Variable causes of social dysfunction in schizophrenia: The interplay of neurocognitive, personal, and intersubjective factors

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Abstract

Schizophrenia exerts its devastating effects mostly by causing a profound and poorly understood inability to function, affecting different aspects of everyday life from daily activities to a lack of social contacts, unemployment, and the consequences of stigmatisation. In empirical studies, social dysfunction is defined as a social performance measure, commonly based on the principles of cognitivism, and usually evaluated in laboratory and everyday settings. In schizophrenia, it is thought to be caused by cognitive dysfunction, related to brain dysfunction. From a medical perspective, schizophrenia is understood as a neurodevelopmental disorder resulting in a pattern of disconnection between important brain areas. Nevertheless, measures of neurocognition do not explain the expected amount of variance in social functioning. Other explanatory models of social dysfunction include structural functionalism, symbolic interactionism, and clinical phenomenology. Phenomenological accounts relate to the classical tradition in psychopathology, which describes schizophrenia as being marked by a certain "Gestalt", which is in turn recognised as a distinctive and pervasive change in an individual's self-experience and attunement to the surrounding world, thus emphasising the subjective experience of others. In the present paper, we intend to empirically explore the dilemma concerning the causes of social dysfunction in schizophrenia and to show how the comprehension, gained via a neuroscientific approach to a complex brain phenomenon can be meaningfully expanded by adding insights from different explanatory models. These models need to be operationalised so that all the data can be incorporated into a comprehensive statistical analysis.

KEYWORDS: schizophrenia, social dysfunction, explanatory models, neurocognition, clinical phenomenology

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Schizophrenia – the current medical perspective

Mental disorders in general, and schizophrenia, in particular, represent a major disease burden for modern societies, being by far the most important cause of chronic disability in the population group between 15 and 44 years of age (Insel 2009). Schizophrenia fully exerts its devastating effect on individuals in their second or third decade of life, not only through clearly noticeable psychopathological symptoms but also by causing a profound and yet poorly understood inability to function in everyday life. The disorder is quite prevalent, affecting 0.5 to 1% of the population. If the schizoaffective disorder and schizotypal personality disorder are considered, the prevalence can be as high as 3%. Together, they comprise a group of clinically related conditions called schizophrenia spectrum disorders (Kandel 2000).

Schizophrenia and related disorders are presently understood as medical syndromes, comprised of heterogeneous signs and symptoms of yet unknown aetiology. Specific diagnostic categories are clinically determined by the presence of typical symptoms described and operationalised in diagnostic manuals, such as ICD-10 and DSM-5 (World Health Organization 1992, American Psychiatric Association 2013), which undergo periodic revisions. Diagnostic criteria currently tend to emphasise objective and observable characteristics, with the addition of a subjective criterion of condition causing a "decline in social function" in order to qualify as a mental disorder.

The most prominent symptoms of schizophrenia are so-called psychotic symptoms such as hallucinations, delusions, and disorganisation of behaviour. Usually, they first appear during the first psychotic episode in late adolescence (Insel 2010), while other less prominent symptoms are present in other periods of life. In childhood, years before the diagnosis is made, more or less subtle anomalies in motor development, cognition or behaviour may be noticed by close relatives (Reichenberg et al. 2010, Sørensen et al. 2010). Later, in adolescence, more alarming emotional and cognitive changes appear, often accompanied by social withdrawal and, in some cases, even attenuated psychotic symptoms. The first psychotic episode is usually preceded by a prodromal period during which social functioning deteriorates significantly, and is then followed by the full development of psychotic symptoms and loss of insight into reality. Psychotic episodes can have a fluctuating course, with periods of complete or partial remission, where patients mostly experience so-called negative symptoms (i.e. lack of motivation, inability to experience pleasure or diminished emotional responsiveness) (Harvey & Davidson 2002, Kandel 2000, Mueser & McGurk 2004). Negative symptoms are usually accompanied by a decline in different cognitive domains, for instance, executive, attentional, memory, and language capabilities (Insel 2010; Uhlhaas & Singer 2010). Psychotic symptoms can be successfully treated with available antipsychotic medications; however, the negative and cognitive symptoms comprise a more treatment-resistant and chronic part of the schizophrenia syndrome, which determines the overall functional outcome (Green et al. 2000).

The course of schizophrenia is far from following the same pattern in different individuals. The first psychotic episode can appear almost unexpectedly or, in contrast, the symptoms can develop slowly but progressively over a period of years. Some patients experience recurrent psychotic episodes without any important decline of function-

ing in between, while others show a progression of negative and cognitive symptoms, resulting in a steady decline in social functioning (Harvey & Davidson 2002; Kandel 2000). Women tend to have a more favourable course of the disorder, with a later onset of the first psychotic episode and less prominent decline in social functioning (Mueser & McGurk 2004). On average, only 15% of the patients experience a full remission of symptoms after the first psychotic episode, while only 20% of them remain regularly employed. Although some experts relate these poor functional outcomes to environmental and psychosocial factors, such as a lack of effective rehabilitation programmes or levels of stigmatisation, they are more likely to be related to the lack of proper understanding of the causes of schizophrenia. This impedes the development of effective preventive and early treatment procedures (Insel 2010).

Neurodevelopmental origins of schizophrenia

With the advancement of brain sciences over recent decades, the medical model became the most prominent and influential way of explaining the origins of schizophrenia. The majority of neuroscientists would agree that schizophrenia is an example of a neurodevelopmental disorder, which means that a disadvantageous combination of otherwise normal gene variants in an individual's genome causes a specific trajectory of brain development and maturation (Schizophrenia Working Group of the Psychiatric Genomics Consortium 2014).

When genetic factors are coupled with additional early or late specific brain damaging events, brain development starts to deteriorate. During early adulthood, when the brain normally reaches its most dynamic and unstable transition phase in development, this sequence of events can finally result in a pattern of partial structural and functional disconnection between important brain areas. This coincides with the appearance of aberrant behaviour diagnosed as symptoms of schizophrenia (Insel 2009).

Epidemiological research has identified numerous possible additional aetiological factors, ranging from early physical traumatic events, maternal starvation, and exposure to toxic substances or infectious agents, to early and late factors that specifically influence the development of the "social brain" or, in other words, parts of the brain responsible for social interactions. The most prominent among these factors are the different social circumstances, such as early emotional trauma and abuse, or growing up in urban environments inside smaller and isolated minority groups. However, they also include important biological influences, such as the abuse of psychoactive substances. The exact timing of environmental factors during brain development is critical for the strength of their individual influence (Tost & Meyer-Lindenberg 2012; van Os et al. 2010).

