, resulting in a similar extension size of PPS, as hypothesized (see the introduction section for the full explanation of study's hypotheses).

Peripersonal Space boundaries after motor training phases

The ANOVA carried out on CP-post values revealed a significant main effect of Experiment ($F_{(1,66)} = 3.77$, $p= 0.05$, $\eta^2_G=0.05$), showing that the two experiments differ in Session 3 (**Fig. 4**). Tukey post-hoc carried out on the significant main effect of Experiment revealed that CP-post values were significantly lower in Experiment 1 than in Experiment 2, thus confirming the effect of motor training in the first experiment only, i.e., after actively using the tool in the extra-personal space (Experiment 1= 1210 ms, SEM= 74.4; Experiment 2= 1415, SEM= 74.4; $t_{(66)}= -1.94$, $p= 0.05$). Moreover, the main effect of SPQ group was not significant ($F_{(1,66)} = 1.62$, $p=0.208$, $\eta^2_G=0.02$) neither was the interaction Experiment by SPQ group ($F_{(1,66)} = 0.69$, $p=0.411$, $\eta^2_G=0.01$).

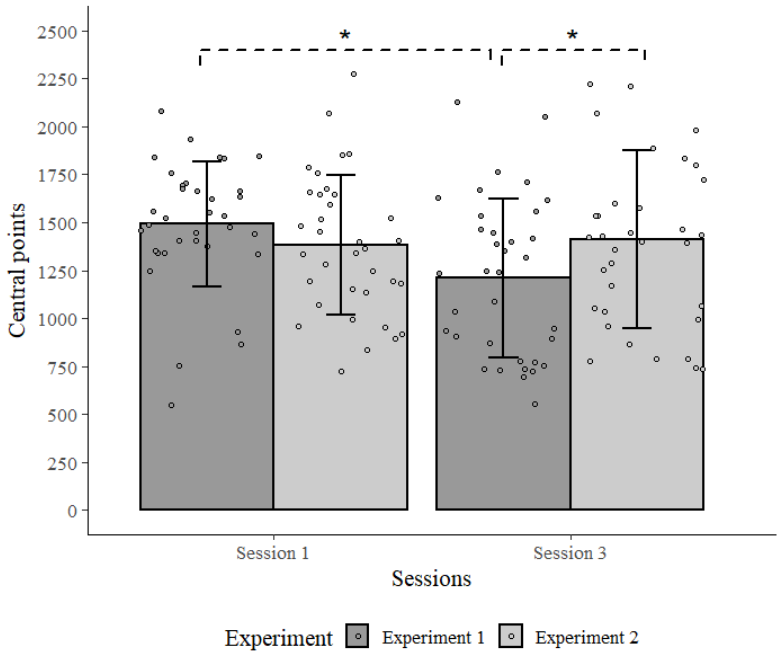

Figure 4. Central points values measured in Session 1 and Session 3, for both Experiments. Error bars depicted SD; * = $p < 0.05$.

Sigmoidal fit analysis

To estimate the location of the PPS boundary, the mean RTs to the tactile targets delivered along with looming sounds were fitted to a sigmoidal function. Consistently with previous literature (Canzoneri et al., 2012; Ferri et al., 2015; Teneggi et al., 2013), a sigmoid model provided a better description of the relationship between tactile RTs and the timing at which the tactile stimuli were delivered, compared to a linear model (commonly used also by previous studies on peripersonal space) (e.g., Canzoneri et al., 2012; Teneggi et al., 2013). Indeed, the R squared of linear and sigmoidal fit for looming sound were entered in a repeated-measure ANOVA with Fit (Linear, Sigmoidal), Condition (Session 1, Session 3), and Experiment (Experiment 1, Experiment 2) as within-subjects factor. Subsequently, the same analysis was carried out for flat sounds.

Results of the ANOVA carried out on looming sounds showed a significant main effect of the factor Fit ($F_{(1,34)} = 50.87$, $p < 0.001$, $\eta^2_p = 0.6$). Post-hoc carried out on this significant main effect showed a higher R squared fit value for the sigmoid model than for the linear model, as previously found by other studies (Linear model: 0.69, SEM 0.02; Sigmoid model: 0.77, SEM =0.02). Moreover, results of the ANOVA carried out on flat sounds revealed the absence of a significant main effect of the factor Fit ($F_{(1,34)} = 2.71$, $p=0.11$, $\eta^2_p = 0.07$), confirming previous evidence that there is no significant difference between R squared values measured for sigmoidal and linear models.

4.3.2 ANOVAs on tactile RTs

We performed ANOVAs on mean RTs to tactile targets measured at baseline in order to 1) verify the specificity of the effects of dynamic, compared to static stimuli on tactile RTs; 2) check the effect of looming stimuli on tactile RTs at different perceived distances of the dynamic sounds. To investigate these aspects, two separate ANOVAs were carried out for each Experiment (Experiment 1, Experiment 2). Specifically, data were entered in repeated-measures ANOVAs with two within-subject factors, Sound (Looming, Flat) and Distance (D1, D2, D3, D4, D5). RTs exceeding more than 2 standard deviations from the mean RTs were considered outliers and trimmed from the analyses.

Whenever appropriate, significant differences were explored performing Newman-Keuls post-hoc comparison, as previously done in other similar studies (e.g., Canzoneri et al., 2012; 2013; Teneggi et al., 2013). Generalized eta-squared (η^2_G) was calculated as effect size measure.

ANOVA – Experiment 1

The ANOVA showed a significant main effect of Distance ($F_{(4,136)} = 44.98$, $p < 0.001$, $\eta^2_G = 0.57$). Moreover, the two way-interaction Sound by Distance ($F_{(4,136)} = 13.76$, $p < 0.001$, $\eta^2_G = 0.29$) resulted significant, due to specific modulation of RTs as a function of the perceived position of approaching compared to flat sounds (**Fig. 5 Panel A**).

Newman-Keuls post-hoc carried out on the significant main effect of Distance revealed that RTs at D1 resulted significantly slower than RTs at D3, D4 and D5 (D1 333.96 ms SEM 9.60; D3 315.78 ms SEM 9.89; D4 296.75 ms SEM 9.68; D5 297.98 ms SEM 9.81; all $p_s < 0.001$). Moreover, the RTs measured at D2 were slower than RTs measured at D3, D4 and D5 (D2 329.74 SEM 9.97; all $p_s < 0.001$) and RTs at D3 were slower than those at D4 and D5 (all $p_s < 0.001$). Post-hoc comparisons carried out on the significant interaction Sound by Distance revealed that RTs measured in response to looming sounds at D1 and D2, when sounds were perceived far from the body, were significantly longer compared to RTs at D3, D4 and D5 when sounds were perceived close to the body (D1 342.02 ms SEM 9.96; D2 336.02 ms SEM 10.55; D3 316.56 ms SEM 10.33; D4 292.55 ms SEM 9.23; D5 285.58 ms SEM 9.05; all $p_s < 0.001$). Moreover, the RTs measured at D3 were significantly slower than RTs at D4 and D5 (all $p_s < 0.001$). Considering flat sounds, RTs measured at D1, D2, D3 were significantly longer compared to RTs at D4 and D5 (D1 325.90 ms SEM 10.06; D2 323.47 ms SEM 9.88; D3 315 ms SEM 9.98; D4 300.95 ms SEM 10.72; D5 310.39 ms SEM 11.08; all $p_s < 0.004$). Furthermore, RTs were slower for looming compared to flat sounds at D1 ($p < 0.001$) and D2 ($p= 0.014$) whereas faster at D4 ($p= 0.05$) and D5 ($p < 0.001$).

ANOVA – Experiment 2

The ANOVA showed a significant main effect of Distance ($F_{(4,136)} = 34.82$, $p < 0.001$, $\eta^2_G = 0.50$). Moreover, the two-way interaction Sound by Distance ($F_{(4,136)} = 10.28$, $p < 0.001$, $\eta^2_G = 0.23$) resulted significant, due to specific modulation of RTs as a function of the perceived position of approaching compared to flat sounds (**Fig. 5 Panel B**), as in Experiment 1.

Newman-Keuls post-hoc carried out on the significant main effect of Distance revealed that RTs at D1 resulted significantly slower than RTs at D3, D4 and D5 (D1 328.71 ms SEM 10.20; D3 306.43 ms SEM 9.88; D4 296.33 ms SEM 10.59; D5 293.98 ms SEM 9.81; all $p_s < 0.001$). Moreover, the RTs measured at D2 were slower than RTs measured at D3, D4 and D5 (D2 322.03 SEM 11.42; all $p_s < 0.001$) and RTs at D3 were slower than those at D4 and D5 (all $p_s < 0.001$). Post-hoc comparisons carried out on the significant interaction Sound by Distance revealed that RTs measured in response to looming sounds at D1 and D2, when sounds were perceived far from the body, were significantly longer compared to RTs at D3, D4 and D5 when sounds were perceived close to the body (D1 338.87 ms SEM 10.86; D2 325.72 ms SEM 11.92; D3 309.22 ms SEM 10.63; D4 290.29 ms SEM 10.30; D5 285.48 ms SEM 9.30; all $p_s < 0.005$). Moreover, the RTs measured at D3 were significantly slower than RTs at D4 and D5 (all $p_s < 0.001$). Considering flat sounds, RTs measured at D1, D2, D3 were significantly longer compared to RTs at D4 and D5 (D1 318.53 ms SEM 10.52; D2 318.33 ms SEM 11.44; D3 303.65 ms SEM 9.44; D4 302.38 ms SEM 11.23; D5 302.49 ms SEM 10.76; all $p_s < 0.03$). Furthermore, RTs were slower for looming compared to flat sounds at D1 ($p < 0.001$) whereas faster at D4 and D5 (all $p_s < 0.01$).

These control analyses clearly highlight the specificity of the effects of looming compared to flat stimuli on tactile RTs, in line with previous studies (e.g., Canzoneri et al., 2012; 2013; Di Cosmo et al., 2018).

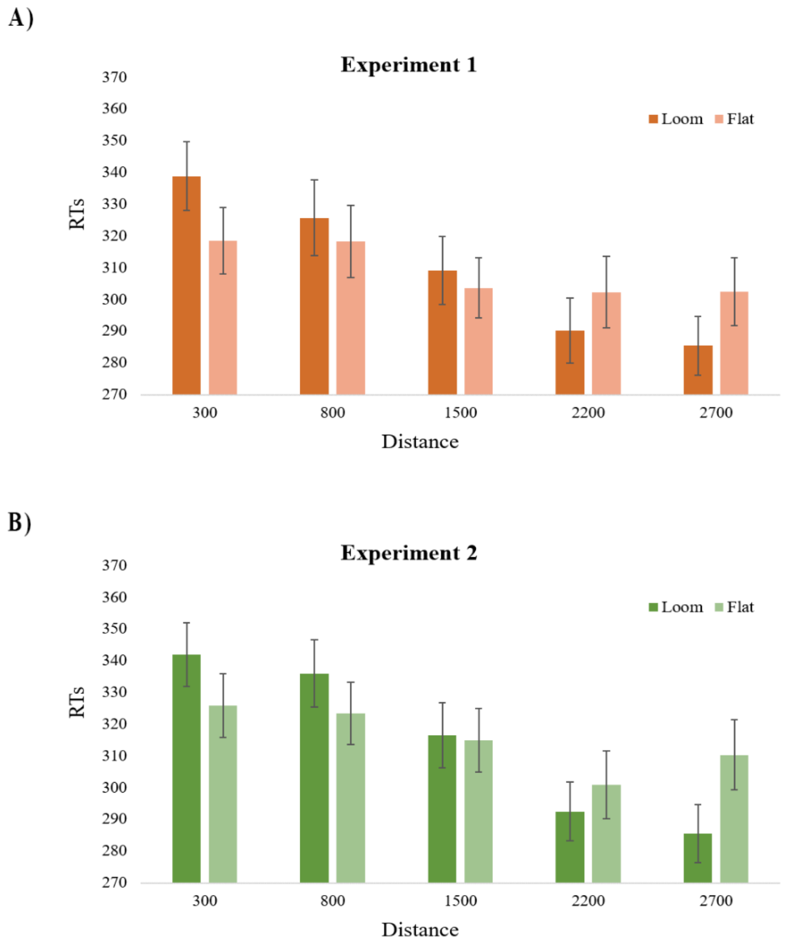

Figure 5. Plots of mean RTs to tactile targets for Experiment 1 (Panel **A**) and Experiment 2 (Panel **B**). Tactile targets were delivered at different temporal distances (D1, 300 ms; D2, 800 ms; D3, 1500 ms; D4, 2200 ms; and D5, 2700 ms) from the onset of either looming (dark pink/dark green) or flat (light pink/light green) sounds. For differences between and within sounds, see text. Error bars represent SEM.

