



The Psychotherapeutic Treatment of Schizophrenia: Psychoanalytical Explorations of the Metacognitive Movement

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Abstract

Metacognition refers to the set of activities which allow persons to have a sense of oneself and of others available to them within the flow of daily experience. These activities range from awareness of discrete aspects of experience to their synthesis into larger, more complex ideas. Following research documenting the existence and influence of metacognitive deficits in schizophrenia, psychotherapeutic frameworks have emerged aiming to improve metacognition in this group. Metacognitive Reflection and Insight Therapy (MERIT) is one such integrative psychotherapy framework. Therapeutic targets and principles of MERIT are intended to be integrative but share common characteristics with psychoanalytical tradition in the treatment of schizophrenia. This paper accordingly explores how psychoanalytic theory can help explain how the effects of MERIT upon metacognition and self-experience in schizophrenia may reflect its effects on repairing the collapse of the boundary/connection between self and the world, mental fragmentation, and the lack of symbolization.

Keywords Schizophrenia · Metacognition · Psychoanalysis · Individual psychotherapy

Metacognitive Psychotherapy in Schizophrenia

Although individual psychotherapy for persons suffering from schizophrenia has been found to be effective in randomized studies (Rosenbaum 2015), little work has explored *how* psychotherapy might contribute to clinical improvement and recovery. One recent approach has suggested that

psychotherapy may promote recovery from schizophrenia by facilitating growth of metacognitive capacity (Lysaker and Dimaggio 2014). Metacognition within this framework, referred to as the integrative model of metacognition, is conceptualized as a spectrum of activities which range from the awareness of discrete experiences in the moment (such as perceptions, emotions and thoughts) to broader, complex senses of self and others which are made on the basis of the integration of considerable amounts of information (Lysaker and Klion 2017; Lysaker et al. 2018). As such, metacognition is foremost an ongoing set of processes that integrate pre-reflective and reflective experiences which include embodied, affective and cognitive elements, and which occur in a variety of ever-changing contexts in the world. Metacognitive processes are necessarily intersubjective as well as dynamic, changing over time as individuals gain and lose capacity to integrate information. As a result, metacognitive abilities are multi-determined and have a bi-directional relationship with a range of psychological, social, and biological processes. When fully intact, metacognition allows a sense of self and others in a manner that is fluid, immediate, and responsive to the social context (Lysaker et al. 2018).

The main protagonists of metacognitive psychotherapy in schizophrenia advocate an integrative psychotherapeutic approach referred to as Metacognitive Reflection and Insight

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Therapy (Lysaker et al. 2019; Lysaker and Klion 2017). MERIT specifically was created to be able to be practiced by therapists from different backgrounds, but as such little work has explored how it theoretically affects the processes which underlie alterations of sense of self and ultimately psychosis. In this article, we accordingly propose to extend existing work on MERIT by exploring how the proposed activities of Metacognitive Reflection and Insight Therapy (MERIT, Lysaker and Klion 2017) can be conceptualized as addressing the basic processes identified by psychoanalysis as laying at the root of psychosis. Our aim is to offer an explanation, through the lens of psychoanalysis, for why and how MERIT affects alterations in self-experience in patients with schizophrenia which may touch essential processes in psychology and the psychotherapy of schizophrenia.

Psychoanalysis, Disintegration of Experience, and Meaning Making in Schizophrenia

In ways that parallel and significantly predate observations made about metacognition, starting with Freud, we can trace the evolving metapsychological descriptions of schizophrenia in psychoanalysis, which stem from in-depth relational clinical experience with people suffering from schizophrenia. Freud considered a withdrawal of libidinal bonds (cathexes) from the external world or from unconscious mental representations of objects, referred to as decathexis, as a central point of the psychotic process, and as a regressive response to intense frustration and conflicts, with a fixation of the libido in the narcissistic objectless phase. In a later phase of restitution, the missing bonds are replaced by hallucinations and delusions as an attempt to re-establish the object relationship. In that way, psychotic symptoms act as a defense against disintegration and anxiety (Kuchenhoff 2018). Freud described a co-occurring formation of psychotic grandiosity with the aid of the metaphor of the amoeba with pseudopodia, describing that this occurs when libido arises from indifferent psychic energy only through cathexes to objects (as pseudopodia), with a distinction between ego-libido and object-libido. Megalomania then results from a superposition of withdrawn libido from objects on primary narcissism (Treurniet 2018) and as such there is an explanation for the grandiosity often found in schizophrenia. In this condition, all events are understood by patients suffering from schizophrenia as being in reference to them and even delusions lead them to see everything as a reference to their persecution. A further consequence of decathexis is a condition that is known as primary process, which occurs in dreams. The withdrawal of cathexes from objects is followed by a severe fragmentation of energetic bonds

