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Mirroring the Self: Testing Neurophysiological Correlates of Disturbed Self-Experience in Schizophrenia Spectrum

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Key Words

Electrophysiology · Emotions · Facial mimicry · Multisensory integration · Schizophrenia · Self-disorders

Abstract

Background: Self-disorders (SDs) have been described as a core schizophrenia spectrum vulnerability phenotype, both in classic and contemporary psychopathological literature. However, such a core phenotype has not yet been investigated adopting a trans-domain approach that combines the phenomenological and the neurophysiological levels of analysis. The aim of this study is to investigate the relation between SDs and subtle, schizophrenia-specific impairments of emotional resonance that are supposed to reflect abnormalities in the mirror neurons mechanism. Specifically, we tested whether electromyographic response to emotional stimuli (i.e. a proxy for subtle changes in facial mimicry and related motor resonance mechanisms) would predict the occurrence of anomalous subjective experiences (i.e. SDs). **Sampling and Methods:** Eighteen schizophrenia spectrum (SzSp) patients underwent a comprehensive psychopathological examination and were contextually tested with a multimodal paradigm, recording facial electromyographic

activity of muscles in response to positive and negative emotional stimuli. Experiential anomalies were explored with the Bonn Scale for the Assessment of Basic Symptoms (BSABS) and then condensed into rational subscales mapping SzSp anomalous self-experiences. **Results:** SzSp patients showed an imbalance in emotional motor resonance with a selective bias toward negative stimuli, as well as a multisensory integration impairment. Multiple regression analysis showed that electromyographic facial reactions in response to negative stimuli presented in auditory modality specifically and strongly correlated with SD subscore. **Conclusions:** The study confirms the potential of SDs as target phenotype for neurobiological research and encourages research into disturbed motor/emotional resonance as possible body-level correlate of disturbed subjective experiences in SzSp.

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Introduction

Contemporary phenomenologically inspired empirical research indicates that disturbance of the basic sense of self may be a core phenotypic marker of schizophrenia spectrum (SzSp) disorders [1–7]. Indeed in SzSp disorder

ders, the basic selfhood seems to be subtly perturbed, unstable and oscillating, resulting in often alarming and alienating experiences that frequently date back to childhood and/or early adolescence. The psychopathological notion of self-disorder (SD) specifically refers to such a *disturbed sense of the basic self*, that entails a variety of anomalous subjective experiences mostly affecting the sense of being a self-present, embodied subject immersed in the world [8]. The 'basic' or 'core' self is indeed a *prereflective, tacit* level of selfhood. The basic sense of self signifies that we each live our conscious life as a self-present, single, temporally persistent, bodily, and demarcated subject of experience and action. It refers to the implicit first-person quality of consciousness, i.e. the implicit awareness that all experience articulates itself in first-person perspective as 'my' experience, constituting the foundational level of selfhood on which other levels of selfhood are built. From a phenomenological perspective, disturbances of the basic sense of self entail various forms of depersonalization, loss of common sense, fading grip on perceptual and situational meanings, distortions of the stream of consciousness, as well as disordered sense of identity and embodiment. Although different in their thematic content, all these anomalous subjective experiences are characterized by subtle, nonpsychotic qualitative changes in the structure of subjectivity [9, 10] implying a fundamental shift in the sense of being a self-coincident subject, endowed with a stable first-person perspective and vitally engaged in the world.

Clinically, SDs encompass a broad range of phenomena that can be reliably explored through systematic checklists such as the Bonn Scale for the Assessment of Basic Symptoms (BSABS) as well as other recent instruments developed from the BSABS, like the Schizophrenia Proneness Instrument (SPI-A, SPI-CY) and the ad hoc constructed Examination of Anomalous Self-Experience (EASE) [11–13].

These not yet psychotic anomalies of subjective experiences antedate the onset of flamboyant psychosis [8, 14–18] and occur in various schizophrenia-related conditions (i.e. full-blown schizophrenia, prodromal/at risk mental states, schizotypy) including unaffected schizotaxic subjects and genetically high-risk individuals [3, 5, 7, 14, 19]. In a recent study [20], the specificity of SDs for the SzSp disorders has been demonstrated in a diagnostically heterogeneous sample, where SDs aggregated with similar levels in schizophrenia and schizotypy. Hence, besides their clinical value for the purposes of early differential diagnosis, SDs constitute a valuable trait phenotype for in-

dexing genetic liability to SzSp disorders [21] (see [22] for a review).