4.3.3 Unimodal tactile RTs

In order to measure the multisensory gain (i.e., speeded RTs) in the audio-tactile conditions, compared to the unisensory tactile, both at Session 1 and Session 3, two separate ANOVAs were carried out for each Experiment. Specifically, RTs were entered in a repeated-measures ANOVA with Condition (Session 1, Session 3), Sound (Looming, Flat), Distance (D0, D1, D2, D3, D4, D5) as within-subjects factors.

Whenever appropriate, significant differences were explored performing Newman-Keuls post-hoc comparison. Generalized eta-squared (η^2_G) was calculated as effect size measure.

Unimodal trials – Experiment 1

The ANOVA showed the significance of the critical interaction Sound by Distance ($F_{(5,170)} = 12.72$, $p < 0.001$, $\eta^2_G = 0.32$). Newman-Keuls post-hoc revealed that RTs measured in the unimodal conditions (D0) were significantly slower than RTs at D3-D5 for looming (D0: 331.98, SEM 10.34; D3: 307.15, SEM 10.65; D4: 291.85, SEM 9.50; D5: 286.46, SEM 9.32; all $p_s < 0.001$) and slower than RTs at D1-D5 for flat sounds (D0: 330.25, SEM 10.83; D1: 322.18 SEM 10.68; D2: 318.67 SEM 10.35; D3: 309.30, SEM 10.04; D4: 297.91, SEM 10.64; D5: 304.91, SEM 10.75; all $p_s < 0.05$), as previously found by other similar studies (e.g., Canzoneri et al., 2012; Di Cosmo et al., 2018).

Unimodal trials – Experiment 2

The ANOVA showed the significance of the critical interaction Sound by Distance ($F_{(5,170)} = 11.10$, $p < 0.001$, $\eta^2_G = 0.25$). Newman-Keuls post-hoc revealed that RTs measured in the unimodal conditions (D0) were significantly slower than RTs at D3-D5 for looming (D0: 335.19, SEM 8.71; D3: 302.75, SEM 9.60; D4: 283.46, SEM 8.87; D5: 277.22, SEM 8.25; all $p_s < 0.001$) and slower than RTs at D2-D5 for flat sounds (D0: 319.94, SEM 9.02; D2: 308.01 SEM 9.73; D3: 296.88, SEM 8.35; D4: 294.43, SEM 9.74; D5: 296.64, SEM 10.16; all $p_s < 0.05$).

4.3.4 Delta CP

The ANOVA showed a significant main effect of Experiment ($F_{(1,66)} = 6.49$, $p= 0.013$, $\eta^2_G =0.09$) and of SPQ group ($F_{(1,66)} = 4.27$, $p=0.043$, $\eta^2_G =0.06$). Tukey post-hoc carried out on the significant main effect of Experiment revealed that Delta CP was significantly lower in Experiment 1 than in Experiment 2, thus showing a peripersonal space expansion only in the first experiment, i.e., after actively using the tool in the extra-personal space (Experiment 1= -280.4 ms, SEM= 87.4; Experiment 2= 34.2, SEM= 87.4; $t_{(66)}= -2.55$, $p= 0.013$) (see **Fig. 6**). For a more comprehensive representation of PPS expansion, see **Fig. 7**. Moreover, for a representation of individual RTs and fitting, for both experiments, see **Fig. 9 and 10.**

Moreover, post-hoc carried out on the significant main effect of SPQ group showed significant lower Delta values for rL-group with respect to rH-schizotypal one (rL-group= -250.8, SEM= 86.1; rH-group= 4.5, SEM= 88.6; $t_{(66)}= 2.06$, $p=0.042$), resulting in greater PPS expansion in rL-schizotypes, regardless of the type of training performed (see **Fig. 8**). For both **Fig. 7** and **Fig. 8** sigmoid fits were normalized between 0 and 1 to improve figures visualization.

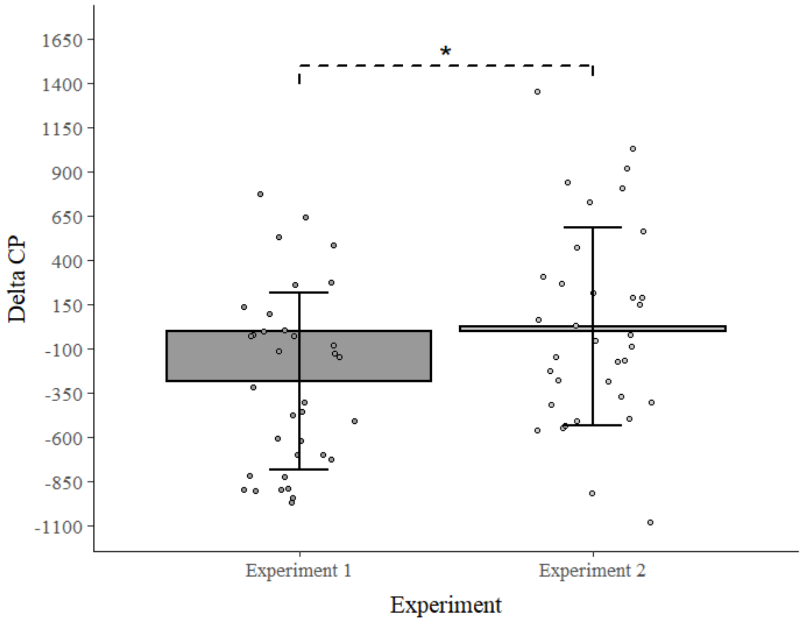

Figure 6. Peripersonal space expansion representation. Delta CP values of Experiment 1 and Experiment 2. Error bars depicted SD; * = p < 0.05.

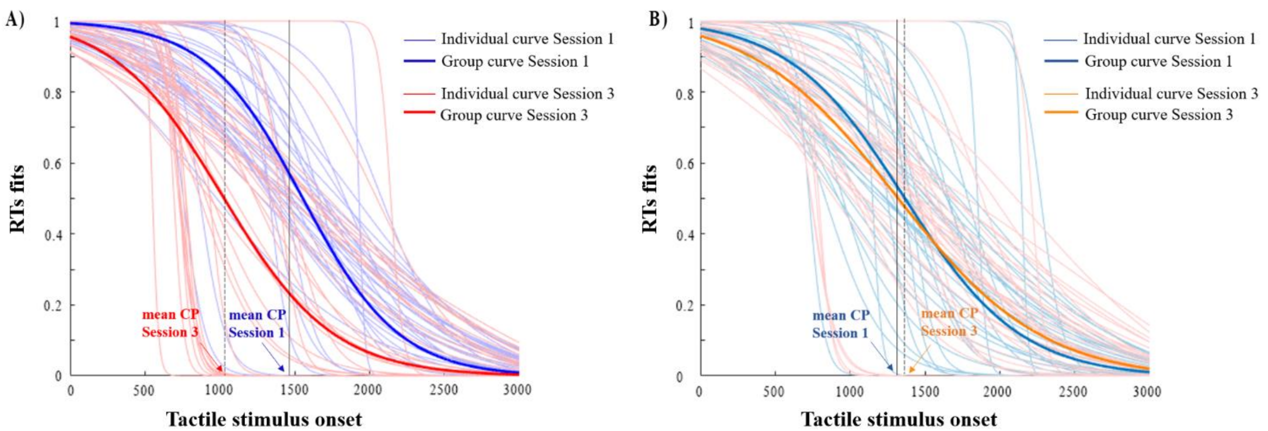

Figure 7. Peripersonal space expansion in Experiment 1 and not in Experiment 2. Panel **A**) shows peripersonal space expansion after Active tool-use (Experiment 1). Panel **B**) shows the absence of peripersonal space expansion after the Observation task (Experiment 2). Both panels show individual normalized sigmoid fits. Continuous lines mark the mean group central point (CP) of Session 1 for both experiments (CP Session 1 Experiment 1= 1492 ms; CP Session 1 Experiment 2= 1383 ms). Dashed lines mark the mean group central point of Session 3 for both experiments (CP Session 3 Experiment 1= 1210 ms; CP Session 3 Experiment 2= 1412 ms).

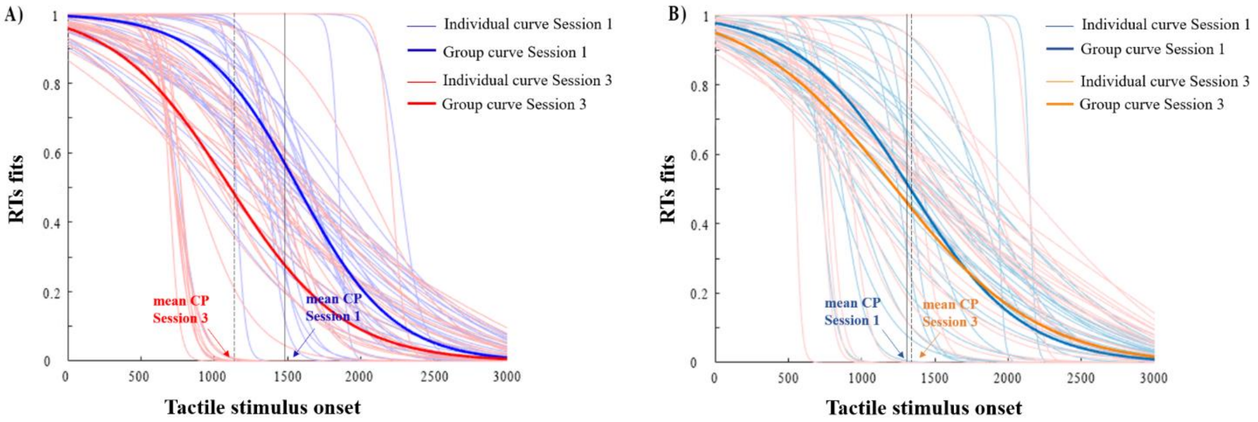

Figure 8. Differences in peripersonal space expansion in relatively-low and relatively-high schizotypes. Panel **A**) shows peripersonal space expansion in rL schizotypes independently from the type of training performed. Panel **B**) shows the absence of peripersonal space expansion in rH schizotypes. Both panels show individual normalized sigmoid fits. Continuous lines mark the mean group central point (CP) of Session 1 for both schizotypal groups (CP Session 1 rL schizotypes = 1496 ms; CP Session 1 rH schizotypes = 1375 ms). Dashed lines mark the mean group central point of Session 3 for both schizotypal groups (CP Session 3 rL schizotypes = 1246 ms; CP Session 3 rH schizotypes = 1379 ms). rL= relatively-low schizotypes; rH = relatively-high schizotypes.