with internal mental objects and psychical dissolution that is characterized by replacement of external physical reality by psychic reality, with a loss of differentiation between them. Other features of primary process include the absence of contradiction, negation or time, forming of substitution and condensation mental products, which brings about a discharge of excitation and is related to the experience of satisfaction (Shaw 2014). This state leads to disruption in the formation of mental representations and to a disturbance of the synthetic function of thinking. The similarities of objects are not recognized according to symbols in thoughts, but in line with sensory-perceptual identity. In Freud's terminology, word-presentations are replaced by thing-presentations (Robbins 2018). On the other hand, the secondary process is formed when the energy of drive cathexes of the primary process becomes bound and does not tend to immediately discharge, but to accept delay (Modell 2014). In this way, a new energy distribution of cathectic energies arises, which results in new directed forces within the ego, which participate in forming personal values or attitudes and are related to thinking (Cutler and Brakel 2014).

The idea of defective synthetic mental functions through the splitting of mental processes can also be found in later years in the writings of Kleinian psychoanalysts. Segal observed a limited differentiation between the symbol and the thing, which is represented by the symbol in schizophrenia. She proposed the term 'symbolic equation' as a basis of schizophrenic concrete thinking, where symbols are felt and treated as though they were identical with original objects. The reason for this is that the person, in order not to be separated from the object, violently projects fragmented parts of the ego and internal objects on an external object that identifies with it, together with the symbol as a creation and function of the ego (Hinshelwood 2018). Thus the symbol falls out of its triangulation function (the ego, the object, and the symbol) that is necessary for development of the capacity for thinking and objectivity (Coelho 2016). According to Bion, the capability of emotional and mental processing emerges through an early relationship when an infant uses a primary object as 'container' for endangering unthinkable emotional experience. This then can process projected split-off fragments of experience and pass them back to the child in an acceptable form. Later, an infant can identify with this containing function, which is a basis for his/her mental processing (Mawson 2017). Later, De Masi (2016, 2017) described this process as emotional unconsciousness, through which people can intuitively perceive emotional nonverbal signs and communications, process them and react unconsciously in return. In schizophrenia, due to a deficit function of the primary container or severe emotional trauma, the emotional unconsciousness is hypothesized to be damaged, resulting in the inability to perceive

and respond to emotions, to construct a sense of personal identity, to make self-observations, and to be aware of her/his mental and emotional processes.

Psychoanalysis to Disintegration in Psychotherapy

Although Freud was pessimistic about the possibility of creating transference within a patient with schizophrenia, many other psychoanalytical schools were not (Kuchenhoff 2018). They inferred that a therapeutic relationship, which is the agent of change, could be formed with the healthy non-psychotic parts of patient's egos, and allowed that a rudimentary symbiotic relationship could be formed on the basis of primitive defense mechanisms—splitting and projective or introjective identification. In this respect, psychoanalytical schools proposed slow stepwise models of progress of the therapeutic relationship, in which the patient and the therapist undergo a mutual process of change and development, starting potentially from very undifferentiated stages.

In relation to an early undifferentiated relationship in the therapy, Ogden (2018) thought that a sparse emotional contact between patient and therapist was due to hidden inner aggression which makes it impossible for patients to externalize and to offer to the therapist for his/her unconscious mental processing. Instead, the patient focuses his/her aggressive mental forces on his/her own capabilities to experience or to think. Consequently, objects and behaviors of the outside world are emotionally equivalent for patients and they can only physically differentiate between them (Ogden 2018). Many psychoanalytic authors derived the origin of this deficient intersubjectivity in a therapeutic relationship from early attachment relationships between child and caregiver. According to Anzieu (2016) a lack of the most crucial interactions between mother and child, e.g. exchange of smiles, solidity of holding and handling, synchronization of rhythms, blocks further differentiation between the subjective and outer world of an infant, between the part and the whole, or between reality and imagination. Consequently, the body is felt as two-dimensional without any 'inside'. Instead of differentiation, only an 'adhesive' bond which resembles the child's fantasy of having a common area of skin with the mother, developmentally persists. Thus, there is an absence of potential space for symbolization and otherness. For patients without the capacity for differentiation, Anzieu (2016) recommended reconstruction of those structures which enable the symbolic understanding of body limits as a basis for further recovery of the patient's identity and past. In this case the therapist uses interplay of his/