Up to now, however, little is known about the electrophysiological bodily correlates of SDs [23, 24]. This is particularly important given the marked gap between patients' complaints (that generally entail disturbing experiences) and the most prominent schizophrenia etiopathogenetic theories and therapeutic practices (which are by large postulated at a brain level of description and analysis). Until now, nobody has ever found a direct association between phenomenological experience (i.e. the experiential level) as measured by systematic checklists and electrophysiological evidence (i.e. the body level) in schizophrenia disorder. Therefore, the current study was designed to focus on the convergence between contemporary emotion neuroscience and phenomenological investigations of SzSp vulnerability [25].

Recent findings strongly support an impairment of emotional resonance in patients with schizophrenia, likely rooting these deficits to abnormalities in the mirror neurons mechanism [26–30]. Particularly, the disruption in patients with schizophrenia of the low-level mechanism of facial mimicry [25, 31, 32], which normally occurs when someone perceives the facial expression of someone else's emotion, compromises patients' emotional empathy and understanding [33–36].

A phenomenological account of the implicit functioning of the body in everyday perception and action turns the traditional notion of the physical body into a living medium of the individual's relation to the world [37, 38]. According to this view, subtle distortions of these embodied mediating processes would be a crucial feature of schizophrenia, which – indeed – has been phenomenologically reconceptualized by Fuchs [39] as a disorder of embodied intersubjectivity [40]. Thus, the aim of this study is to investigate whether a direct connection between congruent motor facial mimicry in response to emotional stimuli and anomalous subjective experiences (i.e. SDs) exists in SzSp, in line with a previous study documenting the specificity of SDs in such a diagnostically heterogeneous sample [20]. Facial mimicry (electrophysiologically measured by means of facial electromyographic activity, EMG) has been proved to be a mirror motor resonance proxy [31, 41, 42]. For the purpose of this study, we employed a novel electrophysiological paradigm that was specifically designed to evoke congruent facial mimicry through multimodal (i.e. audio and/or video) emotional stimuli. This paradigm was previously demonstrated to be able to detect specific deficits in facial mimicry in schizophrenia patients [25].

Table 1. Demographic variables and psychopathological characteristics of the SzSp sample

Characteristic	Mean	SE	Range (scale range)
Age, years	34.17	1.63	25–49
SAPS	23.12	3.83	1–58 (0–170)
SANS	47.41	4.12	15–83 (0–125)
BSABS	41.72	4.01	29–86 (0–103)
Length of illness, years	11.19	1.17	2–24
Age at first recognized psychotic episode	24.06	1.04	19–34
Number of hospitalizations	3.38	0.44	0–7
Dose of typical and atypical antipsychotics	26.31	4.74	
Dose of atypical antipsychotics	19.56	3.77	
Dose of typical antipsychotics	6.75	1.35	

Drugs are expressed as the cumulative value measured in dose-years in the form of (chlorpromazine equivalent in mg) × (time on dose measured in years) [46]. SAPS = Scale for the Assessment of Positive Symptoms; SANS = Scale for the Assessment of Negative Symptoms.

Methods

Sample

The sample included 18 outpatients (13 males, 5 females, mean age \pm SE: 34.17 \pm 1.63 years) and was recruited at the Psychiatry Division of Parma University, Department of Neuroscience. All participants were diagnosed with a SzSp disorder (i.e. schizophrenia or schizotypal personality disorder according to DSM-IV diagnostic criteria) [43] and were clinically stable (i.e. with no current psychotic symptoms) at the time of the experimental assessment. Data from 14 participants included in this group were previously reported in a separate validation study [25] using the same paradigm. This study focused on different questions than the one currently at stake, namely the comparison of behavioral and EMG data detected from schizophrenia patients with respect to healthy participants. The results reported in the current study are therefore entirely original, while considering clinical data acquired from the BSABS interview.

