Review

Impaired Corollary Discharge in Psychosis and At-Risk States: Integrating Neurodevelopmental, Phenomenological, and Clinical Perspectives

Michele Poletti, Alfonso Tortorella, and Andrea Raballo

ABSTRACT

The brain is increasingly viewed in contemporary neuroscience as a predictive machine; its products, such as movements and decisions, are indeed accompanied by predictions of outcomes at distinct levels of awareness. In this conceptual review, we focus on corollary discharge, a basic neurophysiological mechanism that is allegedly involved in sensory prediction and contributes to the distinction between self-generated and externally generated actions. Failures in corollary discharge have been hypothesized as potentially relevant for the progressive development of positive psychotic symptoms such as passivity delusions and auditory verbal hallucinations. We articulate this framework adopting three confocal lenses, namely, the neurodevelopmental, phenomenological, and clinical perspectives. Converging evidence from these research domains indicates a possible developmental cascade leading to increased lifetime risk of psychosis. That is, early childhood alterations of corollary discharge mechanisms, endophenotypically expressed in motor impairment, may concur with a progressive fading of the feeling of self-agency on one's own experiences. Combined with other age-dependent situational challenges occurring along development, this may progressively hamper the ontogenesis of the embodied self, thereby facilitating the emergence of anomalous subjective experiences such as self-disorders (a longitudinal index of schizophrenia spectrum vulnerability) and broadly conceived clinical high-risk states. Overall, this condition increases the risk of developing passivity symptoms, phenotypically expressed in a severity gradient ranging from intrusive thoughts to passivity delusions and auditory verbal hallucinations. Empirical and clinical implications of this framework, as well as future scenarios, are discussed.

Keywords: Corollary discharge, Obsessive-compulsive disorder, Schizophrenia spectrum disorders, Self-disorders, Sense of agency, Sensory prediction

https://doi.org/10.1016/j.bpsc.2019.05.008

The brain is increasingly viewed by contemporary neurosciences as a predictive machine that makes sense of the world by predicting what we will experience and then updating these predictions as the situation demands. In this framework, actions and decisions are accompanied by predictions of outcomes, and in a reverberating feedback loop the mismatch between predictions and outcomes enables an ongoing recalibration to achieve planned goals. These predictions are generated at distinct levels of awareness—from nonconscious sensory predictions generated for movements to conscious predictions generated during decision making (1–4).

In this review, we focus on a specific basic neurophysiological mechanism—corollary discharge (CD)—that is crucially involved in sensory prediction. Briefly, CDs are copies of motor commands used to form a prediction of sensations from self-generated actions, which are identified in single-cell recordings from a range of organisms (e.g., insects, crustaceans, primates) and in multiple sensory domains (e.g., visual, auditory) (5,6). The motor system continuously compares these internally predicted outcomes with actual perceived outcomes

and, if necessary, updates predictions based on received sensory feedback (6,7). Being involved in the prediction of sensations from self-generated actions, leading to sensory attenuation in case of congruent matching between sensory expectations and sensory consequences, CD mechanisms contribute to, among other mechanisms (8), the distinction between self-generated and externally generated actions (5).

In a historical perspective, Feinberg (9,10) was the first to hypothesize that CD mechanisms analogous to those involved in sensorimotor predictions could also be involved in the distinction between endogenous and externally induced neural events of consciousness and that the alteration of these mechanisms in patients with schizophrenia could be involved in the development of psychotic symptoms such as passivity delusions and hallucinations. The presence of an altered sensory prediction in schizophrenia spectrum disorders (SSDs) was empirically confirmed (11,12), and this mechanism was involved in causal models of psychotic symptoms, for example, in terms of altered source monitoring (13). Delusion of control and auditory verbal hallucinations (AVHs) were

especially framed within this paradigm (14,15); for example, a failure in the sensory prediction of inner speech (16,17) could be involved in its external misattribution (18–20), and AVHs would indeed emerge at the zenith of the external misattribution of inner speech, experienced and thematized in terms of hearing one's thoughts spoken aloud and/or externalized commenting voices (21).

Starting from this empirical and theoretical background, we extend this framework in three intertwined directions: neurodevelopmental, phenomenological, and clinical.

The first direction concerns the developmental dynamic of the impaired sensory prediction (based on altered CD mechanisms) detected in adult subjects with psychosis in light of the neurodevelopmental hypothesis of schizophrenia and the clinical staging of psychosis. Indeed, if psychosis is as an end-stage phenomenon preceded by premorbid and prodromal stages and clinically emerging during late adolescence or early adulthood, in which stage (along disease progression) does the alteration of CD mechanisms occur?