her attention, preoccupation, and active intervention. Along with this, the therapist's words could replace the original tactile contact (Werbart 2019). The therapist should maintain a stable therapeutic setting, not make interpretation and not be forced into action (Ogden 2018). Alternatively, the therapist should assist the patient to differentiate, to establish a working alliance, to support better understanding of his/her feelings, attitudes, and subjective motives in a concrete situation in the interpersonal field (Rosenbaum 2015).

As the patient becomes more able to differentiate, changes in the therapeutic relationship begin to come strongly to the foreground. These may be manifested as a loosening of boundaries between patient and therapist. In this context, Ogden (2018) described that aggressive orientation towards a patient's own mental content is transferred to the therapist, limiting his ability to think or experience. The therapist can then identify with this projection and sense his/her own insignificance. The crucial task for the therapist is to form thoughts that continue to be useful. Implicit reactions of the therapist and reflections upon countertransference lead to internalization processes on the side of the patient. According to Searles (2018), the therapist experiences hopelessness and anger, which he/she reverses into solicitous care of the patient under the pressure of guilty feelings. The therapist should 'survive' the attack by the patient, who can subsequently identify with him.

In the further progress of the therapy, the confusion between the patient and the therapist begins to be resolved in the way of a gradual separation between both. According to Ogden (2018), inner destructive forces are redirected from the therapist towards the own mental space of the patient, resulting partly in the ability to contain one's own painful, fearful thoughts and feelings, and partly also in an increase of blocking, fragmentation, projection, or introjection, which also give rise to psychotic symptoms. On the other hand, this change frees the therapist and gives him/her more space for empathy and interpretation. The therapist is felt as a separate person whose loss could be feared and mourned. These processes open up a space for elaboration of unconscious hatred with the aid of containment and interpretation. In this phase, gradual disillusionment with narcissistic collusion should take place (Frosch 2014), which means total compliance of the patient with the idealized therapist. The resulting breaking down of psychotic grandiosity results in more activity and responsibility by the patient for his own progress. However, the therapist must also recover his personal grandiosity and covert devaluation in the therapeutic dyad. In the late phases of psychotherapy, psychotic symptoms recede and the patient opens up to the world of relationships and is enriched by new possibilities of introspection (Ogden 2018).

MERIT as a Transtheoretical Integrative Framework in the Psychotherapy of Schizophrenia

Metacognitive Reflection and Insight Therapy (MERIT) is a novel integrative approach to psychotherapy for schizophrenia (Lysaker and Klion 2017). The development of MERIT was informed by a range of psychotherapy theoretical traditions and in particular by empirical work suggesting that relatively more severe deficits in metacognition are commonly found in schizophrenia and linked to poorer concurrent and prospective outcome (Lysaker et al. 2019). MERIT utilizes the integrative model of metacognition, which as noted above, frames metacognition as a fundamentally intersubjective phenomenon which includes a spectrum of mental activities that range from discrete to synthetic. MERIT was developed to offer a practice framework intended to guide therapists to target metacognitive deficits and help an individual to regain or develop a newly enhanced capacity for metacognition. In this regard, MERIT understands the core problems in schizophrenia in a manner similar to how psychoanalysis does: disturbed synthetic function of thinking, together with fragmentation of inner psychic experience; impoverished mental representations; inability to create the sense of own self and to make use of own thinking processes for complex reflection of oneself and the surrounding world to manage life adequately. It also shares with psychoanalysis a common therapeutic target: the enhancement of the synthetic functions of thinking, with the aim of creating more stable representations of the self and others.