The final stage of the pathological neurodevelopmental processes seems to consist of a structural and functional disconnection in brain networks, causing dysfunctional processing of information between neurons in the brain (Andreasen 2000; Insel 2010; Mueser & McGurk 2004; Selemon & Goldman-Rakic 1999). Early brain-imaging research in patients with schizophrenia confirmed the existence of numerous structural brain changes in different regions. These are mostly reductions in volume of the neuropil, small connecting parts between individual neurons (Coyle 2006; Meyer-Lindenberg et

al. 2001). These structural brain changes were shown to be correlated with the extent of disturbances of different cognitive processes in schizophrenia (Barch 2005; Lesh et al. 2011). These findings were later confirmed by a large number of functional imaging studies, showing a direct relationship between disordered brain function and cognition (Anticevic et al. 2011; Minzenberg et al. 2009; Van Snellenberg et al. 2006). The latest advances in the neuroscientific research of schizophrenia follow the development of imaging techniques for determining the architecture and function of large brain networks (Cole et al. 2013; Power et al. 2011). Network imaging studies have now directly confirmed the existence of differences in schizophrenia in both network structure (Ardekani et al. 2005; Cabral et al. 2013; Den Heuvel et al. 2010; Zalesky et al. 2011), and functional relationships between large functionally independent brain networks (Anticevic et al. 2013; Cole et al. 2014; Repovš et al. 2011). Presently, these anomalies seem to be the most sensitive measures of brain dysfunction in schizophrenia. Although they are still not sufficiently sensitive to be used as biomarkers for individual diagnostic purposes, they are able to identify group differences even in the absence of overt behavioural differences between patients and healthy control subjects (Anticevic et al. 2012).

In parallel with the rapid advance in imaging studies, there have been many attempts to integrate these findings with different other neurobiological and electrophysiological findings in schizophrenia. The most promising theories relate functional imaging measures of network disconnection with disturbances in local and long-range synchronisation of electrophysiological activity in inhibitory and excitatory neuron networks (Anticevic et al. 2013; Lesh et al. 2011; Lewis & Sweet 2009; Uhlhaas & Singer 2010).

Based on these discoveries, brain, and cognitive dysfunction seems to have prevailed in modern medical theories concerning the causes and mechanisms of schizophrenia. Moreover, the advance of neuroscience has produced a number of unexpected and intriguing questions in the entire field of psychiatric research. It is now known that clinically delineated mental disorder categories such as schizophrenia, mood disorders, and personality disorders have more in common than we would expect, as they show similarities from genetic background and brain dysfunction, to disturbances in cognition and similar therapeutic response to different classes of psychotropic medications. In addition, the same functional brain changes observed in patients can be shared in varying degrees among their otherwise healthy relatives, and are sometimes thought of as underlying the positive aspects (e.g. creativity and intellectual abilities) of their personalities. This has led some prominent neuroscientists to propose that we should never study patients with schizophrenia alone, but always in a larger, family related settings to truly gain insights into the causes of the disorder (Andreasen 2006).

Social dysfunction in schizophrenia

Part of the answer to this interesting question about the origins of schizophrenia lies in the crucial but often overlooked criterion of social dysfunction, which needs to be present to establish the clinical diagnosis of schizophrenia, and therefore delineates ill from healthy, but possibly related, individuals.

Nosological definitions of schizophrenia and related disorders changed considerably in the past, reflecting prevailing etiological theories and shifting between narrow, dichotomous categories and wider, continuum-like definitions (Harvey & Davidson 2002). The reasoning underlying present classification criteria originates from the 1970s, when far-reaching changes were introduced in psychiatric classification. They were mostly targeting the "subjective part" in the diagnostic process, while favouring reliability over validity. This process was supposed to make psychiatry more compatible both with the rules of research in the natural sciences, and with the idea that mental disorders are 'more likely brain disorders exhibiting psychological symptoms than psychological disorders caused by psychodynamically acting traumatic events and interpersonal conflicts in lives of the affected individuals' (Insel 2009).

Before that, it was widely accepted that schizophrenia was marked by a certain unique "Gestalt" (defined as a salient unity or intrinsic organisation of diverse phenomenal features, based on reciprocal part-whole interactions), which was mainly recognised as a distinctive and pervasive change in an individual's self-experience and his attunement to the surrounding world and social relations. This was hard to describe but easily recognised by experienced clinicians (Parnas 2012). It was famously called the "praecox feeling". In other words, it was this particular form of impairment in social life and not the specific clinical symptoms that suggested the character of schizophrenia for some psychotic states and not for the others (Stanghellini & Ballerini 2002).

Social dysfunction in schizophrenia is understood as a complex phenomenon, affecting different aspects of patients' lives, from everyday activities to lack of social contact, unemployment and the consequences of stigmatisation. As an enduring trait-like characteristic of schizophrenia, it is present long before the first psychotic episode and does not depend solely on any single psychopathological symptom (Stanghellini & Ballerini 2002, 2007). From the medical perspective, it is thought to be mainly related to cognitive disturbances and brain dysfunction in individuals with schizophrenia, although this hypothesis has been questioned in the light of recent empirical studies. For example, consistent problems with social functioning have been identified even in samples of patients with schizophrenia without cognitive abnormalities (Penadés et al. 2010).

Most of the empirical data on social dysfunction comes from studies dealing with the question of what patients are unable to do in social settings. They either employ the macro-social measures (e.g. global psychosocial functioning, impairments in relationships, occupational or leisure activities) that are related to the real-world functioning or they focus on micro-social measures derived from laboratory assessments of social performance, such as role-playing or problem-solving tests (Stanghellini & Ballerini 2007). These studies have shown that both types of measures are significantly but modestly related to cognitive deficits in patients, with cognition explaining a smaller share of the social outcome variance in groups of younger patients with recent onset of the disorder (Milev et al. 2005). Nevertheless, macro-social measures are thought to be less consistent due to their dependence on external and environmental factors, as well as on weak correlations with specific psychopathological domains and composite cognitive scores, which on average explain only around 20 to 40% of the social function outcome variance

(Cohen et al. 2006; Stanghellini & Ballerini 2011; Strassnig et al. 2015). Micro-social measures, in contrast, seem to be more related to cognitive deficits, probably due to their laboratory task nature, however, they are less relevant for real-world settings, where patients live and need to function (Stanghellini & Ballerini 2007).

Another significant criticism is that these kinds of studies emphasise the idea of social dysfunction in a behavioural-functionalistic way, focusing on socially defined and observable negative outcomes of actions, which could, in theory, be based on an unknown number of subjective mental states with different mixtures of negative and positive features (ibid.).

Explanatory models of social dysfunction

Anthropology has long remained isolated from brain sciences, mainly because of the latter's early reductionist approach with theoretical models that proposed ideas contrary to the basic foundations of socio-cultural anthropology. This has recently changed substantially, as reductionism has been largely replaced in cognitive (neuro)sciences with more complex, multi-causal, and ecologically valid accounts of brain development (Downey 2012). The present situation is more in line with the classic observation by Victor Turner:

> My career focus mostly has been on the ritual process, a cultural phenomenon, more than on brain neuroanatomy or neurophysiology. But I am at least half convinced that there can be genuine dialogue between neurology and culturology, since both take into account the capacity of upper brain for adaptability, resilience, learning, and symbolizing, in ways perhaps neglected by ethologists *pur sang*, who seem to stop short in their thinking about ritualization at the more obviously genetically programmed behaviors of the lower brain (Turner 1973).