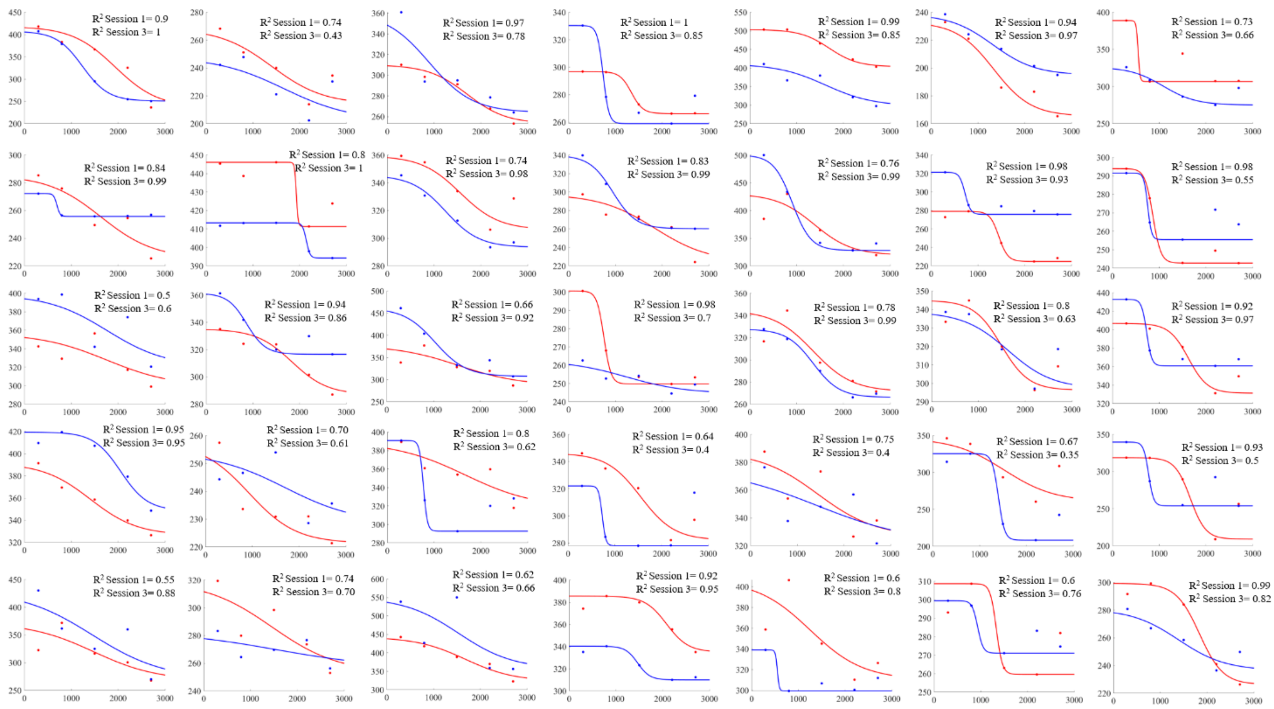

Figure 9. Reaction times and fitting for each participant in Experiment 1. Red lines mark the individual fitting of Session 1; blue lines mark the individual fitting of Session 3. R^2 indicates the individual goodness of fitting for Session 1 and Session 3, respectively.

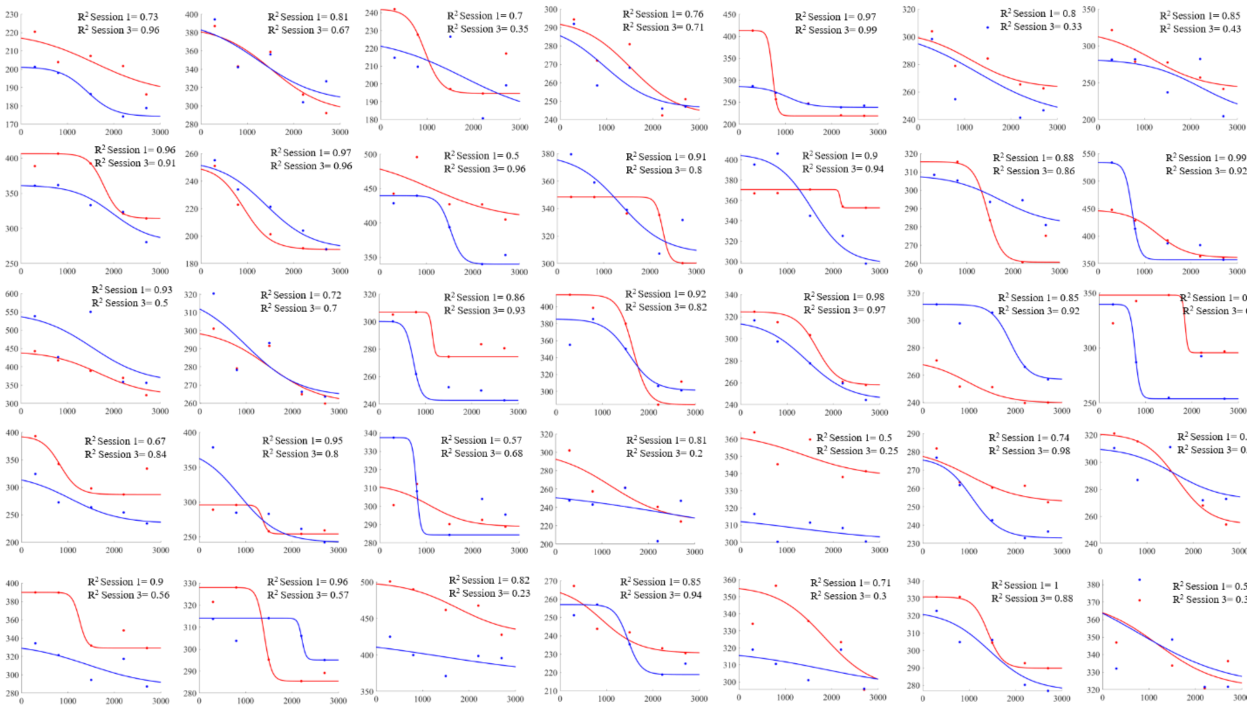

Figure 10. Reaction times and fitting for each participant in Experiment 2. Red lines mark the individual fitting of Session 1; blue lines mark the individual fitting of Session 3. R^2 indicates the individual goodness of fitting for Session 1 and Session 3, respectively.

4.4 Discussion

In the present study, we have investigated the plasticity of PPS, along the schizotypal continuum, after using a tool (Experiment 1), or after observing another person doing the same (Experiment 2). To accomplish this goal, two groups of participants underwent an adapted version of the widely used audio-tactile interaction task (Canzoneri, Magosso, & Serino, 2012), to measure individuals' PPS boundary both before and after the two different training sessions with a tool. In Experiment 1 participants were asked to use a tool to move fifty small objects placed in their extrapersonal space, whereas in Experiment 2 participants only had to observe the confederate performing the same activity with the tool, passively holding a tool of the same length themselves. Delta CP results are in line with previous evidence showing how actively using a tool affects PPS representation. Previous studies in monkeys (Iriki et al., 1996; Ishibashi et al., 2000), healthy humans (Bassolino et al., 2010; Maravita et al., 2002; Serino et al., 2007) and neuropsychological patients (Farnè et al., 2005; Farnè & Làdavas 2000; Maravita et al., 2002) have shown that after tool-use, visual or auditory stimuli presented in the far space interact with somatosensory stimuli on the hand holding the tool (Farnè & Làdavas, 2000; Làdavas & Serino, 2008; Maravita 2006; Maravita & Iriki, 2004). Indeed, under normal conditions, the external cues are associated with tactile stimulation when occurring near the body, i.e. within the PPS. Tool-use, however, allows physical interactions with external stimuli placed at farther spatial locations, resulting in the expansion of PPS boundaries.

The effect of tool-use in the mapping of PPS is thought not to be restricted to the active use of the tool but to extend also to the mere observation of others acting with a tool (Costantini et al., 2011). Our results seem not to be in line with those previously reported, as no significant change was found in the position of PPS boundary after the observation of the confederate performing the action with the tool (main effect of Experiment). However, it should be added that differently from the study by Costantini and colleagues, where participants had to perform a reaching task that involved a goal-directed action, which resulted in the change of PPS boundaries, we used a multisensory integration task in order to capture participants' PPS boundaries. Consequently, in our study the mere observation of the action executed by the confederate may have been insufficient to remap the observers' peripersonal space, thus triggering its expansion. A more recent study by Serino and colleagues (Serino et al., 2015) provides additional support to explain our findings. Specifically, according to these authors, who found that peripersonal space expanded after synchronous audio-tactile training (without tool-action), multisensory areas captured the synchrony between the tactile stimulus applied to the hand and the auditory stimuli in the far space, hence associating these two different stimuli as if they occurred from an equivalent sector of space. Thus, the temporal contiguity of somatosensory stimulation applied to the body and visual and/or auditory external cues seems to be crucial to induce PPS plasticity. Accordingly, D'Angelo and colleagues (D'Angelo et al., 2018) recently found that the sense of agency for a virtual hand projected in the far space extends PPS, only in a synchronous condition (i.e., participants actively moved their hand, receiving proprioceptive information, and perceiving a visual stimulus that responded synchronously to their movements in a different position). These findings therefore highlight the relevance of intentional action to actively create an association between different stimuli occurring in space. Thus, it is possible that in an observation task, as in the asynchronous condition of the previously mentioned studies, the mere occurrence of proprioceptive and visual and/or auditory stimuli per se might be not sufficient to induce PPS expansion.

Importantly, a recent study by Galigani and colleagues (2020) has shown how an observation tool-use training does not induce any modulation either on body representation or on PPS remapping, confirming our findings. Furthermore, Bruno and colleagues (Bruno et al., 2019) have recently shown an increased arm length estimation after performing active tool-use training, without any modulation in the passive condition, in which participants were instructed to maintain a relaxed posture while a robot passively moved their arm. This suggests that only when there is congruency between action goals and bodily movements, plasticity of body metric representation occurs. Thus, although further research is needed, all these results seem to indicate that not only body- but also space-representation, in the case of passive tool-use observation, might be sensitive to intentional action and/or the goal of the action. These two elements could be crucial in order to associate two different sensory stimuli and, as a consequence, trigger PPS plasticity.

Furthermore, the present study extends previous knowledge about individual differences in the plasticity of peripersonal space. Indeed, our results demonstrated a significant main effect of SPQ group, showing lower Delta CP values in the relatively low schizotypal group than in the relatively high one, resulting in greater PPS expansion in the first group, regardless of the type of training performed. Our results are congruent with previous research showing that the extent of PPS varies across individuals, not only depending on the dimension of the body (Longo & Lourenco, 2007), but interestingly also depending on individual personality traits (Ardizzi & Ferri, 2018; Di Cosmo et al., 2018; Lourenco et al., 2011; Noel et al., 2018; Sambo & Iannetti, 2013). Indeed, our findings corroborate recent reports showing a relationship between PPS plasticity and individual personality traits (Hunley et al., 2017), as demonstrated by the fact that individuals high in claustrophobic fear are characterized by decreased PPS plasticity (i.e., less PPS expansion). Thus, PPS expansion may not be experienced equally across individuals. Moreover, the different functional plasticity of PPS along the schizotypal spectrum here demonstrated, raises some interesting psychopathological questions, especially considering the alterations in the motor field associated with both full-blown schizophrenia and high schizotypal traits. Indeed, high schizotypal individuals have been associated with impairments in motor coordination and motor sequencing (Kaczorowski et al., 2009), psychomotor dyscontrol (Lenzenweger & Maher, 2002; Roché et al., 2015), thought to reflect deficit in visuo-motor integration mechanism, deficits in pre-pulse inhibition and in oculomotor tasks (Ettinger et al., 2014) and hand precision movements (Mittal & Walker, 2007; Mittal et al., 2007; Walker et al., 1994; see also Hirjak et al., 2018 for a recent review). Moreover, high schizotypes are also more susceptible to experimental distortions of corporeal awareness (Burrack & Brugger, 2005), including also perceptions of alterations in the size and shape of one’s own body (Chapman et al., 1978), suggesting altered awareness of physical body boundaries. Additionally, several studies reported abnormal sense of agency and blurred self-other boundaries in schizophrenia (Ferri et al., 2014; Ferroni et al., 2019; Hur et al., 2014; Jeannerod, 2009; Sandsten et al., 2020; Synofzik et al., 2009), extended also to the sub-clinical domain (Asai et al., 2008; Asai & Tanno, 2007b, 2007a, 2008; Thakkar et al., 2011). Coherently, a more recent study showed implicit loss of self-body knowledge in schizophrenia for the first time identifying a specific alteration of the sensory-motor processes of self body-parts (Ardizzi et al., 2020). Drawing from all these findings, we can speculate that individuals with relatively high schizotypal traits, despite not being part of the highest end of SPQ distribution, may be characterized by general lack of plasticity of their PPS, consequently highlighting a potential functional alteration of the boundaries between their own body and the environment. This is also consistent with the definition of personality disorder - which includes the schizotypal personality – as a disorder characterized by rigid and inflexible behaviours (*DSM-IV-TR*, 2000) (e.g., impairments in cognitive flexibility, Bowman & Turnbull, 2009; Ettinger et al., 2014; Völter et al., 2012), thus enhancing the poor adaptability of schizotypy, potentially emerging also at this motor level.