MERIT as an integrative practice is defined by the presence of eight elements or activities which should take place in each session. Each is suggested to both independently and synergistically promote the development of metacognitive capacity (Lysaker and Klion 2017). The first element of MERIT, which entails a focus on the patient's agenda, presumes that the patient has come to a session with some hopes or wishes that ought to be reflected. The patient could initially be unaware of his agenda, or the agenda could be contradictory. Dialogue or discussion of interpersonal processes as the second element of MERIT highlights the therapist's sharing his/her own thoughts about the patient or his/her agenda and mutually reflecting upon them. The dialogue promotes the patient's awareness of the therapist's mind and the reflections about the presence of another mind in general (De Jong et al. 2016). The third element is a focus on personal narratives concerning experiences from the patient's life. In the beginning, the patient may be able to recount fragments and will only later be capable of presenting more coherent and lengthy narratives. The fourth element, which

consists of identifying psychological problems from the material of the previous elements, emerges from the first three 'content' elements. The therapist helps the patient to understand life challenges and to develop a greater self-awareness. The fifth element, by discussing interpersonal processes between the patient and the therapist, enables the patient to develop a greater awareness of how he/she is relating to the therapist. The therapist stimulates thinking about how the patient perceives and relates to the therapist, and enhances more complex reflections on the therapeutic relationship. The therapist eliciting discussion on the progress of therapy is referred to as the sixth element. The patient can obtain a better awareness of how a session or the therapy affects him or her positively or negatively. The seventh element encourages the therapist to reflect with the patient on him/herself and other people. The eighth element comprises the therapist's facilitation of the patient's use of his/her unique self-knowledge and knowledge of others to respond to psychological or social difficulties and challenges faced (referred to in MERIT as metacognitive mastery). Research that supports MERIT, using open and randomized trials, as well as qualitative studies and case work has been summarized elsewhere (Lysaker et al. 2019).

Psychoanalytic View of MERIT's Elements

We now turn to explore how and why the MERIT framework may potentially address some of the core difficulties which psychoanalysis posits at the root of psychosis (the collapse of the boundary/connection between self and world, mental fragmentation, the lack of symbolization, the deficit function of the primary container). For this reason, we chose the first six elements of MERIT (agenda, dialogue, narrative focus, psychological problem, reflection on interpersonal process, reflection on progress) to discuss these therapeutic components from a psychoanalytical point of view. We do not explore the final two elements which pertain to the need to intervene or relate to the patient in ways that match the patient's maximal capacity for metacognition, as these rely on the use of a specific assessment system that is beyond the scope of this paper.

Agenda

Dealing with a patient's unconscious agenda is one of the crucial tasks of the therapist. The potential of the therapy could be utilized if the therapist is more aware of and work with what unconscious motifs or related affects are hidden within the patient's behavior, speech or appearance. The tradition of Kleinian psychoanalysts uses the term, 'the total situation', as a form of the complex transference in which

the patient uses projection and introjection and transfers important object relations, emotions, and defenses from the past to the present (Joannidis 2018). It includes all that the patient brings into the relationship, not only what he or she is saying, but also how it is being said and how the therapist is being used. For instance, very rapid speech by the patient, not allowing the therapist to say anything, might be understood as an unconscious fear of the therapist's intrusion. Rather than using more complicated interpretations of the patient's emotional state the therapist simply describes the current situation to the patient. This better corresponds to the patient's insufficiently formed emotional self- and object-representations and by limited symbolic functions. Only the therapeutic support of differentiation in self and objects can bring about later recovery of the agenda.

Dialogue

A dialogue foreshadows the active role of the therapist in the treatment of psychoses. It highlights a felt presence of the therapist by the patient, which is perceived as necessary for the support of the fragile interpersonal border between both. Sharing thoughts about the patient is closely linked to the therapist's function as the container, by which he or she can synthesize countertransference feelings and observation of the patient. In this way, the therapist can present the split material from the patient as a coherent whole. Then, in a new and more acceptable way, the patient can understand his or her mental material with the aid of the therapist's reaction. Moreover, acceptance of the therapist's container by the patient means a better building up of his/her own containing functions (Mawson 2017).