At present, there are other relevant controversies in brain sciences, deserving a greater participation in a wider debate, for example, the theoretical explanations of the meaning and purpose of the newly discovered mirror neuron system in the brain (see later). Another important argument relates to the implications of neuroplasticity research, which show the brain as being much more flexible and adaptive than previously thought. This offers another perspective for integrated research besides the better-established question of which brain systems support social behaviour: namely, on how cultural influences sculpt brain plasticity (Downey 2012).

Critical current approaches in cognitive (neuro)sciences that can widen the brain-cognition perspective on characteristics of social dysfunction in schizophrenia were divided by Stanghellini and Ballerini (2002, 2007) according to different explanatory models, which broadly fall into categories of deficit, stigma and coping models and include the following:

Behaviourism/functionalism, in which social skills denote how individuals routinely adopt suitable behaviours to achieve goals and fulfil needs. The disease process in schizophrenia is thought to disrupt the implementation of these skills. This model emphasises the behavioural aspects of an individual in situations of social interaction. All

psychiatric disorders include an impairment in social skills, with differences appearing more in the quantitative than the qualitative level. The strengths of the model lie in its offering of easy and repeatable measurements, although it lacks insight into the subjective experiences of patients and cannot reliably differentiate between schizophrenia and other types of psychiatric disorders.

Structural functionalism, in which the core phenomenon is social adjustment, which is the capacity to participate in social life by behaving according to the expectations of others. In this context, normality refers to socially established norms organised in patterns of socially appropriate behaviour called "social roles", which depend on the ability to adopt and internalise the rules of a specific socio-cultural environment. Disability is considered as a consequence of the disease, which causes deviances from social rules and expectations at different levels. The characteristics of this model are quite similar to those found in the behaviourist/functionalist model.

Cognitivism, in which different subsets of cognitive processes jointly form social cognition, which is perceived as the ability to correctly understand, predict and respond to the states of mind and intentions of others. Cognitivism is the prevailing approach to empirical research in schizophrenia. Social cognition, as a specific subtype of cognition, relies on three types of cognitive or "social" patterns, where role patterns denote a similar concept to that of social roles in structural functionalism, while "person" patterns are based on personal features or specific representations of individuals. Together, these interact with event patterns, which are coherent and causally related time linked sequences of events anticipated by the individual, who learns to apply proper social patterns according to circumstances. Therefore, social cognition is a deeper social competence model, which bypasses behavioural and normative reductionism, while it assumes rather than explains how individuals understand the manifestations of others' minds. As a result, it seems to endorse a disembodied and dis-embedded conception of mental processes that are neither taking place within the lived body (especially the emotional body), nor interacting with the environment.

Symbolic interactionism, in which social functioning is based on the ability to interact with others through a commonly shared set of symbols, known as "social knowledge". According to this model, objects and events provide meaning, which is derived from social interactions and guides future behaviour. That is, an individual experiences himself indirectly through the ability to adopt the point of view of others. It develops throughout one's life and culminates in adulthood as an ability of the self to adopt the point of view of the whole community or the "generalised other". The advantage of this model lies in the introduction of the idea of intersubjectivity through the concept of adopting the point of view of others.

Psychoanalysis, in which social competence is based on the emotional ability to maintain stable relationships. In this model, disturbances are attributed to structural conflicts within an individual mind, such as pathological ways of developing object relationships. The model emphasises early mother-child relationships and thus introduces the phenomenon of early, primordial intersubjectivity.

Phenomenology, in which the social world is a product of the individual mind.

In this model, all social facts are not considered as independent entities, but rather the contents or "phenomena" of the individual intentional mind. Phenomenology emphasises the subjective dimension of social activity and describes the social world as made of meanings, which are understood and shared by every individual. This gives an experience of reality provided by objects and events in the world. Intersubjectivity is considered to be a primordial and given dimension that does not need to be attained, but that allows the establishment of meanings through interpretation in a spontaneous, intuitive and unreflective manner. The interpretative order, or common sense, is valid for everyone and is constructed from shared facts and procedures, available in an undiscussable manner to all individuals belonging to the same cultural context. Common sense establishes strong moral and emotional values, and deviances from it are viewed as deviances from a shared reality.

Neural correlates of social dysfunction are generally researched with the framework of cognitivism, while symbolic interactionism functions as a foundation for different psychosocial and phenomenological approaches. Nevertheless, all explanatory models can potentially include interactional relations at various levels between neural correlates and subjective or environmental factors, which are better captured in another type of theoretical approach to social dysfunction. According to this point of view, specific factors can be assigned to broader categories, independently of the explanatory model to which they best adhere (Stanghellini & Ballerini 2007):

Trans-personal factors include environmental factors that influence the life of the individual but are not under his control. These include stigma and the amount of social support, such as availability of social and psychiatric facilities, and family resources, which correlate especially with macro-social measurements of functional outcome. Stigma is reinforced through different sources and represents a significant influence that hinders the inclusion of patients in society, as well as their acceptance of appropriate treatment (Gaebel et al. 2002). Culture as a mixture of external artefacts (roles and institutions), internal values (beliefs, attitudes, epistemology, consciousness), and biological functioning is a source of complex socio-cultural processes that are involved in identifying, describing, labelling, and intervening in cases of behavioural or mental deviance. Not only patients but also mental health professionals, communities, and institutional settings contribute to differences in the prevalence of identified cases of mental disorders across cultures (Draguns & Tanaka-Matsumi 2003). Schizophrenia spectrum disorders occur in all cultures and geographical areas with a similar rate of incidence in different populations. While the course and prognosis of schizophrenia are extremely variable across populations, the outcome seems to be consistently better in developing countries, although the reasons for this are not clearly understood (Kulhara et al. 2009; Sartorius 2008).

Sub-personal factors include everything that is not directly involved in the personal experience of the social world. The main sub-personal factor is neurocognition, which includes different cognitive domains relevant for social functioning, such as working memory, attention, vigilance, processing speed, verbal and visual learning and memory, and reasoning and problem solving. As already mentioned, neurocognition is clearly related to social functioning, but this relationship is probably quite complex and

mediated through different hierarchical levels. It seems quite probable that neurocognition is a prerequisite for higher level social cognition, which in turn, is a prerequisite for social functioning (Addington et al. 2006).

Personal factors include many different concepts. Among them, there are social cognition, coping resources and non-cognitive factors. We have already referred to *social cognition* as the ability to understand, predict and correctly respond to the intentions of others. As such, social cognition is necessarily a broad construct including several sub-components:

a) *Emotion perception* is the ability to perceive and evaluate the emotions of others, based on their facial expressions, vocal prosody and bodily gestures. Emotion perception seems to be deficient in schizophrenia in different aspects, but the extent of the deficits is controversial (Bigelow et al. 2006);

b) *Social perception* relates to how accurately an individual can understand the exact goals and intentions of other people, that is, their mood states and the level of intimacy of their mutual relationship. This ability was shown to be deficient in patients with schizophrenia (Sergi et al. 2006);

c) *Theory of mind* (ToM) is another important aspect of social cognition that has to do with understanding the internal states of others. ToM can be divided into two general categories: *Theory theory* presupposes that there is a cognitive mechanism or learned ability capable of determining the intentions and behavior of others in a theoretical/analytical way, while *simulation theory* states that the internal states of others automatically cause the activation of similar experiences in ourselves, so that consequently, we understand others by recognising our own internal states. Patients with schizophrenia show deficits on more challenging laboratory ToM tasks, but not in everyday settings. In general, measures of social cognition can explain a larger amount of variance in the functional outcome than neurocognitive measures alone can (Couture 2006).