In conclusion, the present study demonstrates the absence of a significant effect of the observation task in modulating PPS boundaries, independently from individual schizotypal traits; furthermore, it provides new evidence of individual differences in the plasticity of peripersonal space. Thus, these findings, showing a similar extension size of PPS but a different functional plasticity of PPS boundaries in a low-to-medium spectrum of schizotypy, representative of the schizotypy distribution in healthy population, seem to suggest a potential dissociation between the two mechanisms underlying the alterations of the extension size and plasticity of PPS. Consequently, it emerges that the altered motor adaptability here demonstrated in healthy individuals with relatively high schizotypal traits, might precede the impaired extension of PPS previously found in high schizotypes and schizophrenic patients (Di Cosmo et al., 2018), even though all these assumptions have to be confirmed by future studies in these latter cohorts of individuals. In the light of these new findings, further studies should also deepen our understanding of the mechanisms underlying the observation task, taking into account the potentially relevant role of the intentional action and the temporal and contingent matching of body stimulation with multisensory stimuli from others sector of space.

Some limitations of the present study should be highlighted. First, the application of a between-subjects design probably prevented us from finding a significant interaction between Experiment and SPQ group factors. Further studies will adopt a within-subjects design, in which the same group will perform both Active and Observation motor trainings, to better elucidate the potential influence of individual schizotypal traits on peripersonal space plasticity. Second, in accordance with the main aim of the present study, we randomly recruited participants, consequently with different severity levels on the schizotypal dimension. An a priori sampling of people with high and low schizotypal traits could be implemented in further studies to better investigate the potential functional alteration of peripersonal space in the sub-clinical domain. Furthermore, it should be mentioned that, as recently demonstrated (see Hobeika et al., 2018; Hobeika et al., 2020; Holmes et al., 2020; Kandula et al., 2017), the paradigm here adopted has some intrinsic limits that must be taken into account for future studies focused on peripersonal space (e.g., foreperiod effects due to looming stimuli). Lastly, I am completely aware that, although the decision to choose a female confederate was due to specific reasons (see Methods section), the absence of gender-balanced confederates could represent a potential limit to the present study. Thus, further studies are needed to clarify the role of gender as a potential variable in influencing the plasticity of participants' peripersonal space.

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Chapter 5

5. Looking for your boundaries: insights into peripersonal space plasticity in schizophrenia

5.1 Introduction

The integration of multisensory bodily inputs has been recently proposed as a key mechanism underlying the experience of oneself within a body, which is perceived as one's own (sense of body ownership), which inhabits a specific location in space (self-location), and from which the external world is perceived (first person-perspective), i.e., the main components of bodily self-consciousness (Blanke, 2012; Blanke and Metzinger, 2009; Blanke, Slater and Serino, 2015). Multisensory integration of bodily inputs commonly occurs within a limited sector of space immediately surrounding the body, i.e., the peripersonal space (PPS, Graziano and Cooke, 2006; Làdavas, 2002; Rizzolatti et al., 1997). It has been suggested that PPS indexes the *spatial self*, i.e., the experience of being a bodily self in space (Blanke, Slater and Serino, 2015; Noel et al., 2015, 2017; Salomon et al., 2017) and represents the space where the individual interacts with external stimuli. Neurophysiological data have described bimodal and trimodal neurons in the monkey's brain located in the ventral premotor cortex and in the posterior parietal cortex with visual and/or auditory receptive fields (RFs) anchored to tactile RFs centred on specific body parts (Rizzolatti et al., 1997). The existence of multimodal frontoparietal brain regions in the human brain coding for PPS has been subsequently confirmed by several neuroimaging studies (Brozzoli et al. 2011; Brozzoli, Gentile, and & Ehrsson 2012; Ferri et al. 2015; Makin, Holmes, and Zohary 2007; Sereno and Huang 2006). Thus, it follows that PPS is a multisensory sector of space where tactile and proprioceptive information of specific parts of the body and visual/auditory inputs coming from the environment are efficiently integrated (Gross and Graziano, 1995; Rizzolatti et al., 1997; Serino, 2019). PPS is not fixed, rather it dynamically shapes through experience. For example, it has been widely demonstrated that tool use can shift the boundaries between peri- and extra-personal space. In a seminal study Iriki and colleagues (1996) showed that the hand-centred visual RFs of monkeys' neurons in the intraparietal sulcus extended after a motor training with a rake used to retrieve food placed outside PPS. Then, the plastic property of PPS has been also demonstrated in humans by several behavioural studies conducted both in neuropsychological patients (Berti and Frassinetti, 2000; Farnè, Iriki, and Làdavas 2005; Farnè and Làdavas, 2000; Maravita et al., 2001) and in healthy participants (Bassolino et al. 2010; Canzoneri et al., 2013; Serino et al., 2007) demonstrating how tool use extends the boundaries of PPS. Thus, it follows that PPS is a multisensory interface mediating interaction between the body and the external environment (Graziano and Cooke, 2006). Despite the relevance of PPS for bodily self experiences, few studies have investigated the extension of PPS along the schizophrenia spectrum in order to better delineate the self boundaries.

Schizophrenia has been described as a psychiatric disorder associated with abnormal bodily experiences. These anomalies include an attenuated sense of self-presence, disturbance in the tacit fluidity of the field of awareness, hyper-reflexivity and more interestingly for the present study, blurred body boundaries (Sass and Parnas, 2003). Specifically, from a clinical standpoint, abnormal spatial self experiences have also been reported in schizophrenia (Stanghellini et al., 2020). Indeed, anomalies of space experiences have been highlighted, including the disruption of the coherence of the environmental space, such as disintegration of the appearance of external objects and itemization of external world experiences. *"Walls moving"; "Short road seemed miles and miles as if it opened up and swallowed me"; "For a while it seemed big and open then too close to me"* (Examples of patients' sentences – from Stanghellini et al., 2020).

Thus, as PPS represents the space of the bodily self (Noel et al., 2015), it has recently grasped the attention of the psychopathological literature focused on self-disorders. Indeed, narrower PPS boundaries have been recently described either in people with high schizotypal traits or in schizophrenia patients, when compared with low schizotypal traits and healthy controls, respectively (Di Cosmo et al., 2018). Other studies have reported different results, showing a larger extent of PPS in schizophrenia (Holt et al., 2015; Park et al., 2009), related also to positive symptoms severity (de la Asuncion et al., 2015; Schoretsanitis et al., 2016). Despite different evidence has been reported regarding the extension of PPS in schizophrenia, all these findings support the idea that the integration of body-centred and external spatial information is altered in both high schizotypy and schizophrenia (for a review see Noel et al., 2017).

Interestingly, a recent study by or group (Ferroni et al., 2020) has investigated the functional property of PPS along the schizotypal continuum, demonstrating a greater PPS expansion in the relatively-low schizotypal group than in the relatively-high one, regardless of the type of training performed (i.e., motor and perceptual trainings; see Chapter 4). This study, which shows a similar extension of PPS but a different plasticity in a low-to-medium spectrum of schizotypy, seems to suggest that the altered motor plasticity demonstrated in the relatively-high schizotypal individuals might precede the impaired extension previously found in high schizotypes and schizophrenic patients (Di Cosmo et al., 2018). Thus, taking into account also the idea of a dynamic continuum ranging from personality variation to psychosis (Debbané and Mohr, 2015; Lenzenweger, 2006; Raine, 2006), it follows that investigating the plasticity of PPS could be crucial to better delineate the altered extension of self-boundary in schizophrenia.

Hence, the aim of the present study was to investigate the plasticity of PPS after a motor training with a tool in schizophrenia. In order to assess the extension of PPS, we used an adapted version of the audio-tactile interaction task developed by Canzoneri et al. (2012), as done in our previous study

on schizotypy described in Chapter 4 of this thesis (Ferroni et al., 2020). Considering previous evidence on schizophrenic patients, characterized by bodily self disturbances such as blurred body-boundaries, we hypothesize a lesser plasticity of PPS boundaries among schizophrenia patients.
It should be added that the results of the present study are preliminary, due to the delayed and still ongoing recording of the data because of the COVID-19 pandemic.

5.2 Methods

14 patients with schizophrenia (SCZ; mean age 37.86 SE 3.62, 9 males) and 20 healthy controls (HC; mean age 26 years SE 0.35, 10 males) were included in the present study. The current number of HC and SCZ does not cover the entire final range of participants. The expected analyses will be carried out comparing the two groups and, on each group, separately in order to check also the potential expansion of PPS within each group. The most conservative power analysis that requires the largest number of participants is obtained for the repeated-measures ANOVA considering within interactions ($1-\beta = 0.95$, $\alpha = 0.05$ and effect size $f = 0.25$) with a total sample size of n. 50 participants (25 participants for each group). Moreover, it should be declared that the HC sample will be matched for age and gender when the SCZ recruitment will be finished.

SCZ were recruited among patients seeking treatment at the Psychiatric Unit of the University Hospital of Parma. All 14 patients were under medication during the period of the study, and medication was based on a low-medium dose of a single atypical antipsychotic drug. Indeed, in order to check for the potential effect of the pharmacological treatment on patients' performance, we converted patients' treatment in chlorpromazine equivalents, following the standard practices for antipsychotics (Woods, 2003). Then, we correlated them to patients' performance (i.e., reaction times measured in response to tactile targets at each experimental condition) and no significant correlation was found (see Results section 5.3.2). HC were recruited through fliers posted in meeting places. Inclusion criteria for SCZ were I) a diagnosis of Schizophrenia according to DSM-IV-TR criteria (First et al., 2002), and II) stable phase of recovery (i.e., with no acute symptoms for at least 6 months post morbid). SCZ patients were evaluated and recruited for the study after a clinical stabilisation to assure that they were able to participate in the study. Inclusion criterion for HC was the absence of current or past psychiatric or neurological illnesses as determined by their clinical history, assessed by means of a general psychopathology questionnaire. Exclusion criteria for all participants were: I) substance abuse or dependence; II) pathological conditions likely affecting cognition or interfering with participation in the study (i.e., presence of neurological and vascular disorders, dysmetabolic syndrome and mental retardation); III) abnormalities of touch or hearing. Participants' handedness was assessed by the Edinburgh handedness inventory (Oldfield, 1971). Written informed consent was obtained from all participants after full explanation of the procedure of the study. The study was approved by the Local Ethical Committee (AVEN) and were carried out in accordance with the Declaration of Helsinki (1964 and subsequent amendments).