The second direction is phenomenological and concerns the subjective experience associated with impaired CD mechanisms. In this perspective, the distinct levels of self-awareness (see Figure 1A) described by phenomenology, and particularly the sense of ownership (SoO) and sense of agency (SoA), may provide a useful heuristic framework.

The third direction is clinical and addresses the potential psychopathological manifestations triggered or somehow consolidated by altered CD mechanisms. Empirical studies showed that some characteristic psychotic symptoms such as passivity delusions and AVHs are associated with a failure of CD mechanisms in terms of external misattribution of self-generated actions; however, to better characterize the underlying pathogenetic sequence, it is crucial to define whether altered CD mechanisms are all-or-none phenomena limited to the genesis of psychotic symptoms or whether they could be expressed through a gradient of severity spanning across several symptomatic manifestations.

NEURODEVELOPMENTAL PERSPECTIVE

In the sensorimotor domain, CDs are copies of motor commands used to form a prediction of the sensation from self-generated movements and represent a neurophysiological process identified in single-cell recordings from a range of organisms and in multiple sensory domains (5). CD mechanisms contribute, among other mechanisms (8), the distinction between self-generated (accompanied by CD) and externally generated (not accompanied by CD) actions; for example, if sensory predictions of self-generated actions match sensory consequences, sensations are felt as less intense (i.e., sensory attenuation) (22).

Empirical evidence from developmental studies indirectly suggests that CD mechanisms are likely to have an early onset in human development; by 2 months of age, neonates are already able to discriminate precisely between self-stimulation and exogenous stimulation (23,24), and the integrity of CD mechanisms is probably needed for such discrimination.

If CD mechanisms have an early origin and are altered in adult subjects with psychosis, a fundamental issue is the timing of occurrence of potential alterations and the beginning of the related endophenotypic effects. Both the neurodevelopmental hypothesis of schizophrenia (25) and the clinical staging model of psychosis (26) consider psychotic manifestations as end-stage phenomena preceded by premorbid and prodromal manifestations, which become progressively more specific along disease progression. In this respect, the following questions remain unanswered:

1. Which are the critical stages, along the neurodevelopmental trajectory leading to psychotic symptoms, during which alterations of CD mechanisms occur?
2. Do they occur in late clinical stages (i.e., triggering frank psychotic symptoms such as passivity delusions and AVHs), or do they rather exert a more temporally remote action already in premorbid and/or prodromal stages (e.g., triggering a set of endophenotypic manifestations not directly related to psychotic symptoms)?

Although not directly evaluated, several empirical lines of evidence indirectly suggest that alterations of CD mechanisms may have an early premorbid origin, triggering complex long-term developmental dynamics that may result in psychotic symptoms in young adulthood.

First, motor coordination impairment in childhood is presumed to be subtended by copotentiating impairments in two key basic processes involving movement circuits: CD mechanisms and the sensory feedback to estimate actual body states (27–29). In comparison with typically developing peers, in children with motor coordination impairment the sensorimotor remapping is marked by a larger discrepancy between sensory and motor signals in order to maintain continuous learning and adaptation; that is, these children have difficulties in processing error signals used for adjusting action that arise from comparing sensory feedback with CD. The deficiencies in error signal processing may be due to noisier or inefficient sensory feedback and impaired CD mechanisms, both of which have been directly documented in this condition (30,31). Inspired by Wolpert et al.'s internal model (4), another model of childhood motor impairment—the internal deficit model (32)—suggests that these children have difficulties in generating or using predictive estimates of body position as means of correcting actions in real time; this would also affect their ability to learn new internal models or modify existing ones. Thus, even within the internal deficit model, impaired CD mechanisms may be causally involved. Finally, neuroimaging studies have not yet collected robust evidence, but they preliminarily support the idea that performance deficits of these children tend to map to functional and structural issues in a distributed neural network (e.g., frontoparietal and parieto-cerebellar structures, corticospinal tract) that enables motor control and learning and could be characterized by both early deviance and maturation delay (33).