Coping resources are the ability of the individual to deal with stressful events and their consequences, and it is reduced in patients with schizophrenia. This is probably related to neurocognition, personality traits, and the presence of psychopathological symptoms (Stanghellini & Ballerini 2007).

Among *non-cognitive personal factors* influencing social dysfunction in schizophrenia, we can identify emotional experience, empathy attitudes, personal values, and phenomenologically delineated subjective and intersubjective factors. Social functioning is undoubtedly strongly dependent on motivational and emotional factors, such as the expectation of interpersonal reward, ability to feel pleasure, the experience of rejection, and interactions between emotion and cognition (Anticevic 2012, Velligan et al. 2006). Patients show changes in empathic abilities mostly on the level of cognitive perspective taking, while affective empathy (i.e. the concern for others) seems not to be altered (Haker et al. 2012, Montag et al. 2007).

Currently, a large body of neuroscientific research exists about the neural correlates of social cognition and non-cognitive personal factors. We now believe that social behavior exhibiting a capacity for imitation and intersubjective communication is already present in infants, and relies on the existence of a mirror neuron system comprising different types of neurons that are active, either when we are thinking about the intentions of others

(mentalising), or when we automatically share the experience of the same mental states when observing others (neural resonance). Mirror neurons probably exist in parallel with other neurons in major brain areas and activate only in the context of intersubjective events. This characteristic makes them ideal candidates for neural correlates of different types of complex processes, such as the theory of mind and empathy (Zaki & Ochsner 2012). Prosocial behavior, in general, was also shown to be related to different neurobiological factors. For instance, hormones, such as oxytocin and testosterone. can promote or inhibit the empathy towards others (Bartz et al. 2010; Zak et al. 2009).

Turning to phenomenological descriptions of intersubjectivity, Stanghellini and Ballerini propose an overall crisis of intersubjectivity in schizophrenia, based on changes in the system of values of the individual that can be captured in terms like *antagonomia*, which reflects the purposeful choice of patients to take an eccentric stance when faced with the common sense values of others, and *idionomia*, which reflects a feeling of radical uniqueness and exceptionality of one's being with respect to common sense and others (Stanghellini & Ballerini 2007, 2011).

More generally, phenomenologically delineated intersubjective factors are probably best expressed through Bleuler's classical concept of *autism* and its later conceptualisations, which depict the patient's detachment from the social surroundings and immersion into the private world, either filled with an unusual but imaginative inner life or empty and cold (Parnas et al. 2002; Henriksen et al. 2010). This lack of attunement to the outer world is pre-reflexive in nature and places the emphasis not so much on social performance (and its deficits), but on the subjective experience of other people, the ability to understand their mental structure and the communitarian common sense in general, to make emotional contact and establish mutual relationships. Instead of *social dysfunction*, different terms like *perplexity* or *dis-sociality* are proposed as being more appropriate, since they point to qualitative rather than quantitative changes in social performance (Henriksen et al. 2010; Stanghellini & Ballerini 2011). Detachment from the social world can perhaps also represent a protective factor, as in the concept of "positive withdrawal", which lowers the risk of patients experiencing another psychotic episode (Corin 1998).

Phenomenological accounts of schizophrenia

Broader phenomenological accounts of changes in the subjective experience of patients with schizophrenia have gained momentum in the last decade, building on the rich history of the continental tradition in psychopathology and clinical phenomenology research, and culminating in organised empirically based research that combines philosophical insights and clinical work in specialised interdisciplinary research institutions (Parnas & Henriksen 2014). They have shown that the characteristically described Gestalt of schizophrenia can be operationalised as disorders of basic prereflective self-experience, by using semi-structured interviews performed by experienced clinical phenomenologists. The construct of self-disorders is remarkably internally consistent (Nordgaard & Parnas 2014), it appears early and remains present throughout the lifetime of affected individuals with different types and severity of diagnoses from the schizophrenia spectrum. It correlates well with depressed mood and suicidality (Skodlar & Parnas 2010) and social dysfunc-

tion (Haug et al. 2014), possibly because of its proposed impact on dysfunction of social cognition (Nelson et al. 2009), but appears to be unrelated to neurocognitive dysfunction (Haug et al. 2012b).

Self-disorders are pervasive experiences that qualitatively change the individual's first-person, subjective experience of himself as a conscious, active and embodied agent in the world (Parnas 2003). Anomalies of this kind do not reach a psychotic intensity, meaning that patients can retain a critical distance towards them, which is characteristically expressed through their use of metaphors or expressions such as "as if" sentences when they describe their experiences.

Self-disorders include changes in the whole spectrum of the phenomenological concept of *presence*, which includes the pre-reflective self-experience or *ipseity* (as opposed to the consciously reflected *narrative* self) and the individual's sense of embeddedness in the world, together with his loss of understanding of common sense, appearance of autism and perplexity (Parnas 2003). The disturbance of ipseity is the basis for more complex anomalies of self-experience. The simultaneous experience of the body as being part of the embodied self, a living spatiotemporal agent in the world and body as a separated physical object, that can be observed by the self, is changed in the direction of a clearly noticeable experiential distance between the body and the subjective self. Changes in experience can influence motor and language actions, which can appear as if happening automatically or outside the patient's willful intentions (Hirjak et al. 2013). Similarly, the stream of consciousness can change, bringing about the loss of the natural flow of thoughts and changing the subjective experience of the content of thought. Thoughts can appear as being anonymous, spatially localised or with other new sensory qualities. The increase in experiential distance between the self and the thought content can result in a process of hyper-reflective internal self-monitoring. The combination of ipseity disturbance and hyper-reflectivity was suggested as the main foundation for theoretical accounts of self-disorders in individuals with schizophrenia spectrum disorders (Parnas 2003; Raballo & Parnas 2012; Sass et al. 2011). As mentioned above, disturbances in self experience extend to the usually unreflective embeddedness of the self in the outside world through a lived and subjective embodied experience. Patients can experience transitivistic phenomena marked by difficulties in differentiating between self, body and the environment, especially in relation to other persons. Experiential anomalies can together lead to existential changes, expressed through different types of reorientation of the individual towards idiosyncratic preoccupation with supernatural and metaphysical ideas, or solipsistic feelings of centrality and specialness of his position in the world and universe (Parnas 2003; Raballo & Parnas 2012).