Narrative focus

Narration in schizophrenia is remarkable from two aspects—its character and content. As to the nature of discourse in schizophrenia, it lacks cohesiveness, usual space–time structure, or intelligible causal relations. A further characteristic of the schizophrenic narrative is its concreteness, related to the symbolic equation described by Segal (Hinshelwood 2018). The common differences between words, things, body states, and actions are missing. Words and sentences lose their representative and symbolic nature. Instead of reflection or self-awareness, we find equivalence, immediacy, and action (Martens 2012). From the developmental point of view, the disturbances of cohesion, time, space, causality, and symbolic functions in a schizophrenic narrative might be seen as 'regression' or insufficient maturation from the early stages of infant development. Consequently, differentiation and cohesiveness in the narrative might arise from

attachment-related experiences. In this context, narration in psychotherapy could contribute to the maturation of representative and symbolic functions of the patient in the therapeutic relationship. The strengthening of the concept of time through narration has the effect of improved reality-testing and social-emotional awareness (Martens 2012). But there is also another aspect to narration as a therapeutic agent. The lack of cohesiveness in the narration in schizophrenia might also be related to the split of emotional experience from conscious awareness. The narration to the analyst of the patient's past may reveal a hidden connection and links which, up to that time, had existed as unbound fragments and which could be experienced as a surprise on the patient's side. Creating 'sutures' between consciousness and split fragments of experience enables old memory traces related to a previous split-off experience to be endowed with a new meaning as the patient speaks and organizes the facts of his or her history to relate them to the therapist (House and Slotnick 2015). In this way, with the aid of narration, the history of the patient with new meaningful contexts can be created.

Psychological Problem

Patients suffering from schizophrenia are often unaware of their psychological problems. They often tend to act them out, or the content of the problem may be revealed in psychotic symptoms. The therapist can facilitate understanding of the symptoms in the relationship between patient and therapist, or the patient's current interpersonal conflicts (Curtis 2014). For instance, hallucinations can be understood as mentally 'unmetabolized' residues of interpersonal, hostile or destructive traumatic experiences. Von Haebler (2015) used the expression 'appellation' (Benennung) for the therapist verbalizing emotions which are not yet fully crystallized in patients. When the patient can 'learn' how to translate symptoms, the therapeutic dialogue can move more into the realm of interpersonal issues or psychological distress. In this respect, patients also face serious dilemmas in the interpersonal sphere. Mentzos (2015) described such dilemmas as an extreme need by the patient for a symbiotic bond with the object, simultaneously with the wish to abandon it and to free himself from it, in other words, the dilemma between the loss of the self or of the object that results in extreme anxiety or the formation of a psychotic symptom. The patient may react by clinging to the object and be at least partially aware of his or her need, but unaware of the fear of destruction. For instance, he or she may then show undifferentiated dependency on a parent, despite hallucinations or obsessive thoughts with an aggressive content that disavow the destructive fear of the parental object.

Reflection on Interpersonal Process

Facilitation of reflection on the process within the therapeutic couple is a cornerstone of the psychoanalysis. Interpretation is the standard tool for enhancing reflection on the interpersonal process. However, in the context of psychosis, usual interpretations of the verbal content of a patient's narration may induce distress on the side of the patient, interfering with the desired reflection because of lower metacognitive functions, hand in hand with the reduced ability for symbolization and a concrete form of thinking. Therefore, instead of interpretations of the transference, the therapist may rather use a description of the current interpersonal situation, referring to the non-verbal cues of the patient. The therapist's reactions to the patient should capture the way in which the patient communicates, what is missing in his or her narrative, and why, rather than the verbal content. Usual transference interpretations can be used only later in the therapy when the patient distinguishes between the therapist as a real person and ideas about the therapist (Carsky and Rand 2018). The other methods of easing the patient's acceptance of transference interpretation are called 'analyst-centered interpretations' as described by Steiner, e.g. "You experience me as...". The patient must get rid of his dangerous mental content and project it on the therapist. Thus, it is more thinkable for the patient to observe it on the person of the therapist than when the therapist 'pushes' the projected material back on to the patient in the form of patient-centered interpretations, e.g. "Inside you there is..." (Busch 2015).

Reflection on Progress

Progress in the therapy is poorly recognizable for patients in psychosis where primary process of thinking prevails with its characteristic feature of timelessness. Reflection on progress strengthens formation of inner representations comprising better established concept of time. Along with this, reflection on progress can also improve realistic self-esteem in patients. However, there could also be a danger of negative therapeutic reaction as a result of his or her unconscious fear of change, when the therapist begins to praise the progress of the patient. In this case, the therapist perceives this anxiety through countertransference and tries to relieve it through an emphasis on progress and thus exacerbates the fear of change in the patient (Yerushalmi 2017).