Before inclusion, all patients were screened to rule out any history of neurological and vascular disorders, alcohol or drugs abuse and mental retardation. Clinical features were documented with the Scales for the Assessment of Positive and Negative Symptoms [44, 45], whereas disturbances of subjective experience were explored through the BSABS [2, 11] (see the online suppl. material section for details; for all online suppl. material, see www.karger.com/doi/10.1159/000380884). Since all patients were under psychopharmacologic treatment with antipsychotics, cumulative measure of lifetime drug exposure was calculated following Andreasen et al. [46]. Demographic and clinical features of the sample are provided in table 1.

Written informed consent was obtained from all participants before entering the study, after the treating clinician gave them an

exhaustive explanation of the study. The Ethics Committee of the University of Parma approved the study that was carried out according to the ethical standards of the 2013 Declaration of Helsinki.

Experimental Paradigm: Stimuli and Procedure

The experimental paradigm consisted of the following procedure (see [25] for details and empirical validation): participants were presented with 2-second colored video clips portraying positive (Laugh), negative (Cry) and neutral (Control) emotional stimuli in visual (i.e. Video) and/or auditory (i.e. Audio) modalities. Video or Audio modalities were either in isolation (i.e. Video or Audio alone) or combined (i.e. Audio-Visual). The Audio-Visual combination was either congruent (Audio-Visual Congruent, AVC), i.e. Audio and Video conveying the same emotion (e.g. Cry) or incongruent (Audio-Visual Incongruent, AVI), i.e. Audio and Video conveying contradictory information (for example, in AVI Cry participants saw an actor laughing but heard crying whereas in AVI Laugh participants saw an actor crying but heard laughing). Participants were requested to recognize and quantitatively rate the emotional value of the perceived stimuli, while EMG activity of corrugator supercilii and zygomaticus major muscles (whose activity is evoked by the perception of negative and positive emotions, respectively) was recorded. For further details about stimuli, experimental procedure and EMG recording, see the online supplementary material section and Sestito et al. [25].

Data Analysis

EMG activity data and behavioral rating scores were analyzed following the same procedure defined in the validation study [25]. The BSABS interviews were conducted by a senior psychiatrist (C.M.) with extensive research interview experience and principal translator of BSABS into Italian, together with experienced psychiatrists (E.L., M.T., R.F., G.D.P.) specifically trained in the use of BSABS. A total amount of 103 items were assessed for presence/absence (98 principal items plus 5 items exploring coping strategies). Patients were inquired about the anomalies of experience present since illness onset. The average period elapsed between BSABS and EMG assessments was 82.50 \pm (SE) 20.96 days. In order to explore possible relations between electrophysiological evidence and phenomenological experiences thought to constitute a distinctive phenotype of schizophrenia psychopathology, EASE-analog subscales were constructed from the available BSABS data. BSABS items were indeed grouped into seven rational scales [2, 47] representing essential dimensions of the SzSp experiential pathology: Diminished Affectivity, Disturbed Contact, Perplexity, Cognitive Disorder, Self-Disorder, Cenesthesias and Perceptual Disorder. To ensure good internal consistency, each scale was subjected to an item analysis, intended to maximize α coefficient [48]. For further details about behavioral and EMG data analyses, see the online supplementary material section.

Results

EMG Data

The specific aim of EMG analyses was to detect significant EMG activations with respect to the control condition, in different emotions (Laugh and Cry, that is,

positive and negative emotions domain), modalities (AVC, AVI, Audio and Video) and time epochs (T1: 0–500 ms; T2: 500–1,000 ms; T3: 1,000–1,500 ms; T4: 1,500–2,000 ms), and consider them in the subsequent correlation analysis with BSABS subscores. Indeed, the inclusion in the current paradigm of Control stimuli – i.e. effectively judged as emotionally neutral by both patients and healthy participants (see the online suppl. material section and the previous validation study [25]) – allowed us to consider them in post hoc comparisons in order to detect significant EMG activations in the experimental conditions.

EMG activations in SzSp participants emerged in the corrugator muscle for negative emotions (i.e. Cry) during the following conditions: AVC Cry, only at T3 (i.e. the time epoch spanning from 1,000 to 1,500 ms after stimulus onset); in Audio Cry at T1 and T2 (i.e. from 0 to 1,000 ms after stimulus onset); in Video Cry at T2, T3, T4 (i.e. from 500 to 2,000 ms after stimulus onset); finally, no activations were found in AVI Laugh.