The empirical research on symptoms of self-disorders at first employed different instruments for detection of a wider group of related "basic symptoms" of schizophrenia (BSABS, SPI-A). Later, this was replaced by the construction of a more focused instrument named the Examination of Anomalous Self-Experience (EASE) (Parnas et al. 2005), which divides anomalies in five basic interview related domains, that are theoretically and also empirically understood as parts of the same experiential change, the Gestalt of schizophrenia (ibid.).

Research question and methods

In the present study, we intended to explore further the dilemma concerning the importance of different factors in the social functional outcome in schizophrenia spectrum disorders, by showing the interrelations between empirical data on disorders of self experience, clinical symptoms, social dysfunction, cognitive functioning and brain function measures, gathered with validated clinical procedures, phenomenological interviews, and electrophysiological brain imaging. We purposefully chose a group of patients with relatively recent onset of illness and who are currently in a stable remission, with a relatively good social functioning status. To achieve these conditions, patients were recruited from the outpatient services at the University Psychiatric Hospital in Ljubljana. With these inclusion and exclusion criteria, we attempted to avoid the expected larger effect of neurocognitive factors related to longer disease duration and investigate whether we can identify different meaningful social functioning factors in such a homogeneous sample of younger patients with schizophrenia. Neurocognitive factors were evaluated by measuring the performance of patients in a visual working memory task and by analysing simultaneous electrophysiological recordings of their brain function. We only included male subjects in this study, in order to exclude the influence of sex on the variability of neurocognitive function. The chosen visual working memory task depends on the activation of a frontoparietal brain network, that was shown to be essential for basic cognitive control abilities (Barch & Ceaser 2012) and is simultaneously potentially related to disturbances in mirror neuron system, the theoretical neural correlate of higher social cognitive functions (Zaki & Ochsner 2012). Patients with schizophrenia usually show two possible sources of dysfunction on working memory tasks: problems with maintaining a larger number of items in memory and problems with filtering out the influence of distracting items (Park & Gooding 2014). Therefore, the task was designed in such a way to include both conditions, and a group of healthy control subjects was included to allow us to empirically determine which are the most critical of the neurocognitive measures in our research sample. The control group was age-matched to the patient group, but not education matched since patients with schizophrenia, especially males, on average attain lower levels of education than the general population.

Clinical evaluation of patients

The clinical status of each patient was evaluated by two experienced psychiatrists who are the co-authors in the study. The presence of clinical psychopathological symptoms was determined with the Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987), which is a standard measure of clinical symptoms in schizophrenia research. Summary scores were calculated for each patient for the Total score and the Positive, Negative and General symptoms subscales. Social functioning was determined with the Personal and Social Performance Scale (PSP scale) (Morosini et al. 2000). The PSP is a 100-point single-item rating scale subdivided into 10 equal intervals. The ratings are based mainly on the assessment of patient's functioning in four main areas through defined operational criteria: socially useful activities, personal and social relationships, self-care, and disturb-

ing or aggressive behaviours. For the purposes of statistical analysis, we determined and used all five PSP scores (PSP overall score, PSP activities, PSP relationships, PSP self-care, PSP aggression).

Evaluation of anomalies of subjective self-experience and disturbances in intersubjectivity

Phenomenological interviews were carried out and evaluated according to the structure and items contained in the Examination of Anomalous Self-Experience instrument (EASE) (Parnas et al. 2005), by one of the co-authors of the study (Borut Škodlar), who was extensively trained in the use of EASE by the instrument's authors. Interviews were recorded and later evaluated for the presence or absence of each specific EASE item, which gave the overall summary score, following the usual practice in EASE related studies: each item is scored on a five-point Likert scale (0–4). For the purpose of the analysis, the Likert scale is dichotomised between 0 and 1 (absent or questionably present) versus 2, 3, and 4 (definitely present, all severity levels) (Haug et al. 2012a).

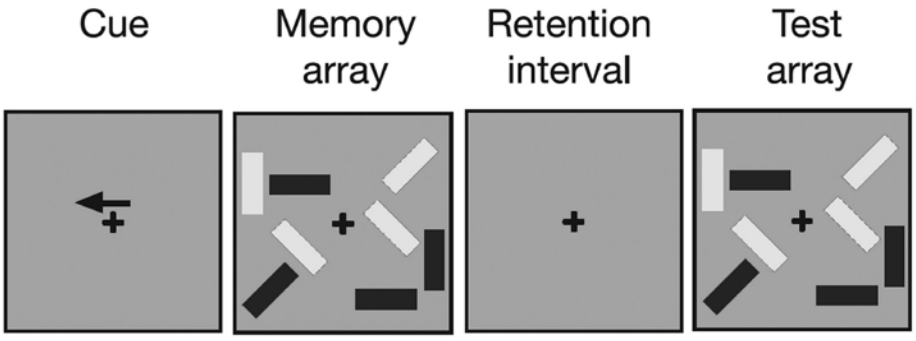
Relative percentages of present items were additionally determined for separate EASE domains, which include Cognition and stream of consciousness, Self-awareness and presence, Bodily experiences, Demarcation and transitivism, and Existential reorientation.

Cognitive task and electrophysiological measures of brain function

The visual working memory task was designed according to a methodology (Vogel et al. 2005; Vogel & Machizawa 2004) to elicit specific electrophysiological brain activity related to working memory in posterior brain areas, the so-called contralateral delay activity (CDA). Subjects were seated in front of a computer screen, their task being to remember specific combinations of orientations of up to four items for a short period (2.5 seconds) and answer whether one of the items had changed direction (Figure 1). There were three different conditions in the task, where they needed to maintain either two (low memory load, condition 2) or four items (high memory load, condition 4) or exhibit successful inhibition of two distracting items presented together with two memory items (distractor condition, 2+2). Because CDA is an event-related brain potential, determined by the technique of averaging together electrophysiological brain responses in repeating task trials to reduce noise and artefacts in the recording, each condition was repeated 200 times. There was a practice session performed before the start of the recording, where subjects needed to attain at least a 75% success rate to exclude the possibility that they were answering by chance. For each trial, only items presented in one of the visual hemifields (Figure 1, arrow) were relevant, because CDA is a lateralised event-related response, exhibiting bigger amplitude changes in the contralateral hemisphere. The electrophysiological signal on pairs of analogous electrodes in posterior areas of the left and right hemispheres was subtracted to obtain the final differential amplitude curve (CDA). Event-related potentials are known to have a very good time resolution but a low spatial resolution, so they are primarily used to follow the time sequence of cognitive events during each trial. In previ-

ous studies, CDA amplitude changes (relative changes in amplitude negativity during the working memory retention phase of each trial) were shown to be related to the average working memory capacity of individual subjects, and that they closely follow the current working memory load, efficiency at adding and removing items from working memory and inhibition of the distracting items (Luck & Vogel 2013; Vogel et al. 2005; Vogel & Machizawa 2004).

Figure 1: Visual working memory task. Subjects need to remember the orientation of red (grey) items and inhibit the distracting items in blue (black), on the left part of the screen (Vogel et al. 2005).