Second, childhood motor impairment is longitudinally associated with an increased risk of schizophrenia (34,35) and schizotypy (36), and the childhood anamnesis of subjects who will develop schizophrenia is characterized by increased rates of later achievement of motor milestones (37) and motor impairment (38) [see (39) for an illustrative example derived from childhood home movies].
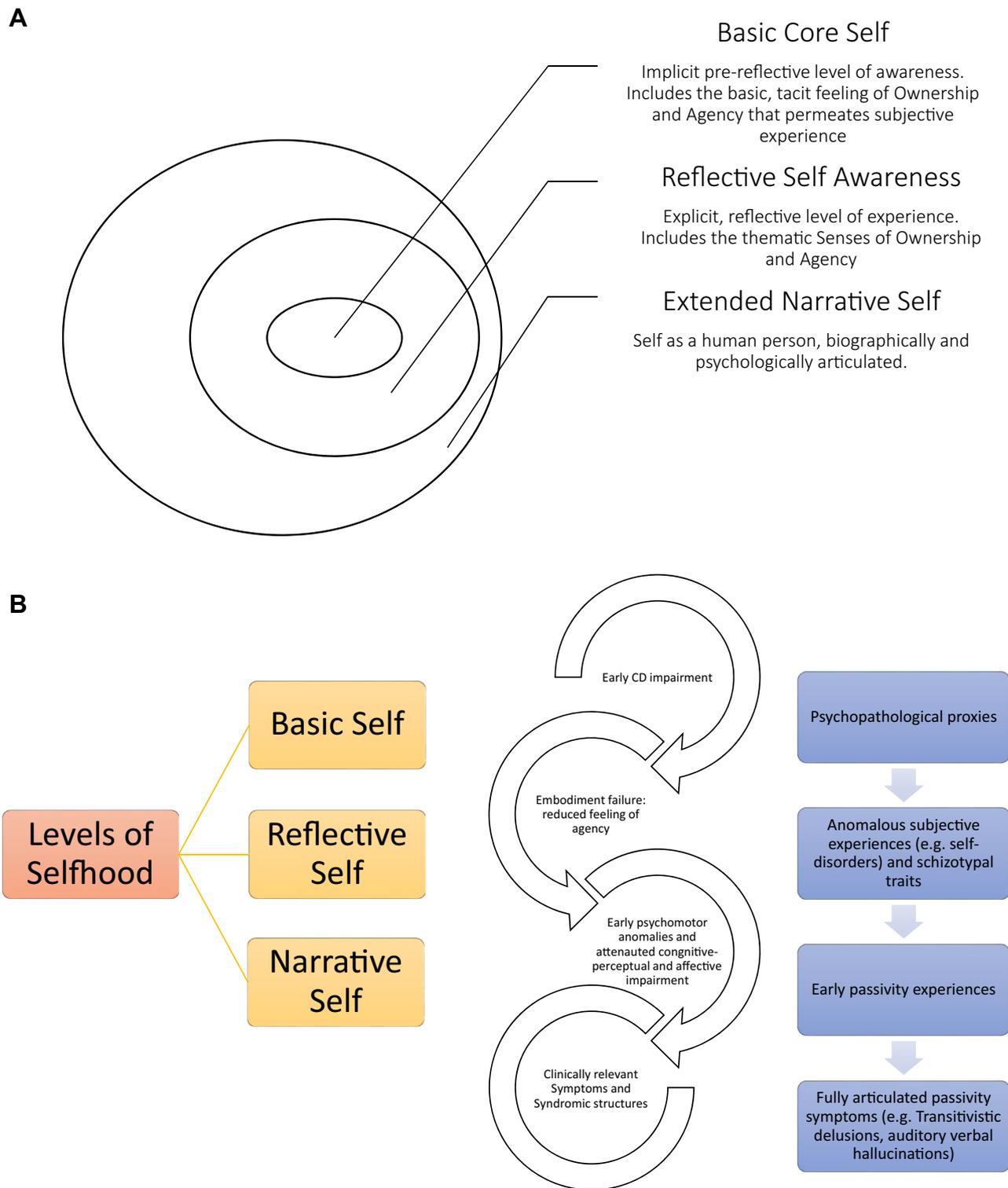
A

Basic Core Self

Implicit pre-reflective level of awareness.
Includes the basic, tacit feeling of Ownership
and Agency that permeates subjective
experience

Reflective Self Awareness

Explicit, reflective level of experience.
Includes the thematic Senses of Ownership
and Agency

Extended Narrative Self

Self as a human person, biographically and
psychologically articulated.