Furthermore, the analysis performed on the zygomatic major muscle EMG responses to positive emotions (i.e. Laugh), on the other hand, yielded no significant results. For additional details regarding EMG data analyses, see the online supplementary material section.

Correlations between EMG Activations and BSABS a priori Scales

After item analyses, five out of the original seven a priori scales were retained for the subsequent correlation analysis, reaching a satisfactory internal consistency (α value ≥ 0.55): Diminished Affectivity, Cognitive Disorder, Self-Disorder, Cenesthesias and Perceptual Disorder (see Appendix for item composition and α coefficients). Prior to formal analysis, we examined correlations between age and sex and the dependent variables (BSABS a priori scales: Diminished Affectivity, Cognitive Disorder, Self-Disorder, Cenesthesias, Perceptual Disorder). Pearson's correlation analysis showed a significant correlation between Perceptual Disorder and age ($r_{18} = 0.481$, $p < 0.05$, two-tailed) whereas no significant correlations emerged between sex and the dependent variables.

A multiple regression analysis was conducted in order to determine the variance explained in the five dependent variables (BSABS a priori scales: Diminished Affectivity, Cognitive Disorder, Self-Disorder, Cenesthesias, Perceptual Disorder) including the EMG activations (AVC Cry T3; Audio Cry T1 and T2; Video Cry T2, T3, T4) as predictors. Moreover, semipartial correlations were calculated for variables supposed to be dependent on each other –

Table 2. Pearson's correlations between EMG activations and Self-Disorder subjective experience domain as measured by a priori scales of Parnas et al. [2]

Self-Disorder	R	R ²	p
AVC Cry (T3)	0.024	0.001	0.924
Audio Cry (T1)	0.648	0.420	0.004**
Audio Cry (T2)	0.579	0.335	0.012*
Video Cry (T2)	-0.151	0.023	0.551
Video Cry (T3)	-0.028	0.001	0.911
Video Cry (T4)	-0.154	0.024	0.542

* $p < 0.05$; ** $p < 0.01$. T1 = Time epoch 0–500 ms; T2 = time epoch 500–1,000 ms; T3 = time epoch 1,000–1,500 ms; T4 = time epoch 1,500–2,000 ms.

that is, EMG activations occurring during consecutive time epochs T1, T2, T3 and T4. This procedure allowed an estimation of the independent contribution of each EMG activation recorded in a given time epoch above and beyond the variance accounted for by the other ones.

Results showed that only the Self-Disorder subscore reached significance ($F_{6,11} = 5.83$, $p < 0.01$, $R = 0.872$, $R^2 = 0.761$), for which the overall regression model accounted for 76.1% of the variance. The significant predictor variables for SD were the EMG corrugator supercillii muscle activations detected in the Audio Cry condition, both in T1 ($t = 3.41$, $\beta = 0.65$, $p < 0.01$) and T2 ($t = 2.84$, $\beta = 0.58$, $p < 0.05$; table 2).

Semipartial correlation coefficients for conditions in which EMG activations occurred during consecutive time epochs (i.e. Audio and Video Cry conditions) were calculated. Only the correlation between SD and the EMG activation of the corrugator muscle occurring during the first time epoch (T1) in the Audio Cry condition was significant ($t = 2.92$, $\beta = 1.89$, $p < 0.05$) whereas a negative correlation emerged between SD and the EMG corrugator activation recorded during the Video Cry condition in T4 ($t = -2.26$, $\beta = -0.88$, $p < 0.05$; table 3).