Brain responses were recorded with a continuous electroencephalogram, using a 128-channel system BrainAmp with the active electrode system actiCap (Brain Products GMBH, Germany). Each recording was preprocessed using standard techniques (Repovš 2010) to reduce the influence of different types of noise and artefacts in the signal and epoched into separate trials to enable averaging of the signal according to experimental conditions. CDA amplitude was measured in the time window of 500 to 900 milliseconds after the presentation of a memory array. We decided to calculate and analyse the following two measures:

a) behavioral, cognitive task measures – *memory capacity K*, calculated according to Vogel and Machizawa (2004) for each condition (K2, K4, K2+2), *response accuracy* for each condition (Acc 2, Acc 4, Acc 2+2) and *response reaction times* (RT 2, RT 4, RT 2+2), and
b) electrophysiological CDA related task measures – *relative difference in CDA amplitude between conditions 2 and 4* (CDA 4-2, for which bigger difference corresponds to better maintenance processes in working memory (Vogel and Machizawa 2004)) and *filtering efficiency FE*, which is defined as the relative distance of CDA amplitude in condition 2+2 against amplitudes in conditions 2 and 4 (the position being closer to the one in condition 4 signifies a lower ability to inhibit distracting items (Vogel et al. 2005)).

Statistical analyses

Mixed design ANOVAs with a Greenhouse-Geisser correction were used to test whether there is any significant effect on the primary measures of interest (memory capacity K and CDA amplitude), or on the secondary measures of interest (average reaction time and response accuracy) in three different conditions (within-subjects factor: condition C2, condition C4, and condition C2+2), for two participant groups (between-subjects factor: patients and controls), and interaction between these two factors. Significant results were investigated further by means of a simple main effects analysis with Bonferroni correction.

The Pearson product-moment correlation coefficient was computed to assess the relationship between the difference of CDA negativity in conditions C4 and C2 (computed as C4-C2), and maximal memory capacity, defined as memory capacity K4 in condition 4, computed by the formula presented elsewhere (see Vogel & Machizawa 2004)). Pearson product-moment correlation coefficient was used in the same way to assess the relationship between filtering efficiency FE, computed by the formula presented elsewhere (see Vogel et al. 2005) and memory capacity K4 in condition C4.

Spearman's rank-order correlations were run to determine the relationships between PSP scores and other scores (neurocognition, self-disorders, and clinical status).

The relationship between social functioning, self-disorders and cognitive functioning was further explored by means of linear regression modelling. The aim of this analysis was to find an optimal set of variables representing self- disorders and neurocognitive functioning to describe social functioning. Social functioning, the dependent variable in the model, was represented by three potential variables: Overall PSP score, PSP Activities score and PSP Relationships score. The potential independent variables included a set of self-disorder related variables (total EASE score, EASE Cognition score, EASE Presence score), a set of neurocognitive variables (Memory capacities K4, K2, K2+2, Filtering efficiency, CDA amplitude 4-2, reaction times and accuracies at different conditions), and a set of clinical PANSS scores.

Results

Demographic data

Fourteen male patients (1 left-handed) were included in the study, 10 diagnosed with schizophrenia spectrum diagnosis (schizophrenia or schizoaffective disorder) and four with schizotypal disorder. All patients were taking atypical antipsychotic medication and were, at the time of this study, in stable symptomatic remission, attending outpatient services at the University Psychiatric Hospital Ljubljana. The average duration of disease in patients was 6.0 years (SD=3.4), and the average number of hospitalisations was 2.8 (SD=2.1). The control group of healthy participants included 15 male subjects (1 left-handed, 1 ambidextrous). There were no differences between groups regarding age (control group M=26.8 years, SE=5.5, patient group M=27.8 years, SE=3.8, p=0.606) but there was a significant difference regarding education (control group M=14.4 years, SE=1.2, patient group M=13.4 years, SE=1.1, p=0.023).

Evaluation of clinical symptoms and anomalies of self-experience

Patients scored 76.5 points (SD=15.7) on average on the PANSS Total score, which translates to a mild to moderate expression of psychopathological symptomatology (PANSS minimum score = 30, maximum score = 210). Overall, the group PSP score was 54.4 (SD=8.1), which indicates mild to moderate social functioning disability. All PSP scores in our patient group ranged between 42 and 73, which is consistent with our intention of choosing a homogeneous sample regarding social dysfunction. Patients attained an average EASE score of 17.9 points (SD=6,5), with the majority of items scored in the domains of Cognition and stream of consciousness, and Self-awareness and presence, which is consistent with other EASE-related studies (Parnas & Henriksen 2014).

Comparisons of neurocognitive factors between patient and control group

The patient group significantly differed from the control group regarding behavioural performance on the visual working memory task on the primary measure of memory capacity in the distractor condition C2+2 (patients' K2+2 Mean=1.6 SD=0.4 vs control's Mean=1.8 SD=0.2; p=0.048). The other two conditions did not differ regarding memory capacity (patients' K2 Mean=1.7 SD=0.2 vs control's Mean=1.8 SD=0.1; p=0.055 and patients' K4 Mean=2.2 SD=0.9 vs control's Mean=2.5 SD=0.8; p=0.190). Regarding secondary measures, patients had higher reaction times and lower accuracy on average in all three conditions, although differences were not statistically significant.

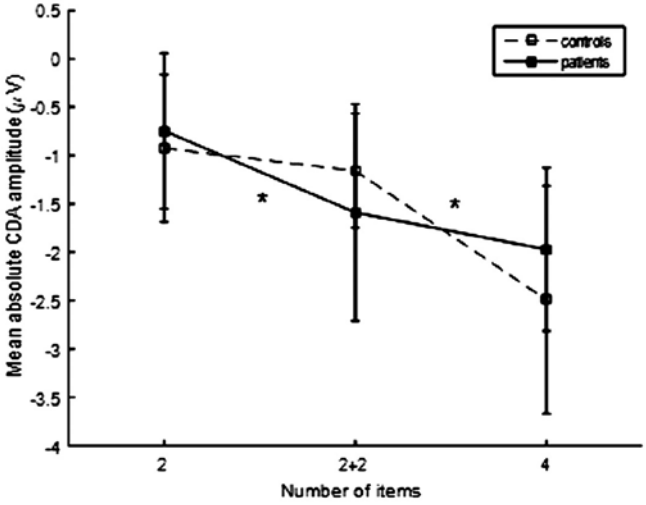


Figure 2: Differences in mean absolute CDA amplitudes between subject groups for trial conditions

Regarding the absolute CDA amplitude, ANOVA showed a significant interaction effect between condition and group ($F(1.602, 43.246)=5.035$, $p=0.016$). Further analysis revealed that the two groups did not differ significantly in any of the three conditions, however, condition C4 (M= -2.491, SE=0.266) was different from conditions C2 (M= -0.927, SE=0.202, $p<0.001$) and C2+2 (M=-1.158, SE=0.229, $p<0.001$) in the control group, while in the patient group the baseline condition C2 (M= -0.747, SE=0.209) was different both from C4 (M= -1.972, SE=0.275, $p<0.001$) and C2+2(M=-1.59, SE=0.237, $p<0.001$); see Figures 2, 3, and 4.