Clinical scales

SCZ were evaluated by means of the structured clinical interview for DSM-IV Axis I disorders (SCID-I) to establish Axis I diagnoses (First et al., 2002). Patients were evaluated with the Assessment of Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, and Opfer, 1987) that measures symptoms severity in schizophrenia. Disturbances of subjective experience were investigated through the Examination of Anomalous Self-experience scale (EASE; Parnas et al., 2005). For patients' clinical scale, see **Table 1**.

EASE (Examination of Anomalous Self-Experience)

The EASE is a semi-structured psychometric tool for a qualitative and quantitative assessment of experiential or subjective anomalies of self-awareness. The EASE cannot be used alone to diagnose schizophrenia, but it's a valuable and consistent tool for differential diagnosis between schizophrenia spectrum disorders and non-spectrum psychotic disorders in first-episode patients (Haug et al. 2012; Parnas and Henriksen 2014; Parnas et al., 2005a). Studies demonstrated an association between Anomalous Self-experiences (ASEs), low self-esteem, depressive symptoms and poorer social functioning in schizophrenic patients (Haug et al. 2014, 2016). Moreover, it is long known that the onset of the illness may be predated or accompanied by characteristic ASEs that Berze (Berze 1929) described as the *schizophrene Grundstimmung*, i.e. a "schizophrenic elementary condition of life" which brings "eternal destruction instead of living creation" and often develops sneakily over many months or even years before the psychotic onset. ASEs have thus been proposed as phenotypic vulnerability features for early detection and diagnosis of schizophrenia and schizotypal disorder (Koren et al. 2013; Parnas et al. 2005b; Parnas, Carter, and Nordgaard 2016). A recent prospective, observational study of first-episode psychosis patients showed that high levels of perplexity and self disorders were the best predictors of the subsequent development of schizophrenia

The EASE items are grouped into five domains:

- *Cognition and stream of consciousness* (e.g., thought interference, thought block, attentional disturbances, ambivalence)
- *Self-awareness and presence* (e.g., diminished sense of basic Self, derealization, I-split, loss of common sense, anxiety, hypohedonia)

- *Bodily experiences* (e.g., mirror-related phenomena, somatic depersonalization, motor disturbances)
- *Demarcation/transitivism* (e.g., confusion with the Other, passivity mood)
- *Existential reorientation* (e.g., solipsistic-like experiences, existential or intellectual change)

The authors were inspired by the weighty phenomenological descriptions of the subtle pathological phenomena that underlie ASEs and successfully developed a practical and much needed “bridge” between theoretical discussion and clinical practice.

PANSS (Positive and Negative Syndrome Scale) for Schizophrenia

Since its development, the PANSS remains one of the most widely used psychometric tools for the assessment of schizophrenia symptoms and the patients’ response to treatment (Kay, Fiszbein, and Opfer, 1987). The PANSS is composed of 30 items grouped under a Positive Scale (PS), a Negative Scale (NS), a General Psychopathology Scale (GPS) and a Composite Scale (CS), which are assessed on a “past week” reference period by using data from clinical observation and both patient and caregiver reports. The items in the PS and the NS were empirically chosen among the most “crucial” symptoms which are regarded as primary rather than derivative (e.g., disorientation may be secondary to hallucinations) and they represent most different spheres of functioning (e.g., cognitive, affective, social and communicative). The GPS provides a parallel measure of severity of psychopathology that can also serve as a control measure for interpreting the other scores. The CS score is calculated by subtracting the NS score from the PS score, in order to express the degree of predominance of one syndrome over the other for phenotypical characterization.

n.		14
Male, n.		9
Age, years		37.86; SE 3.62
Edinburgh (Handedness)		0.60; SE 0.13
Scales	**Subscales**	
Illness duration (mean; SE)		15.64 years; SE 3.46
Chlorpromazine Equivalent Dose (mean; SE) *		482.57 mg/die; SE 94.35
PANSS (mean; SE)	Total	82.29; SE 5.51
	Positive Scale	16.21; SE 1.57
	Negative Scale	23.07; SE 1.48
	General Psychopathology Scale	43; SE 3.41
EASE (mean; SE)	Total	17.45; SE 1.63
	EASE 1	6.55; SE 0.80
	EASE 2	7; SE 0.62

EASE 3	1.09; SE 0.40
EASE 4	0.64; SE 0.25
EASE 5	2.18; SE 0.49

Table 1. SCZ= Schizophrenia patients. PANSS= Assessment of Positive and Negative Syndrome Scale; EASE = Examination of Anomalous Self-experience; EASE 1= Cognition and Stream of Consciousness domain; EASE 2 = Self-awareness and presence domain; EASE 3 = Bodily experiences domain; EASE 4 = Demarcation/Transitivism domain; EASE 5 = Existential Reorientation domain. * Chlorpromazine equivalents were calculated following standard practices for antipsychotics (Woods, 2003).

Procedure

The experimental procedure consisted of three sessions. First, participants performed the Peripersonal Space task (i.e., PPS task – Session 1) in order to measure the individual PPS boundary at baseline. After this session, they took part to Session 2 (i.e., training phase, see below). Lastly, participants were submitted again to PPS task (Session 3) in order to measure PPS boundaries after actively using a tool. The total procedure was carried out on the same day.

a) Session 1 and 3: PPS task

The location of participants' PPS boundary was measured using an adapted version of the well-established PPS task procedure (Canzoneri, Magosso, and Serino, 2012; Ferri et al., 2015a; Ferri et al., 2015b; Ferroni et al., 2020; Teneggi et al. 2013). The audio-tactile interaction task used here includes a bimodal stimulation (tactile and auditory stimulations), as it has been shown that stimuli from different sensory modalities interact more effectively when presented within the same portion of space (Stein and Meredith, 1993). Tactile stimuli were delivered at different temporal delays from the onset of the sound, for the sound to be perceived at different distances from the body. Hence, the looming sounds used in this paradigm (see below) allowed for the measuring of participants' PPS boundaries, as the distance where sounds affected tactile reaction times. Thus, we recorded participants' reaction times (RTs) to a tactile stimulus applied to the hand while dynamic looming or flat sounds were presented. Since it has been shown that close but not far sounds boost tactile RTs (Bassolino et al., 2010; Serino et al., 2007; A. Serino, Canzoneri, and Avenanti, 2011), we predicted that RTs to tactile stimuli would decrease as a function of the sound's source perceived approach, in the case of dynamic sounds.

Auditory stimuli were samples of pink noise (or 1/f noise) of 3000 ms duration with flat or increasing (looming) intensity levels. The sounds were sampled at 44.1 kHz. Sound intensity was manipulated using Soundforge 4.5 software (Sonic Foundry) so that "looming sounds" had exponentially rising acoustic intensity from 55 to 70 dB, whereas "flat sounds" had constant 62.5 dB acoustic intensity. Auditory stimuli were presented by two loudspeakers (see below). The looming sounds were emitted by both near and far loudspeakers, arranged so that the far loudspeaker activated at the maximum intensity and its intensity decreased up to silence along the trial, whereas the near loudspeaker activated at the minimum intensity and its intensity increased up to the main value along the trial. In this way, the looming sounds gave the impression of a sound approaching towards the participant's body.

Tactile stimuli were delivered by means of constant-current electrical stimulators (DS7A; Digitimer) via pairs of neurological electrodes placed on the hairy surface of the participant's right index finger. The electrical stimulus was a single, constant voltage, rectangular monophasic pulse. At the beginning of each session, the intensity of the tactile stimulus was set to be clearly above the threshold of each participant (Canzoneri, Magosso and Serino, 2012). The stimulus duration was equal to 100 μs. The presentation of auditory and tactile stimuli, as well as the recording of participants' responses, were controlled by custom software implemented in MATLAB (The MathWorks 2015).

During the experiment, participants were blindfolded and comfortably seated behind a table with their right arm resting palm down. The audio-tactile apparatus, which was mounted on the table, consisted of two loudspeakers, one placed near participants' right hand and the other at a distance of 100 cm from the near loudspeaker (i.e., far from the participant), and a constant-current electrical stimulator controlling a pair of neurological electrodes attached to the participant's right index finger (See **Fig. 1**). During each trial, either a looming or a flat sound was presented. Along with the auditory stimulation, in 60% of the trials, participants were also presented with a tactile stimulus. The tactile stimulus was delivered at varying temporal delays from the onset of the auditory stimulus. Five different temporal delays that resulted in five distances from participants' body were used: 300 ms (D1); 800 ms (D2); 1500 ms (D3); 2200 ms (D4); and 2700 ms (D5). The remaining trials (40% of total) were catch trials with auditory stimulation only (either looming or flat sounds) or unimodal tactile trials (with only vibration). Unimodal tactile stimuli served as baseline trials. In these trials, the tactile stimulation was delivered during silence periods, preceding sounds administration, namely at -700 ms (D0). These baseline trials were used to control for a potential confounding effect due to expectancy. Each trial was followed by an inter-trial interval of 1000 ms. Each participant was presented with a random combination of 18 target stimuli for each temporal delay for the looming and flat sounds, randomly intermingled with the catch trials. Following the procedure adopted by previous studies (Teneggi et al., 2013; Ferroni et al., 2020), trials were equally divided into two blocks for a total of 120 trials, lasting about 8 minutes each. Participants were asked to respond as fast as possible to the tactile target, when present, by pressing a button on the laptop with their left index finger, trying to ignore the auditory stimulus. Each trial was repeated if participants failed to answer to the tactile target.

Participants performed this task both before and after the Session 2.

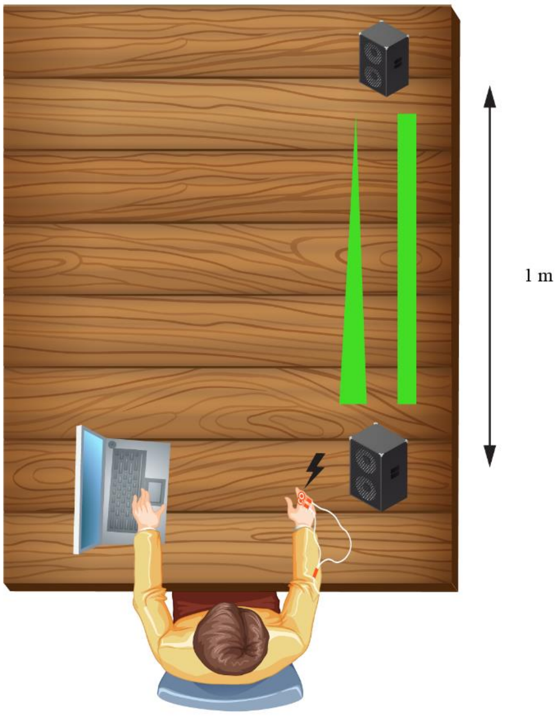

Figure 1. Experimental setting of PPS task. The green shapes represent the two adopted sounds (rectangular shape = flat sound; triangular shape = looming sound).

b) Session 2: Active tool-use

The tool used for the training session was a garbage clamp 75 cm-long composed of an ergonomic handle with a lever (12 cm), a 60 cm-long rigid aluminium shaft and an articulated 'hand', composed of two curved plastic 'fingers' (13 cm each). Participants were instructed to move 50 small coloured objects (green and red), placed on two marked areas of the table, in the far space (85 cm from participants' chest). Participants sat along the short side of the table holding the tool with their right hand and were requested to use the tool in order to grab and move one object at a time across the two areas (see Ferroni et al., 2020). All objects were moved from one marked area to the other and then repositioned on the initial area for a total of 100 movements (see **Fig. 2**). Session 2 lasted around 8 minutes.