B

Levels of Selfhood

Basic Self

Reflective Self

Narrative Self

Early CD impairment

Embodiment failure:
reduced feeling of
agency

Early psychomotor
anomalies and
attenauted congnitive-
perceptual and affective
impairment

Clinically relevant
Symptoms and
Syndromic structures

Psychopathological proxies

Anomalous subjective
experiences (e.g. self-
disorders) and schizotypal
traits

Early passivity experiences

Fully articulated passivity
symptoms (e.g. Transitivistic
delusions, auditory verbal
hallucinations)

Figure 1. Levels of self-awareness **(A)** and their psychopathological articulation along with the developmental cascade **(B)**. CD, corollary discharge.

Within motor impairment, oculomotion is particularly relevant. Indeed, CD mechanisms have a crucial role in maintaining perceptual stability across eye movements (40). The smooth pursuit system reveals a maturation delay in children with motor impairment (41), and impairments in smooth pursuit tasks (42,43) and double step (44) are reported in SSDs since

prodromal, ultra-high-risk states. Impairments of CD mechanisms while performing a double-step task have been shown in patients with schizophrenia (45), and prediction errors in oculomotor tasks have been related with clinical symptoms [for a review, see (46)]. The continuity of impairment from premorbid through prodromal to clinical stages, as well as their accurate assessment, strongly suggests the potentiality of oculomotor prediction tasks to study CD mechanisms in SSDs (47) even in non–clinically overt conditions and in genetically high-risk subjects (e.g., with schizotaxia).

Third, genetic risk for SSDs during childhood is associated with phenotypic impairments at the motor level, as highlighted by familial high-risk studies on offspring of subjects with a diagnosis of schizophrenia (48). Possible effects of the schizophrenia-related genetic load are early and substantial at the phenotypic level, as confirmed by distinct empirical evidence; a study reported early abnormalities in intermodal integration (e.g., an infant's ability to link movement with visual perception and integrate perception across modalities) in 8-month-old offspring of parents with schizophrenia (49), and the schizophrenia polygenic risk score [i.e., proxy values generated by combining multiple genetic markers, obtained through genome-wide association studies, into a single score indicative of specific lifetime risk for a disease (50,51)] is associated with early phenotypic manifestations (52), including nonoptimal overall infant neuromotor development at 2 to 5 months of age (53).

Fourth, along the stages describing the neurodevelopmental trajectory to psychosis, empirical studies have documented impairments that are consistent with altered CD mechanisms in prodromal or ultra-high-risk individuals (54,55) and in nonclinical subjects with high scores on the Schizotypal Personality Questionnaire (56); both these groups present an abnormality in suppressing cortical responsiveness to sensations resulting from their own motor actions as auditory stimuli during vocalizations.

In sum, CD mechanisms probably represent a uniquely informative opportunity and plausibly a key neurophysiological domain to better understand the link between motor impairment and developmental liability to psychosis. Indeed, several subtypes of motor abnormalities, including athetosis, chorea, dystonia, bradykinesia, tics, and stereotypies, are elevated in clinical stages of schizophrenia, even among drug-naïve individuals (57), but only motor lag and motor coordination impairment emerge relatively early during developmental years (35,38), and these domains are mainly dependent on sensorimotor integration provided by CD mechanisms.

Available empirical evidence, on the basis of the tight intertwine between CD integrity and harmonic motor development, strongly suggests that an alteration of CD mechanisms could occur relatively early along the neurodevelopmental trajectory that increases the risk of later psychotic states. However, is motor impairment just an indirect phenotypic proxy of broad neurodevelopmental alterations putatively associated with prospective risk of developing psychosis (i.e., akin to an epiphenomenic flag) or, rather, is it a pathogenetically central kernel (e.g., a direct manifestation of a latent pathophysiological mechanism causally involved in the neurodevelopment of psychosis) (58)? In the next sections, we present and discuss data and hypotheses on this issue.

PHENOMENOLOGICAL PERSPECTIVE

The predictive account of brain function posits that the brain continually generates online models of the world, on the basis of current context and past experiences, and constantly updates them when the prediction and the actual input do not match (1–3). At the sensorimotor level, this continuous activity of prediction is based on CD mechanisms (4–7), mediating sophisticated sensorimotor and neurocognitive operations (e.g., perceptual stabilization, motor sequencing, sensorimotor learning) and contributing to the subliminal scaffolding of the experiential field.