Discussion

In this article, we have sought to use a psychoanalytic conceptualization of how alterations in mental synthetic function and intersubjective space in schizophrenia occur

in order to understand how a novel therapeutic approach, MERIT, may be an effective treatment in schizophrenia. Specifically, we have explored how the first six of the eight MERIT elements may address the kinds of fundamental collapse of self-experience described by a psychoanalytical approach. It follows that MERIT allows for the establishment of an intersubjective space in which patients can symbolize psychological pain and then both practice and tolerate integration slowly having less need for fragmentation and greater metacognitive capacity.

One implication we see from these reflections is that research and therapeutic practice concerning synthetic metacognition and psychoanalytic understanding could have mutually enriching influence. The metacognitive approach might provide operational definitions for psychoanalytic concepts in schizophrenia related to self-disturbance and the emotional, cognitive, and social disruptions associated with psychoanalytic understanding of fragmentation. For instance, the capacity to organize self-experience, to understand others in a coherent manner, or to see oneself from an outside perspective could all be operationalized within the framework of integrated metacognition. Operationalized in this manner, and correspondingly utilizing the associated measurement scales (e.g. the MAS-A as a marker for disruptions in self-experience), psychoanalytical therapists might better quantify and track progress in psychotherapy. On the other hand, psychoanalysis, with its rich descriptions of psychosis, may continue to offer clinicians and researchers insights into deeper processes in schizophrenia, particularly as related to disruptions in intersubjective space and mental fragmentation, difficulties which can lay at the core of psychosocial dysfunction (Hamm and Lysaker 2016).

Additionally, both psychoanalysis and MERIT can be seen to share some common aims and attributes in regard to the psychotherapy literature for schizophrenia. Both draw attention to the emotions of people suffering from schizophrenia, such as fears of disintegration, anger, envy, or sadness, feeling of loss or unbearable psychological pain, which tackle behavior, interpersonal relations, or the psychotherapeutic process. Both approaches also highlight the importance of intersubjectivity in therapy and recognize that this is a process that unfolds emotionally on both sides—the patient and the therapist. The approaches share an interest in pursuing meaning-making, the cultivation of insight, and aim to promote movements from states of fragmentation to integration. All of these shared aims seem to us a valuable shared contribution to a field in their emphasis on personal recovery in schizophrenia and may offer a modality in which clinicians can assist persons in moving toward personal recovery, which seems particularly important at a time when contemporary treatments are often narrowly focused on symptom relief and skill remediation (Leonhardt et al. 2017).

Turning to future directions, one area of apparent difference between the metacognition and psychoanalysis research that this paper has not explored at length concerns the developmental roots of metacognition itself. The metacognitive literature has contended that there are likely multiple pathways to metacognitive compromise, but has attended less to developing or aligning with a particular model of developmental psychodynamics. Future work might more thoroughly use the operational concepts of metacognition to explore and further elaborate models of the development of these basic psychological structures and their possible disruption in schizophrenia.

One potential avenue for understanding this may be found in the work of Stern (Michels 2017), who, on the basis of observational infant studies, has described the phases of creation of a ‘sense of self’, within the interaction and early relationship between a child and primary caregiver. For example, he has described how early in life there is evidence that after the formation of the first signs of regulatory organization during the first two months of life, there are further phases of establishing the layers of self. In this period, basic mental capacities arise, such as the sense of authorship of one’s own actions, volition, proprioceptive feedback, predictability of consequences, the sense of being a non-fragmented physical whole, early inner qualities of emotions patterned by experience, and the sense of continuity in time. Later, but even before children start to represent and imagine things in their minds and to use language as a new tool for relatedness, they discover that they have their own mind, just as others have their minds and that inner subjective experience can be shared, which opens up the world of intersubjectivity, empathy or shared fantasy (Michels 2017). It is thus possible that for some, disturbance in attachment play a role in the development of metacognitive deficits (Beebe 2014; Brown 2017). It is also possible that the recovery of metacognitive capacity, regardless of its etiological roots, follows a developmental course similar to what Stern has described. Following this, future research might look to integrate findings from observational infant studies, studies from early childhood trauma, and psychological therapies for schizophrenia, to deepen the understanding of the intersubjective therapeutic processes necessary for effective treatment.

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Compliance with Ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research Involving Human Participants and/or Animals This article does not contain any studies with human participants or animals performed by any of the authors.

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