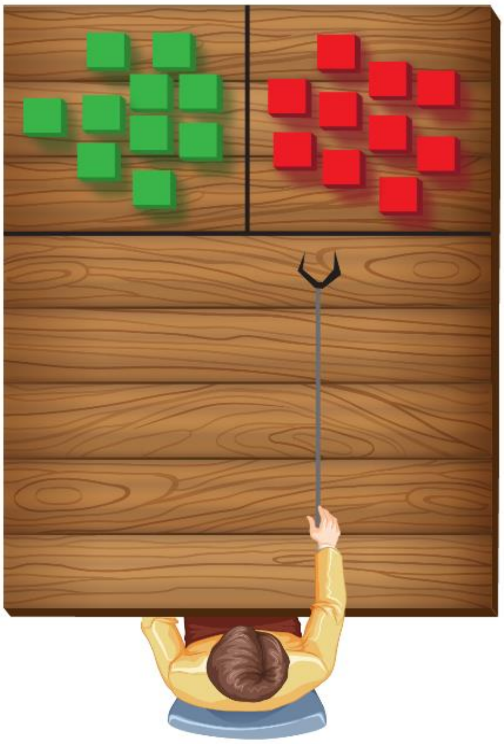

Figure 2. Qualitative representation of the training phase. This figure represents a graphical illustration of the training sessions in which only few coloured objects are reported. Please see the main text for the complete explanation of the procedure. Panel shows the Active tool-use Session 2, in which participants were instructed to move the 50 small coloured objects one at time, with the garbage clamp.

5.2.1 Data analyses

In order to verify the effectiveness of the PPS protocol followed and to check the expected expansion of PPS, we first ran the analyses considering only on the control group. Thus, in order to check the different modulation of looming compared to flat sounds on tactile RTs (considered as a preliminary step in order to proceed to consider only looming stimuli as experimental variables) and to control for a potential confounding effect due to expectancy, a repeated-measures ANOVA was carried out on control group (Results section 5.3.1 – Unimodal tactile RTs). Then, to verify the expansion of PPS, a repeated-measures ANOVA was carried out considering only the looming stimuli (Results section 5.3.1 – Looming tactile RTs). After the assessment of the PPS expansion among healthy controls, we checked for these assumptions also in the SCZ group. Due to the small sample size for SCZ group, only a qualitative representation of the results is reported (Results section 5.3.2). Lastly, we compared the performance of the two groups considering only the looming stimuli in order to check for a potential, and preliminary, difference in terms of PPS expansion (Results section 5.3.3).

Differently from several previous studies (e.g., Canzoneri et al., 2013; Ferroni et al., 2020; Teneggi et al., 2013), the sigmoidal fit analyses will not be carried out due to the low goodness of fit of the clinical sample. For this reason, only RTs analyses are here reported.

5.3 Results

5.3.1 Healthy controls

Unimodal tactile RTs

As previously described, in order to measure 1) the multisensory gain and 2) verify the specificity of the effects of dynamic, compared to static stimuli on tactile RTs, a repeated measures ANOVA was carried out. Specifically, RTs were entered in a repeated-measures ANOVA with Condition (Session 1, Session 3), Sound (Looming, Flat), Distance (D0, D1, D2, D3, D4, D5) as within-subjects factors. RTs exceeding more than 2 standard deviations from the mean RTs were considered outliers and trimmed from the analyses. Whenever appropriate, significant differences were explored performing Newman-Keuls post-hoc comparison. Partial eta-squared (η^2_p) was calculated as effect size measure.

The ANOVA showed a significant main effect of Distance ($F_{(5,95)} = 21.57$, $p < 0.001$, $\eta^2_p = 0.53$). Crucially, the two-way interaction Sound by Distance resulted significant ($F_{(5,95)} = 4.39$, $p < 0.001$, $\eta^2_p = 0.19$). Newman-Keuls post-hoc revealed that RTs measured in the unimodal conditions (D0) were significantly slower than RTs at D3-D5 for looming (D0: 337.46, SE 14.40; D3: 311.89, SE 12.84; D4: 294.81, SE 11.56; D5: 287.64, SE 11.01; all $p_s < 0.001$) and slower than RTs at D2-D5 for flat sounds (D0: 330.30, SE 12.33; D2: 319.07 SE 12; D3: 310.15, SE 12.07; D4:296.80, SE 13.07; D5: 304.11, SE 12.98; all $p_s < 0.038$), as previously found by other similar studies (e.g., Canzoneri et al., 2012; Di Cosmo et al., 2018; Ferroni et al., 2020). Moreover, RTs measured in response to looming sounds at D1 and D2 were significantly slower than RTs at D3-D5 for looming (D1: 345.43, SE 12.23; D2 332.43, SE 12.37; all $p_s < 0.002$). Furthermore, RTs measured at D3 were significantly slower than RTs at D4 and D5 (all $p_s < 0.016$). Considering flat sounds, RTs measured at D1 were significantly longer compared to RTs at D3-D5 (D1: 332.40, SE 12.89; all ps < 0.001). Moreover, RTs measured at D2 and D3 were significantly longer compared to RTs at D4 and D5 (all ps < 0.032). Lastly, RTs were slower for looming compared to flat sounds at D1 (p= 0.05) whereas faster at D5 (p= 0.014). This control analysis highlights the specificity of the effects of looming compared to flat stimuli on tactile RTs, in line with previous studies (e.g., Di Cosmo et al., 2018; Ferroni et al., 2020). For this reason, we proceeded to consider only looming stimuli as experimental variables (see below).

Looming tactile RTs

Reaction times were entered in a repeated-measures ANOVA with Condition (Session 1, Session 3) and Distance (D1, D2, D3, D4, D5) as within-subjects factors. RTs exceeding more than 2 standard deviations from the mean RTs were considered outliers and trimmed from the analyses. Whenever appropriate, significant differences were explored performing Newman-Keuls post-hoc comparison, as previously done in other similar studies (e.g., Canzoneri, Magosso, and Serino 2012; Canzoneri et al., 2013; Teneggi et al., 2013). Partial eta-squared (η^2_p) was calculated as effect size measure.

The ANOVA showed a significant main effect of Distance ($F_{(4,76)} = 36.63$, $p < 0.001$, $\eta^2_p = 0.66$). Moreover, the two way-interaction Session by Distance ($F_{(4,76)} = 3.66$, $p = 0.009$, $\eta^2_p = 0.16$) resulted significant (see **Fig. 3**). Newman-Keuls post-hoc conducted on the significant main effect of Distance revealed that RTs at D1 were slower than RTs at all the other distances (D1: 345.43 ms SE 12.23; D2: 332.43 ms SE 12.37; D3 311.89 ms SE 12.84; D4 294.81 ms SE 11.56; D5 287.64 ms SE 11.01; all $p_s < 0.02$). Moreover, RTs at D2 were slower than RTs at D3, D4, and D5 (all $p_s < 0.001$) and RTs at D3 were faster than RTs at D1 and D2 (all $p_s < 0.001$) but slower than RTs at D4 and D5 (all $p_s < 0.003$). Post-hoc comparisons conducted on the significant interaction revealed that RTs measured in Session 1 at D1 and D2 were significantly slower than RTs at D3, D4, and D5 (D1 346.29 ms SE 13.80; D2 342.27 ms SE 14.59; D3 323.47 ms SE 14.63; D4 298.04 ms SE 12.27; D5 290.81 ms SE13.22; all $p_s < 0.001$). Moreover, the RTs measured at D3 were significantly slower than RTs at D4 and D5 (all $p_s < 0.001$). This modulation of tactile perception due to sound position captures the boundaries of PPS in Session 1, before the tool-use training. This boundary was extended after tool-use. Indeed, in Session 3 (i.e., after tool-use) RTs at D3 were no more significantly different than RTs at D4 (D3: 300.31 ms, SE 11.61; D4: 291.57, SE 12.46; $p = 0.18$). Thus, the critical spatial range where sounds became effective in modulating tactile RTs increased to include positions more distant from the body. Indeed, RTs at D3, and not at any other distance, were significantly faster in Session 3 compared to RTs at the same distance in Session 1 ($p < 0.001$).

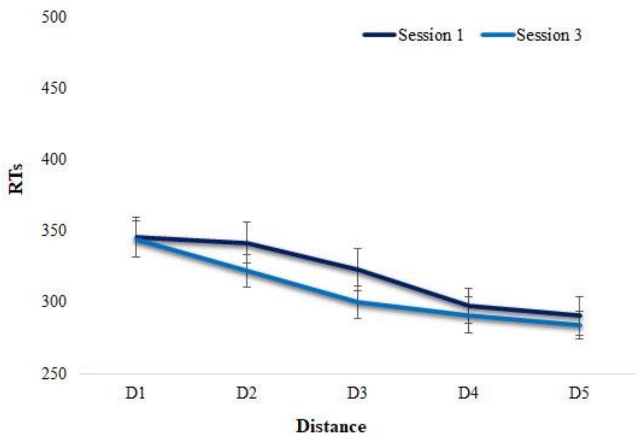

Figure 3. Plot of looming mean RTs (ms) to tactile stimuli in HC measured at Session 1 and Session 3. Error bars represent SE. For differences between RTs measured at five distances (D1-D5), see text.

5.3.2 Schizophrenia patients

The current patients' sample size does not cover the entire final range, as previously stated. For this reason, the control analyses previously conducted in the HC group are not reported for SCZ, due to the current low power of the analysis. Thus, only a qualitative representation of the data is provided (see **Fig. 4 and Table 2**). Mean RTs measured, independently from Sessions, in response to looming and flat sounds, at six distances are shown. Specifically, 1) RTs measured in the unimodal conditions (D0) were qualitatively slower than RTs at D3-D5 for looming sounds, while slower than RTs at D2-D5 for flat sounds. Moreover, 2) RTs were slower for looming compared to flat sounds at D1 while faster at D5, as previously found by a previous study conducted on schizophrenic patients (Di Cosmo et al., 2018). Importantly, individual chlorpromazine equivalents did not correlate with RTs to tactile targets at any experimental condition (all $p_s > 0.1$).

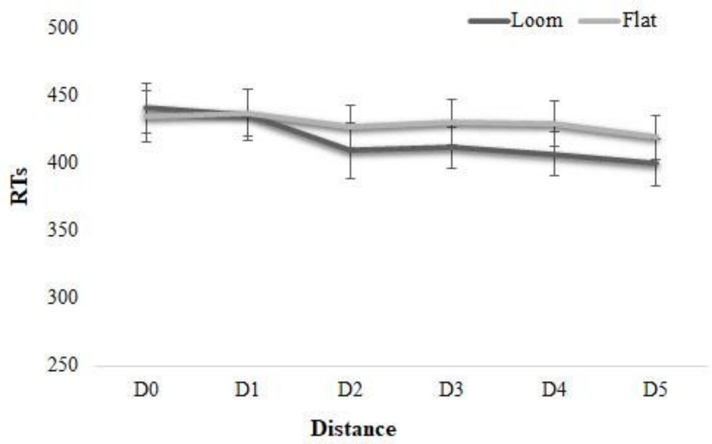

Figure 4. Plots of mean RTs (ms) to tactile targets for looming and flat sounds. Tactile targets were delivered at different temporal distances (D1, 300 ms; D2, 800 ms; D3, 1500 ms; D4, 2200 ms; and D5, 2700 ms) from the onset of either looming (dark grey) or flat (light grey) sounds. Error bars represent SE.

Sound	*D0*	*D1*	*D2*	*D3*	*D4*	*D5*
Loom	436,80	441,16	436,60	409,56	412,02	407,32
Flat	434,61	437,70	427,18	430,85	429,87	419,61
	SE D0	***SE D1***	***SE D2***	***SE D3***	***SE D4***	***SE D5***
Loom	18,29	18,96	20,48	15,07	16,14	17,63
Flat	18,94	17,63	15,89	16,93	16,88	16,34

Table 2. SCZ mean RTs (ms) values for looming and flat sounds. SE = standard error.