The integrity of CD mechanisms is therefore necessary to enable the implicit sense of mineness of psychomotor experience and lend coherence and fluidity to our immediate interaction with the surrounding world. This tacit and implicit level of the stream of consciousness is the focus of the phenomenological analysis of subjective experience (59). In normal conditions, although this immanent level of functioning is always operative in the background of our experience, it is not the object of reflective or conscious awareness and is therefore referred to as antepredicative or prereflective. To this level (which tacitly permeates our interaction with the surrounding world) belong the SoO and the SoA, both of which are crucial for understanding the potential subjective resonances of altered CD mechanisms. SoO describes the immanent automatic feeling of mineness that accompanies our experiences (e.g., the sense that one is the person experiencing certain feelings or thoughts and in general undergoing personal experiences), while SoA refers to the experience of initiating and controlling an action (i.e., the feeling that one is the agent of an action) (59). Although an extensive review of SoO and SoA goes beyond the scope of this article [for review, see (60,61)], we outline some features of these senses that fit with sensorimotor predictions enabled by CD mechanisms.

Regarding SoO, differently conceptualized by bottom-up (mainly based on multisensory integration) and top-down (mainly based on internal body maps) cognitive models (62), the phenomenological approach of Metzinger (63,64) hypothesizes that a conscious self-representation is experienced as mine (a feeling of mineness) if it is transparent, that is, if only its content properties—but not its vehicle properties—become introspectively accessible. In this perspective, transparency occurs when the representational character of a representation's phenomenal content is not corepresented anymore; if this happens, the subject of experience "directly looks through" its own mental representation as if it was in "direct and immediate contact" with the representation's content [see (64), p. 236]. As a consequence, the subject of experience perceives this representational content as real and, if it is self-representational, as mine.

Regarding SoA, it can be distinguished as a feeling of agency—prereflective, low level, and nonconceptual—and a judgment of agency operating at a conscious deliberate level (65). Especially the implicit prereflective feeling of agency is suited for the scope of this review; the feeling of agency, or implicit SoA, is assessed through a behavioral or neurophysiological correlate of voluntary action. In these empirical paradigms, the participants are not explicitly asked about their own agentic experience, but their experience is inferred from a

measured correlate. The most widely used implicit SoA measure is intentional binding (IB); the IB effect refers to the subjective compression of time experienced between a voluntary action and its external sensory consequences. Usually, the time interval is underestimated only when the action is voluntarily but not when it is involuntarily or passively conducted (66).

Although the intertwine among motor control, perception, and cognition is a controversial work in progress (67), we approach the development of SoA according to one of the most explanatory frameworks (14,68,69), namely, the comparator model originally proposed by Frith *et al.* (70). This model takes as its starting point the motor control system and its computational processes (some of which are postulated to inform the SoA) and is mainly based on CD mechanisms. Indeed, if CDs match the actual sensory input (reafference), the movement is felt as self-caused and SoA may arise; on the contrary, in case of recurrent mismatch between CDs and sensory input, SoA may be weaker or absent. Although debated and criticized, provided empirical evidence against the comparator model, it is not strong enough to falsify and reject it, at least in the sensorimotor domain (68).

Although SoO and SoA are intertwined features of the tacit and implicit level of the stream of consciousness, they have been experimentally demonstrated as independent (71,72); indeed, although far from conclusive with respect to both constructs, empirical evidence in favor of an alteration of SoA in SSDs is more substantial (61,73) in comparison with empirical evidence on SoO, which is more controversial (61,74,75).

In sum, 1) CD mechanisms are impaired in SSDs, 2) CD mechanisms contribute to the emergence of SoA, according to the comparator model, in plausible synergy with other mechanisms (61), and 3) SoA is reduced in SSDs. These points jointly suggest that altered CD mechanisms, through their effects on implicit feelings of agency, may have a resonance at the subjective level of experience. If alterations of CD mechanisms occur early and affect the implicit prereflective relationship with the world by interfering with the emergence of the feeling of agency, it is likely that they may longitudinally contribute to trigger the emergence of those subtler subclinical modes of altered subjective experience (i.e., self-disorders) (76) that precede, often by several years, the onset of positive symptoms (77–80). Self-disorders are traitlike nonpsychotic anomalies of subjective experience that have been recursively corroborated as SSD vulnerability phenotypes. They encompass varieties of depersonalization, derealization, and similar distortions of the subjective experience, characterized by a diminished sense of existing as an embodied coherent subject, vitally immersed in the world and author of one's own actions. Self-disorders are clinically closer to initial disturbances of SoA than overt psychotic symptoms and might constitute a more robust (and developmentally earlier) phenotype to anchor the investigation of basic physiological processes as CD mechanisms conferring premorbid (schizotaxic) vulnerability to psychosis.