Discussion

The study confirms that subtle changes in emotional motor resonance can be detected in SzSp patients – specifically, an important change in facial emotional resonance occurs when participants perceive negative emotional stimuli. Such an imbalance in emotional motor resonance (with a proneness to resonate with negative

Table 3. Semipartial correlations between EMG activations and Self-Disorder subscale

Self-Disorder	R	R ²	p
Audio Cry (T1)	0.430	0.185	0.014*
Audio Cry (T2)	-0.257	0.066	0.110
Video Cry (T2)	0.085	0.007	0.578
Video Cry (T3)	0.067	0.005	0.658
Video Cry (T4)	-0.333	0.111	0.045*

* $p < 0.05$. T1 = Time epoch 0–500 ms; T2 = time epoch 500–1,000 ms; T3 = time epoch 1,000–1,500 ms; T4 = time epoch 1,500–2,000 ms.

stimuli along with a missing resonance to positive stimuli) is consistent with the previous literature [25, 49–54] and might result – on a clinical level – in an aberrant assignment of salience [55] to negative stimuli.

Moreover, some of the EMG proxies of such an altered resonance mechanism (i.e. T1 and T2 EMG corrugator facial activations) strongly predict the occurrence of SDs, selectively when the negative stimuli are presented in auditory modality. A further corroboration of such a robust effect emerged when variance accounted for by other variables was controlled, disclosing the earliest EMG corrugator activation detected during the auditory-only modality to be the specific predictor of SDs, and the latest EMG response occurring during the visual-only modality to predict a reversed effect.

Besides being suggestive of a prominent role of the auditory modality for the perceptual salience of negative stimuli in SzSp, this association may indicate that SzSp-specific qualitative changes in subjectivity (at the phenomenological level) are related to subtle alterations of embodied motor resonance (at the electrophysiological level). That is, alterations affecting the low-level mechanism of facial mimicry (i.e. a basic motor resonance mechanism that normally occurs through the lived body when someone perceives the facial expression of someone else's emotion) are associated with the degree of gestalt/qualitative change in the structure of subjectivity experienced by SzSp patients.

Such an association is in line with the phenomenological conceptualizations of the lived body as the medium of subjectivity/consciousness, in the sense that the impairment of a low-level embodied mechanism (facial mimic resonance) is paralleled by characteristic changes in the structure of conscious experience (i.e. SDs). Indeed – on a phenomenological-experiential level – it is through the organization of the perceptual field that the

individual is connected in a 'prereflective' way to the world, precisely through the tacit background of self-awareness that provides the first, elementary basis for his action and cognition [56, 57].

Thus, the results of this study are in line with converging evidence suggesting that the disruption of automatic, perceptual processes may be crucially related to a fragmented experience of the self in SzSp patients (see [58] for a comprehensive overview).

The hypothesis of a disturbed intermodal integration was originally proposed by Parnas et al. [59] as a neurodevelopmental feature that may be relevant to the SDs emerging in individuals who develop schizophrenia. Recently, this hypothesis has been corroborated by a prospective high-risk study [60], supporting the importance of intermodality dysfunction as an early indicator of the vulnerability to schizophrenia. On the other hand, an empirical study [61] discussing the view of schizophrenia as a disease mainly characterized by disturbances in information processing emphasized that an imbalance in sensory stimuli perception might arise from a failure in data-driven bottom-up (specifically in our study, facial or bodily feedback) and predominantly concept-driven top-down (e.g. delusional thinking) loop processes. The disruption in the automatic, low-level ability to appropriately integrate sensory inputs or information with stored material indeed can disrupt the sense of continuity and consistency in the sense of the self. Along a similar conceptual line, Postmes et al. [62] recently argued that sensory processing impairments affecting multisensory integration (i.e. multisensory disintegration) and leading to 'perceptual incoherence' might be implicated in the experiential emergence of SDs. These authors hypothesized that an extreme imbalance in different types of sensory input could hinder their integration within a single unified percept, leading to the well-documented multisensory audiovisual disintegration in schizophrenia [63–66]. Indeed, every single sensory modality with its properties contributes to inform the self about the environment via bottom-up processes, and conflicting sensory inputs result in sensory ambivalence, bringing forth contradictory experiences. As a consequence, sensory amplification (i.e. an increased impact or salience) of any thought or sensory detail occurs on the one hand, and reduced attention to other events takes place on the other, driving patients to a disintegration of their experiential world. This perceptual incoherence might finally result in a misalignment between mind and bodily self, inducing disturbances of subjective experience such as depersonalization, blurred boundaries, cenesthopathies or diminished sense of own-

ership and agency. Thus, any deficits in somatosensory feedback (e.g. a lack of facial motor resonance in response to positive emotional stimuli) plus a selective bias toward the 'single-sensory' modalities as found in our study would function as a 'sensory vacuum' that may undermine the perceived bodily self [40, 67]. We are thus inclined to consider the SzSp alterations in facial motor resonance to Audio-Video emotional stimuli as a proxy of such liability for multisensory disintegration (in the current paradigm: impairment in Audio-Video integration).