Despite the qualitative representation of the results here reported for the SCZ group, the control analyses and check performed in the two groups potentially highlight the general specificity of the effects of looming compared to flat stimuli on tactile RTs, in line with a previous study conducted on schizophrenic patients (Di Cosmo et al., 2018). For this reason, we proceeded to consider only looming stimuli as experimental variables in order to investigate, at a qualitative level, the PPS expansion comparing the two groups. However, it has to be emphasized that all these preliminary results have to be verified with the final sample.

5.3.3 Group differences

Looming tactile RTs

Due to the current small sample size only a qualitative representation of the data comparing the two groups are presented (**Fig. 5**). The qualitative representation of the results highlights the potential different effect of PPS modulation depending on the group. Specifically, in Session 1 HC showed a modulation of tactile RTs from D3 to D4 and D5. In Session 3, in the HC group RTs measured at D3 were no more different than RTs at D4; importantly, RTs at D3 were faster in Session 3 compared to RTs at the same distance in Session 1. Thus, as also highlighted by the analyses conducted considering only healthy controls (Results section 5.3.1), the critical spatial range where sounds became effective in modulating tactile RTs, after the tool-use, increased to include positions more distant from the body. In contrast, in the SCZ group, a different pattern of response compared to HC, can be observed already in the Session 1, in line with Di Cosmo et al.'s study (see Supplementary results of Di Cosmo et al., 2018). Thus, we can hypothesize a modulation of RTs from D4 to D5, i.e., very close to patients' body, as in Di Cosmo et al.'s study. Moreover, differently from HC that showed a different modulation of RTs after the tool-use in the far space, thus underlining a PPS expansion, a lesser pronounced difference between responses given in Session 1 and Session 3 can be observed in the SCZ group (see **Fig. 5**, **Panel B)** and values reported in **Table 3**). Furthermore, RTs at D4 (where we can hypothesize the PPS boundary at Session 1, see above) were not different from RTs at the same distance in Session 3, after the tool-use. Thus, we can speculate that, in the SCZ group, a potential lesser or even absence of PPS expansion might emerge after performing a motor training with a tool in the far space.

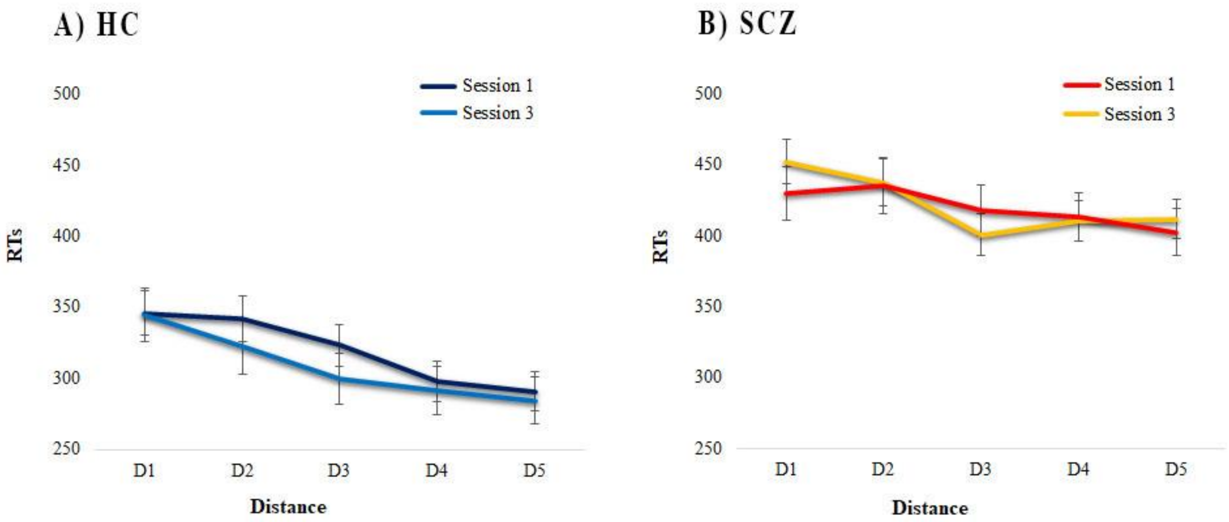

Figure 5. Plot of looming mean RTs (ms) to tactile stimuli in SCZ and HC measured at Session 1 and Session 3. Panel **A)** shows the mean RTs of HC of both Session 1 (dark blue) and Session 3 (light blue); Panel **B)** shows the mean RTs of SCZ of both Session 1 (red) and Session 3 (orange). Tactile targets were delivered at different temporal distances (D1, 300 ms; D2, 800 ms; D3, 1500 ms; D4, 2200 ms; and D5, 2700 ms) from the onset of the sound. Error bars represent SE.

Group	***D1***	***D2***	***D3***	***D4***	***D5***
HC Session 1	346,29	342,27	323,47	298,04	290,81
SCZ Session 1	430,03	435,68	418,09	413,42	402,60
HC Session 3	344,58	322,59	300,31	291,57	284,47
SCZ Session 3	452,30	437,52	401,03	410,63	412,04
	SE D1	***SE D2***	***SE D3***	***SE D4***	***SE D5***
HC Session 1	15,81	16,41	14,98	13,89	13,88
SCZ Session 1	18,90	19,61	17,91	16,60	16,59
HC Session 3	14,12	13,90	11,53	14,28	13,04
SCZ Session 3	16,88	16,62	13,78	17,07	15,59

Table 3. HC and SCZ mean RTs (ms) values in response to looming sounds at Session 1 and Session 3. SE = standard error.

5.4 Discussion

In the present study, we have investigated, for the first time, the plasticity of PPS in schizophrenia. To accomplish this goal, healthy controls and schizophrenic patients underwent an adapted version of the widely used audio-tactile interaction task (Canzoneri, Magosso and Serino, 2012) to measure individuals' PPS boundary both before and after a motor training with a tool in the far space. The results obtained considering only healthy participants are in line with several previous evidence showing how actively using a tool affects PPS representation. Indeed, studies in monkeys (Iriki, Tanaka and Iwamura, 1996; Ishibashi, Hihara and Iriki, 2000) healthy humans (Bassolino et al. 2010; Maravita et al., 2002; Serino et al., 2007) and neuropsychological patients (Farnè, Iriki and Làadavas 2005; Farnè and Làdavas, 2000; Maravita et al., 2002) have shown that after tool-use, visual or auditory stimuli presented in the far space interact with somatosensory stimuli on the hand holding the tool (Farnè and Làdavas, 2000; Làdavas and Serino, 2008; Maravita, 2006; Maravita and Iriki, 2004). Thus, tool-use allows interactions with far stimuli, extending PPS representation.

Comparing the two groups, although at a qualitative level due to the current small sample size (see Methods section), a different pattern of response emerged on controls and schizophrenic patients, both at Session 1 and Session 3, i.e., before and after performing the motor training in the far space. Indeed, among patients, a different pattern of response compared to controls, can be observed in the Session 1, in line with the modulation previously found by Di Cosmo et al. (see Supplementary results of Di Cosmo et al., 2018). Moreover, differently from controls who showed the expected PPS expansion, as shown by the different reaction times modulation after the tool-use, patients did not show a similar pattern of response, rather they seemed to show a similar pattern (less difference) in both Sessions. Indeed, the modulation of reaction times in Session 3 seems to be steep as that of Session 1. Thus, among patients, a potentially reduced or even absent PPS expansion might emerge after performing a motor training with a tool in the far space. These results support and extend previous evidence showing not only how the size of PPS varies across people (Ferri, et al., 2015) depending on several individual characteristics (Ardizzi and Ferri, 2018; Di Cosmo et al., 2018; Lourenco, Longo, and Patham, 2011; Noel et al., 2018; Sambo and Iannetti, 2013) but also how its plasticity seems to depend on individual features (Ferroni et al., 2020).

Moreover, our findings might be congruent with previous research highlighting alterations in the motor domain associated with schizophrenia. Indeed, motor abnormalities have long been recognized as a feature of schizophrenia disorder (Bleuler, 1911/1950; Kraepelin, 1919/1971). Numerous studies demonstrated that both fine and gross motor abnormalities are present in patients with schizophrenia (Blyler et al., 1997; Manschreck, 1986) such as stereotypes, incoordination and repetitive movements. Moreover, also impairments in tasks that require synchronization of movements or switching from one to another have been found (Manschreck and Ames, 1984; Manschreck et al., 1981; 1982). Coherently, a recent study from our group, described in Chapter 3 of the present thesis (Ardizzi et al., 2020), has shown the altered sensory-motor processes of self body parts in schizophrenia, thus further supporting the present findings of the alterations in the motor domain.

Most importantly, several behavioural studies showed how schizophrenia patients are characterized by deficits in motor learning, defined as the process by which individuals learn to use new tools or devices, and in procedural learning (e.g., Bédard et al., 2000; see Bernard and Mittal, 2014 for a review; Pedersen et al., 2008; Schwartz et al., 2003; 1996; see Siegert, Weatherall and Bell, 2008 for a meta-analysis). This has been also confirmed by neuroimaging studies (Exner et al. 2006; Hüttlova et al., 2014; Kasparek et al., 2012; Kumari et al., 2002; Marvel et al., 2007) that provided information about what underlying brain differences might contribute to these deficits. For instance, Kumari and colleagues (2002) showed how patients did not activate key brain regions underlying motor learning processes (i.e., cerebellum and basal ganglia), compared to controls. Taken together, all this evidence highlights motor anomalies and impaired motor learning processes, hence, supporting our findings showing potential alteration of PPS plasticity in schizophrenia.

Furthermore, our results might be supported also by the clinical point of view. EASE is a symptom checklist for semi-structured, phenomenological exploration of experiential or subjective anomalies that may be considered as disorders of basic or 'minimal' self-awareness (Parnas et al., 2005). In particular, the third *(Bodily Experiences)* and the fourth domains *(Demarcation/Transitivism)* of EASE grab our attention, which include anomalies in body experiences and 'spatial' phenomena *[…indicating a loss or a permeability of self-world boundaries, such as feelings of confusion of boundaries between self and others…]*. Thus, taking into account these clinical aspects, it will be relevant to investigate a relation between the potential alteration of PPS plasticity and phenomenological aspects as measured by the EASE.

In conclusion, the present preliminary study seems to confirm previous evidence reported in schizophrenia (Di Cosmo et al., 2018) showing a potential altered size of PPS among patients. Moreover, it reveals a potentially reduced or absent PPS plasticity in schizophrenia. Despite all these results have to be confirmed with the final sample, the evidence here reported in schizophrenia may highlight not only impaired PPS extension but also altered motor plasticity, already found in our previous study among relatively-high schizotypes (Ferroni et al., 2020). Thus, if this picture was confirmed, it would extend the current knowledge of spatial self in schizophrenia, underlining a general alteration of the interface between the self and the environment, revealing how the information about the location of the body parts on which the PPS should be centred (Serino et al., 2015) is altered, both in its size and functional aspects. Lastly, if the absence of PPS plasticity was confirmed also in schizophrenia, it would follow that the altered motor adaptability precedes the impaired extension of PPS boundary previously found in schizotypy and in schizophrenia (Di Cosmo et al., 2018), thus highlighting a dissociation between the two mechanisms underlying these two alterations.