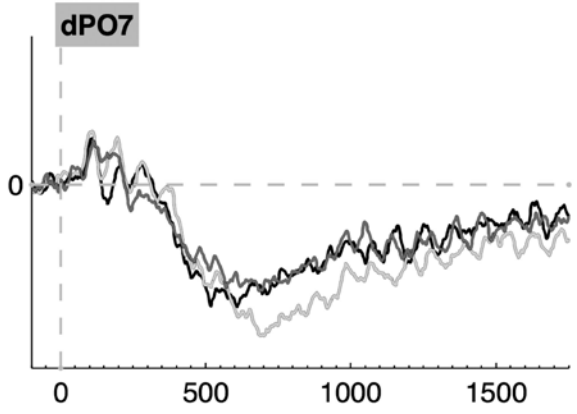


Figure 3: Time course of CDA difference wave for control group (electrode pair in parieto-occipital region; black line condition 2, light-gray line condition 4, dark-gray line condition 2+2)

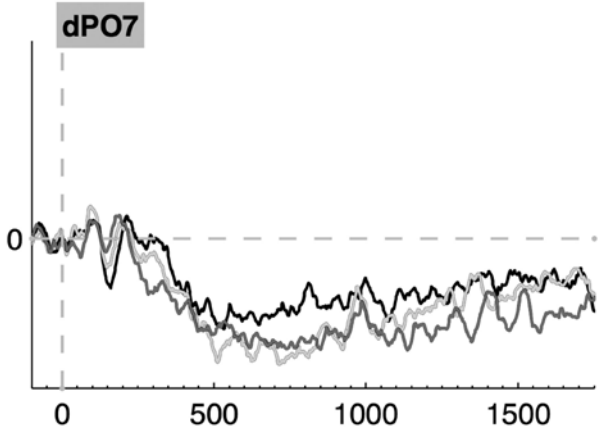


Figure 4: Time course of CDA difference wave for patient group (electrode pair in parieto-occipital region; black line condition 2, light-gray line condition 4, dark-gray line condition 2+2)

Regarding the relation between the increase in CDA negativity (CDA 4-2) and maximal memory capacity (K4), there was no significant correlation between the two variables either in the control (r = -0.474, n = 15, p = 0.074) or patient (r = -0.282, n = 14, p = 0.329) group. However, as shown in the scatterplot (Figure 5), there was a stronger decrease in CDA amplitude in the control than in the patient group.

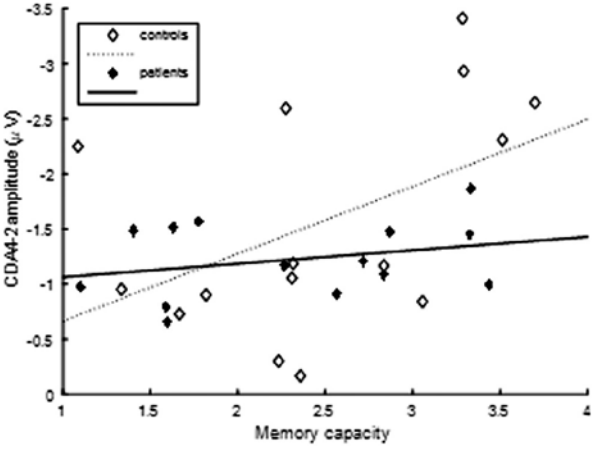


Figure 5: Relation between the increase in CDA negativity (CDA 4-2) and maximal memory capacity (K4); note that the y-axis is inverted

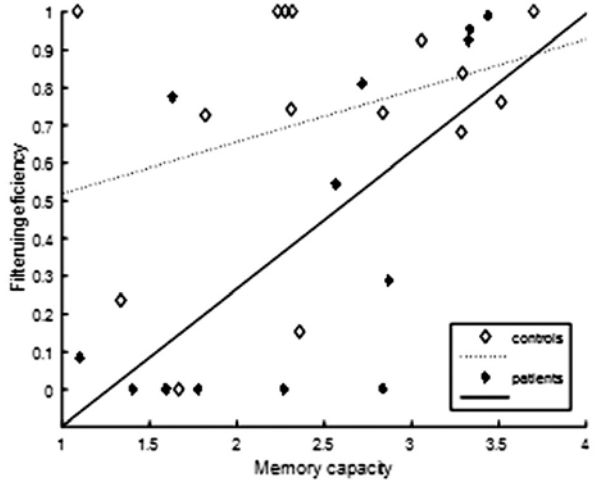


Figure 6: Relation between filtering efficiency (FE) and maximal memory capacity (K4); note that the y-axis is inverted

Regarding the relation between filtering efficiency (FE) and maximal memory capacity (K4) there was a significant correlation between FE and maximal memory capacity in the patient group ($r = 0.684$, $n = 14$, $p = 0.007$), however, not in the control group ($r = 0.329$, $n = 15$, $p = 0.231$). The scatterplot (Figure 6) indicates that in both groups FE tends to increase with increasing memory capacity; however, the effect is stronger (and significant) in the patient group.

Comparisons of neurocognitive and personal factors' relationships with social dysfunction in patient group

Table 1 shows the summary of statistically significant Spearman's rank-order correlations for the chosen variables representing neurocognitive, self-disorders, clinical and social dysfunction factors.

Table 1: Spearman's rank-order correlations (Spearman's rho), showing results only for statistically significant (or very close to significant) relationships

	PSP Overall	PSP Activities	PSP Relationships	PSP Self-care	PSP Aggression
EASE Total					
EASE Cognition			rs = 0.565 p = 0.035		
EASE Presence					
PANSS Total			rs = 0.7 p = 0.005		rs = 0.628 p = 0.016
PANSS Negative					
PANSS Positive					
PANSS General			rs = 0.655 p = 0.011		rs = 0.651 p = 0.012
K2					
K4					
K2+2					
CDA 4-2					
FE	rs = 0.530 p = 0.051	rs = -0.532 p = 0.050			
ACC 2					
ACC 4					
ACC 2+2					
RT 2					
RT 4					
RT 2+2					

Linear regression modelling of the relationship between social functioning, self-disorders, and cognitive functioning

First, a full Pearson's correlation matrix was computed among all variables in order to identify the possible explanatory variables for the three dependent variables. The table also served to identify correlated independent variables and limit their inclusion in each explanatory model. The inspection of the correlation matrix led to four possible multiple linear regression models:

Model 1: PSP overall ~ EASE Cognition + Memory capacity K2+2
Model 2: PSP overall ~ EASE Cognition + Accuracy in condition C2+2
Model 3: PSP Relationships ~ EASE Cognition + PANSS General
Model 4: PSP Relationships ~ EASE Cognition + PANSS total

Second, the analysis of these four models was run separately, evaluating the overall significance of each model, the significance of every independent variable, as well as their interaction. PSP was best predicted overall by EASE Cognition and K2+2 (Model 1), while PSP Relationships was best predicted by EASE Cognition and PANSS total (Model 4).