Certainly, an interpretation of our results along these lines is somewhat preliminary and has several shortcomings that warrant further investigations in future studies. First, the hypothesis of a disturbed emotional motor resonance derived from abnormalities in the mirror mechanism is limited by the lack in our study of direct measures of the entailed neural mechanisms. Second, all patients had chronic disease and were under antipsychotic medications, which might act as confounders in EMG responses. However, most of them were on second-generation atypical antipsychotics (with reduced extrapyramidal side effects) and additionally, the lack of EMG response was emotion- and modality-specific and not casually distributed among conditions, suggesting a minimal influence of such potential confounders on our data. Also, all patients were clinically stable (i.e. with no frank psychotic symptoms) at the time of the experimental session. Third, the small sample size along with an imbalanced gender distribution might have reduced the statistical power and extension of such results to the general population. Finally, in this study BSABS-derived subscores were adopted instead of the ad hoc developed EASE [12] to map SzSp disorders of self-awareness.

In conclusion, despite its intrinsic limitations, the present study provides the first evidence of a positive correlation between SzSp experiential disorders of the self and a specific neurophysiological substrate (in this case a proxy for the mirror mechanism, that is, EMG facial reactions). Indeed, several lines of investigation have reported empathic response deficits in schizophrenia with abnormalities in the mirror neurons mechanism [31–33]. According to this model, involuntary facial mimicry would act as a relevant low-level mechanism contributing to the experience of empathy via processes of simulation and perception-action coupling subserved by a distributed brain network of interconnected systems (see [68] for a review). Besides, this study confirms the potential of SDs as a target phenotype for neurobiological research and encourages research into disturbed motor/emotional resonance as possible body-level correlate of disturbed sub-

jective experiences in SzSp. This may provide a key integrative construct to address future trans-domain research in the neurobiology of vulnerability to schizophrenia.

Furthermore, the paradigm adopted in the current study plays an important heuristic role in mapping the neurodevelopmental processes implicated in SzSp proneness.

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Disclosure Statement

All the authors have declared that there are no conflicts of interests in relation to the subject of this study.

M.S., A.R. and V.G. jointly developed the heuristic structure of the paper. M.S. wrote the first draft, supervised by A.R. All the authors contributed to the final revision of the manuscript.

Appendix 1

A priori scales of Parnas et al. [2] with Cronbach's α coefficients and their BSABS item composition:

-
- Diminished Affectivity (DA; $\alpha = 0.55$)
 - Diminished initiative and dynamism (A 4)
 - Anhedonia (A 6.1)
 - Diminished feelings for others (A 6.3)
 - Diminished need for interpersonal relations (A 6.4)
 - Cognitive Disorder (CD; $\alpha = 0.59$)
 - Thought blockages (C 1.4)
 - Disorder of expressive language (C 1.7)
 - Diminished thought initiative and goal-directedness of thinking (C 1.13)
 - Self Disorder (SD; $\alpha = 0.73$)
 - Psychic depersonalization (B 3.4)
 - Somatic depersonalization (D 1.1)
 - Other optic perception disturbances, including the 'mirror phenomenon' (e.g. impression of a change in one's mirror image) (C 2.3)
 - Cenesthesias (CEN; $\alpha = 0.71$)
 - Electrical bodily sensations (D 5)
 - Sensation of movement, pressure or pulling in the body or on the body surface (D 7)
 - Sensation of lightness, heaviness, levitation, falling (D 8)
 - Sensation of constriction, dilatation, shrinking or expansion of the body (D 9)
 - Perceptual Disorder (PD; $\alpha = 0.62$)
 - Unclear sight, transitory blindness, partial sight (C 2.1)
 - Photopsia (C 2.2)
 - Other optic perception disturbances (C 2.3)
 - Changes of intensity or quality of acoustic perception (C 2.5)
-

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