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Chapter 6

6. General Discussion and Conclusions

The present thesis focuses on the anomalies of self-experiences that have been traditionally associated with schizophrenia spectrum disorders. We started from the idea that the most basic level of selfhood, the minimal self, is grounded in our embodied experience of being a self in a body (Blanke and Metzinger, 2009; Damasio 2000; Neisser 1988, 1993). A disturbance of this basic sense of self was paramount to the psychopathological notion of schizophrenia from very early on (Minkowski, 1927; Schneider, 1950; Schultze-Lutter, 2009).

A core component of the basic self is indeed the *bodily self*, a coherent representation of one's own body and a stable sense of owning it. Patients with schizophrenia commonly report a wide range of anomalous bodily self-experiences (Brent et al., 2014; Chapman, Chapman and Raulin, 1978; Lysaker and Lysaker, 2010; Nelson, Thompson and Yung, 2012), such as perception of alterations in the size, shape or location of their own body parts (Chapman et al., 1978), as well as a disturbed sense of body ownership and self-other boundary (Di Cosmo et al., 2018; Ferri et al., 2014; Peled et al., 2000; 2003; Thakkar et al., 2011; van der Weiden, Prikken and van Haren, 2015). The altered bodily self associated with schizophrenia psychopathology is known to be strictly related to self-recognition and self-other discrimination impairments (Gallese and Ferri, 2014). Consistently, anomalies in face processing (e.g., Ameller et al., 2015; Bortolon, Capdevielle and Raffard, 2015; Chan et al. 2010; Yun et al., 2014) have been found in schizophrenia, possibly underlining a generalized mechanism of identity disruption.

Thus, starting from this point, the aim of the first study of my thesis was to investigate the Enfacement Illusion (EI) (Sforza et al. 2010) proneness among schizophrenic patients. In order to also test the malleability of the Other-Other boundaries after a shared multisensory experience, I decided to include also new non-self related condition in the face recognition task, where, no EI effect was expected, considering the self-specificity of the bodily illusions. Results showed how the EI induced the expected malleability of Self-Other boundary among both controls and patients. Surprisingly, we demonstrated also that the Other-Other boundary was influenced by EI, but in an opposite way in the two groups. Indeed, after the visuo-tactile stimulation, controls decreased the number of frames attributed to the Other when it was paired with the Stranger, whereas patients increased the number of frames attributed to the Other in the same condition. Our results do not confirm patients' higher tendency to be affected by bodily illusions (Ferri et al., 2014; Peled et al., 2000; 2003; Thakkar et al., 2011), probably due to the lesser malleable ownership of the face than the body-parts one. This might be attributed to the particular distinctiveness of the face that has probably anchored patients more to their self-identity than other bodily illusions paradigms, as in the rubber hand or in the full body illusions. Moreover, our negative results could potentially extend previous mixed findings that has showed how the sense of ownership over body-parts or over the full body seems to be unaffected by the illness (Shaqiri et al., 2018).

Interestingly, the two groups differed in the malleability of the Other-Other boundary, as shown by the reduction and increase of the number of frames attributed to the Other in controls and patients, respectively. Despite several studies have focused on the malleability of Self-Other boundary, little is still known about the Other-Other boundary. Thus, we can only speculate that among controls the decrease of the number of frames attributed to the Other might represent a functional adjustment relevant in the social domain. Indeed, as stated by Merleau-Ponty (1964, p.118), *"in perceiving the other, my body and his are coupled, resulting in a sort of action which pairs them…I make it mine; I recover it or comprehend it. Reciprocally I know that the gestures I make myself can be the objects of another's intention. It is this transfer of my intentions to the other's body and of his intentions to my own, my alienation of the other and his alienation of me, that makes possible the perception of others"*. Differently, patients extended in the same way both the Self and the Other, as they showed an equal increment in the number of frames attributed to the Self and to the Other after EI. This result might be supported from a clinical point of view, taking into account how schizophrenia patients often report a disordered sense of uniqueness assigned not only to the Self but also to other people (Cutting, 1991; Margariti and Kontaxakis, 2006). Coherently, delusional misidentification syndromes, like Capgras and Frégoli ones that clearly represent this blurred sense of uniqueness, primarily occur in schizophrenia.

In conclusion, the present study points out a new aspect of the bodily illusions' protocols and schizophrenia disorder, demonstrating how EI is not only confined to self-sphere but it also affects the way we discriminate others, representing a crucial aspect in the social domain.

Besides the diverse findings reported up until now, all the evidence reported in schizophrenia highlights a fragile bodily self, although the nature of this disruption has not been precisely identified yet. Hence, the second aim of my thesis was to test the hypothesis of a specific alteration of the motor roots of the bodily self in schizophrenia. Twenty outpatients with a diagnosis within schizophrenia spectrum (SCZ) and twenty-one matched healthy controls (HC) were required to judge the laterality (left or right) of observed digital images of hands by pressing a left or a right response key, with their respective index fingers. Half of the trials showed participant's own left or right hand displayed at different orientation angles (Self trials). In the other half of trials, the right or left hand of other three people were displayed at different orientation angles (Other trials). We started from the idea that the bodily self has been operationalized in the so-called self-advantage effect (SA_{eff}) that is a faster performance with self than others' right hands, displayed at different orientation angles, in a laterality judgment task requiring sensory-motor mental rotation (Ferri et al., 2011; Ferri et al., 2012). We confirmed the presence of the SA_{eff} among controls, as they showed faster reaction times to self right hands than to other's right hands (Ferri et al., 2011). Moreover, although controls mentally rotated both self and other body-parts in order to answer to the laterality judgment (as shown by the lack of a significant difference in slope values measured in response to self and other right stimuli), only when the motor body representation matched the ownership of the stimuli, the SA_{eff} emerged. Differently, SCZ did not show faster reaction times to self than other's right stimuli indicating, as expected, the absence of the SA_{eff}. Furthermore, a significant lower slope value was found only for self right hand stimuli compared to controls, demonstrating the absence of mental rotation of self stimuli. These findings show, for the first time, the implicit loss of self-body knowledge in schizophrenia, identifying a specific alteration in the sensory-motor processes of self body-parts. This evidence opens new intriguing insights about the basic nature of a breakable minimal self experience in schizophrenia, suggesting the before and below the alterations of body ownership and sense of agency there could be a common altered motor nature of this basic sense of self.

Our experience of being a bodily self depends on the integration of multisensory signals occurring within the peripersonal space (PPS) which represents a multisensory-motor sector of space surrounding our body (Rizzolatti et al., 1981). PPS is the space where the individual interacts with external stimuli. However, through evolution primates have learnt how use tools to reach targets outside the physical limits of their body. Several studies conducted both in monkeys (Iriki, Tanaka and Iwamura, 1996; Ishibashi, Hihara and Iriki, 2000) and in humans (Bassolino et al., 2010; Berti and Frassinetti, 2000; Canzoneri et al., 2013; Farnè, Iriki, and Làadavas, 2005; Farnè and Làdavas, 2000; Maravita et al., 2001; Serino et al., 2007) have showed using a tool to reach objects out of reach extends the boundaries of PPS representation. Interestingly, it has been shown how this plastic property of PPS is influenced not only by the active use of a tool to reach objects in far space, but also by the mere observation of the tool use (Costantini et al., 2011). As PPS represents the space of the bodily self (Noel et al., 2015), it has recently grasped the attention of the psychopathological literature focused on self-disorders. Indeed, narrower PPS boundaries have been recently described either in people with high schizotypal traits or in schizophrenia patients, when compared with low schizotypal traits and healthy controls, respectively (Di Cosmo et al. 2018). Other studies have reported different results, showing a larger extent of PPS in schizophrenia (Holt et al. 2015; Park et al. 2009). Despite different evidence has been reported regarding the extension of PPS in schizophrenia, all these findings support the idea that the integration of body-centred and external spatial information is altered in both high schizotypy and schizophrenia (for a review see Noel et al. 2017). Besides the relevance of the plasticity of PPS, due to its adaptive function, no study so far has investigated the integrity of the functional properties of PPS in schizotypy, such as its plasticity after motor training, crucial in order to better delineate the altered self-boundaries. This represented the aim of the third study of my thesis. Specifically, we tested the PPS plasticity after tool use and after the mere observation of another person using the same tool. In order to avoid including high and low schizotypal individuals characterized by different PPS size (Di Cosmo et al. 2018), thus to better analyse PPS functional plasticity, we randomly recruited participants along the severity continuum of schizotypal traits which is part of the low-to-medium spectrum of schizotypy (e.g., Raine 1991), in which it is reasonable to hypothesize a similar extension size of PPS. In order to assess the extension of PPS, we used an adapted version of the audio-tactile interaction task developed by Canzoneri et al. (2012). We demonstrated the expansion of PPS boundaries after tool-use, whereas no PPS expansion was revealed after the observation task. Moreover, we found a greater PPS expansion in the relatively-low schizotypal group than in the relatively-high one, regardless of the type of motor training they performed. Firstly, our results on the similar size of PPS but with different functional properties in a low-to-medium spectrum of schizotypy, seem to suggest a potential dissociation between the two mechanisms underlying the alteration of both the extension size and plasticity of PPS. Secondly, our findings on the lesser PPS expansion in the relatively-high schizotypes regardless of the type of training underline a potential general functional alteration of PPS with the increase of schizotypal level.

Taking into account the idea of a dynamic continuum ranging from schizotypy to full-blown psychosis (Debbané and Mohr, 2015; Lenzenweger, 2006; Raine, 2006), it is reasonable to hypothesize a lesser malleability of PPS boundaries in schizophrenia. However, no studies until now have investigated this functional aspect of PPS. Hence, this represents the focus of the last study of my thesis that illustrates the preliminary results on schizophrenic patients. Fourteen schizophrenic patients and twenty healthy control participants underwent an adapted version of the audio-tactile interaction task developed by Canzoneri et al. (2012) in order to assess the extension of PPS before and after a motor training with a tool in the far space. We found, although at a qualitative level due to the current small sample size, a different pattern of response on controls and patients, both before and after performing the motor training in the far space. Indeed, among patients, a different pattern of response compared to controls, can be observed in the extension of PPS measured at baseline (i.e., before the tool-use) in line with the modulation previously found by Di Cosmo et al. (2018). Moreover, differently from controls who showed the expected PPS expansion, as shown by the different reaction times modulation after the tool-use, patients seemed to show a lesser difference between the two sessions than controls. Thus, among patients, a potentially reduced or even absent PPS expansion might emerge after performing the tool-use. Our findings may be congruent with previous research highlighting alterations in the motor domain associated with schizophrenia, especially considering the motor learning processes (e.g., Bernard and Mittal, 2014; Pedersen et al., 2008; Schwartz et al., 2003; 1996), thus, supporting our results showing a potential alteration of PPS plasticity in schizophrenia.

In conclusion, the last study highlights a potentially reduced or absent PPS plasticity in schizophrenia, although all these results have to be confirmed with the final sample. The evidence here reported in schizophrenia may highlight not only an impaired PPS extension but also a potentially altered motor plasticity, already found in the previous study among relatively-high schizotypes (Ferroni et al., 2020, here presented in Chapter 4), hence shedding new light on the understanding of the spatial self in psychopathology. Interestingly, a recent study (Costantini et al., 2020) showed that the abnormalities of the body structural representation in schizophrenia are linked to core symptoms commonly taken as phenomenological markers of the disorder. As proposed by the authors, these abnormalities might contribute to more complex bodily self-disturbances that could lead to more *"permeable and blurred boundaries of the body"* (Postmes et al., 2014).

Taken together the data of the present thesis enrich the current state of the art of the minimal self disorder in schizophrenia, empirically supporting the idea of a fragile self. I suggest that this breakable sense of self shatters into a variety of small pieces that enclose multiple interrelated bodily aspects, such as blurred self-other boundaries, implicit loss of self body knowledge and alterations of the peripersonal space both in its size and functional aspects. These abnormal bodily experiences might be related to a common backbone, represented by a distorted motor nature of the minimal self.

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