Model 1: A multiple linear regression was run to predict social functioning (represented by the overall PSP score) from self-disorders (represented by the EASE Cognition score) and neurocognitive functioning (represented by memory capacity K2+2). Both EASE Cognition and K2+2 explained a significant amount of the variance in social functioning (PSP overall), $F(2, 11)=9.41$, $p<0.01$, $R^2=0.6311$. Both EASE Cognition (Beta= -0.497, $t(13)= -2.647$, $p<0.05$) and K2+2 (Beta= 0.520, $t(13)=2.769$, $p<0.05$) significantly predicted the overall PSP score. There was no statistically significant interaction ($p=0.133$).

Model 4: A multiple linear regression was run to predict social functioning (represented by the PSP Relationships score) from self-disorders (represented by the EASE Cognition score) and PANSS Total score. Both variables explained a significant amount of the variance in social functioning (PSP Relationships score), $F(2, 11)=10.368$, $p<0.01$, $R^2=0.6534$. Both EASE Cognition (Beta= 0.5, $t(13)= 2.647$, $p<0.05$) and PANSS total score (Beta=0.0.486, $t(13)=2.571$, $p<0.05$) significantly predicted the overall PSP score. There was no statistically significant interaction ($p=0.654$).

Discussion

The analysis of neurocognitive data revealed that our patient group shows expected characteristics for a sample of younger patients in a stable remission of schizophrenia spectrum disorder. Their behavioural performance in the visual working memory task, which is one of the central proposed cognitive disturbances in schizophrenia, was lower than that of the control group by all measures, but only some of them reached the level of statistical significance. This is reminiscent of other studies of neurocognition in schizophrenia, where an inverted U-shape was proposed as a model to explain discrepant findings of a general cognitive deficit or normal cognitive performance in different cognitive domains

coexisting with hypo- or hyperactivation of different brain regions (Van Snellenberg et al. 2006). It seems that neural correlates can be more telling of an existing disturbance of brain function in cases where patients attain the same behavioural results as those of control groups. This is explained as a case of compensation of function by temporary hyperactivation of brain resources, usually observed as brain hyperactivity, dispersion of brain activation over larger areas, or different types of connectivity patterns between brain areas than observed in healthy subjects performing the same task with the same behavioral efficacy (Anticevic et al. 2012). In our study, from two potential sources of disturbance in working memory processes, maintenance of a large number of items and inhibition of distracting items, we could identify mostly the latter. The patient group was significantly less efficient in the condition with distracting items present, and the brain measures of CDA amplitude changes confirmed this result by showing a reduction in filtering efficiency, with filtering efficiency, in general, showing a larger effect on individual memory capacity in the patient group.

Measures related to inhibition of distracting items were thus identified as the most significant neurocognitive factor in our sample. This finding was corroborated later in the overall correlational analysis of relationships between different patient factors and measures of social function. Filtering efficiency was significantly correlated with the overall score of social function and the ability to perform socially useful, work related activities. Interestingly, other factors, such as clinical symptoms and phenomenologically determined anomalies of self-experience, seemed to be independently correlated with a subdomain of social functioning, namely, the ability to establish and maintain social relationships. This is in line with research on macro-social measures of social dysfunction in schizophrenia and with theoretical assumptions of clinical phenomenology research. We did not observe a correlation between neurocognition and self-disorders, which confirms the findings in a small number of other empirical studies which investigated this relationship (Haug et al. 2012b).

Lastly, the two most efficient joint linear regression statistical models confirmed the correlation analysis and showed that overall social functioning was best predicted by a neurocognitive- and self-disorder-related factor, while functioning in social relationship settings was best predicted by a self-disorder-related factor and a clinical symptom-related factor, while neurocognition did not play the same role as in overall ability to function. The clinical factor identified here, the PANSS general score, is mainly related to less specific bodily symptoms in schizophrenia, which adds some empirical evidence to the proposed influence of body malfunction on pre-reflexive attunement with the surrounding world (Stanghellini & Ballerini 2011). Both models explained up to 65% of the variance in the outcome, which is a much better result than usually found when studying the impact of neurocognition on social dysfunction alone. Therefore, these results show that interdisciplinary approaches can be better suited to explain complex phenomena related to brain function, even when studying small samples. It would not be possible to highlight this interaction without a collaboration of researchers with quite different expertise and theoretical backgrounds. Social functioning is an example of an especially complex phenomenon, spanning different human activities, personal experiences, and

subjective states. Therefore, it is not surprising that brain sciences and humanities on their own can discover many meaningful theoretical and experimental aspects of it. However, as was shown, we believe that it is necessary to integrate first-person and third-person observations and research approaches to further the understanding of this type of questions. Further interdisciplinary studies are needed to make progress in this interesting field.

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Povzetek

Družbeno breme shizofrenije je veliko predvsem zato, ker bolezen povzroči izrazite in obenem slabo razumljene težave v socialnem funkcioniranju bolnikov, ki zajemajo različne vidike vsakdanjega življenja - upad vsakdanjih aktivnosti, umik iz socialnih stikov, brezposelnost, posledice stigmatizacije. V empiričnih raziskavah se sociano disfunkcijo običajno definira glede na teoretična izhodišča kognitivizma, kot mero socialne učinkovitosti, ki se jo lahko preučuje v laboratorijskih pogojih ali v vsakdanjih okoljih.

Za socialno disfunkcijo pri shizofreniji se tako predvideva, da nastane kot posledica kognitivnih motenj, ki so povezane z motnjami v delovanju možganov. Shizofrenijo se z medicinskega vidika sedaj razume kot nevrorazvojno motnjo, kjer patološki proces povzroči motnje v povezanosti pomembnih možganskih omrežij. Kljub temu pa različne mere nevrokognitivnih dejavnikov kažejo, da je s takim pristopom težko razložiti večji delež variabilnosti v socialnem funkcioniranju bolnikov. Drugi možni razlagalni modeli motenj v socialnem funkcioniranju vključujejo naprimer strukturni funkcionalizem, simbolični interakcionizem in klinično fenomenologijo. Fenomenološke razlage so zanimive že zaradi svojih navezav na klasično psihopatološko tradicijo, v kateri je bil za shizofrenijo značilen določen "Gestalt", ki so ga opisovali kot izrazito in trajno spremembo v posameznikovem doživljanju sebe in njegovi uglašenosti z okolico, s pomembnim poudarkom na subjektivnem doživljanju drugih ljudi. V opisani raziskavi skušamo empirično osvetliti omenjeno dilemo o vzrokih motenj v socialnem funkcioniranju pri bolnikih s shizofrenijo in pokazati, kako je možno običajne nevroznanstvene pristope k razlaganju kompleksnih fenomenov, povezanih z delovanjem možganov, nadgraditi z vključevanjem drugih teoretskih pristopov, ki pa morajo biti operacionalizirani do te mere, da lahko vse zbrane podatke smiselno vključimo v skupno statistično analizo.

KLJUČNE BESEDE: shizofrenija, motnje v socialnem funkcioniranju, razlagalni modeli, nevrokognicija, klinična fenomenologija

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