The hypothesis of a contribution of early altered CD mechanisms to the development of self-disorders in SSDs (76) coheres with developmental models of self, stating that the self unfolds from birth through multimodal perception and action

integration, progressively allowing the child to recognize himself or herself as distinguished from others (81–83). Moreover, impairments in the integration of perceptual information across distinct modalities (also enabled by CD mechanisms) were proposed by Parnas *et al.* (84) as possible early neurocognitive triggers of self-disorders (84), and such sensorimotor dysintegration is plausibly considered as an early vulnerability trait factor that could trigger primary diminished self-presence and a disturbed cognitive or perceptual grip on the world (85,86).

In particular, the persistence of altered CD mechanisms along the neurodevelopment, by interfering with the early, prereflective implicit attunement of individual sensorimotor acting with the surrounding world, may concur to the failure in the ontogenesis of the embodied self (see Figure 1B). According to phenomenology, such failure (aka disembodiment) conditions crucial features of the clinical stages of schizophrenia (87), in which perplexity, psychocorporeal dysintegration, fading sense of presence, and expropriation of the privacy of experience (e.g., passivity delusions) might come to the fore. In this perspective, CD mechanisms could exert a progressive longitudinal effect across development and—if altered—might trigger the emergence of (initially nonpsychotic) disorders of subjective experience (e.g., self-disorders). In the next section, we discuss whether this framework fits only with SSDs or might also intercept other psychopathological manifestation.

CLINICAL PERSPECTIVE

As mentioned in the introductory paragraphs, Feinberg (9,10) was the first to suggest that a failure of CD mechanisms, hampering the recognition of self-generated actions and therefore fostering their external misattribution, could be involved in the emergence of prototypical psychotic phenomena such as passivity experiences involving the feeling that individual thoughts, feelings, or actions are under external control. Although the internal model of Wolpert *et al.* (4) was not originally designed to distinguish between the use of CD mechanisms to automatically adjust movements and their use to consciously detect mismatch between the predicted and real outcomes of the action, it is plausible that their impairments might boost or at least increase the proclivity to develop passivity symptoms. This should be realistically contextualized on the background interaction of multiple mechanisms, including action selection monitoring, timing deficits, body representation, and CD mechanisms (46). The hypothesis that impaired predictive mechanisms, together with other neurocognitive mechanisms, are involved in the reduced feeling of agency of patients with schizophrenia with passivity symptoms received preliminary empirical confirmation (14,88,89) and then extended to the development of AVHs (18–21). In this case, it is inner speech that gets externally misattributed and is experienced as one's own thoughts spoken aloud or externalized commenting voices.

The fundamental question we attempt to answer in this section concerns the extension of the psychopathological reverberations of this mechanism. Do effects of altered CDs manifest only in SSDs, or are they expressed through a gradient of severity that could fit with a dimensional continuum, potentially spreading outside SSDs?

Regarding passivity experiences, ante litteram descriptions of disturbances of the senses of ownership and agency could be found in several historical sources. For example, in 1971 Taylor and Heiser (90) differentiated between influenced experiences and alienated experiences. Influenced experiences encompass those in which the patient knew that his or her own thoughts, feelings, and sensations were controlled or imposed on him or her by some external agent (in current terms, preserved SoO and reduced or absent SoA); in contrast, alienated experiences refer to the patient's awareness that his or her thoughts, feelings, and sensations were not his or her own in the sense that they were coming from an outside source (in current terms, reduced or absent SoO and SoA). The authors also acknowledged a continuum between influenced and alienated experiences, including intermediate or hybrid experiences; for example, the subject may be aware of his or her own thoughts, feelings, and sensations as if in some way they were not his or her own while simultaneously feeling that all this was due to some external influence. Subsequently, in 1979 Koehler (91) proposed a passivity continuum ranging from the mildest experience of passivity mood to the most severe negative-passive experience of alienation, passing through intermediated experiences such as general experience of influence, specific experience of influence, experience of influenced depersonalization, positive experience of alienation (e.g., thought insertion), and negative-active experience of alienation (e.g., thought withdrawal).

A similar course is described for AVHs, considered as the end-stage psychotic result of a progressive transformation of the experiential field. Such change was accurately described in terms of psychopathological transition sequences by Ebel *et al.* (92). Such transitions intervene along a coherent sequence leading from nonpsychotic experiential precursors to auditory hallucinations through a series of progressive experiential changes of increasing severity. These include basic disturbances of the thought stream (e.g., thought interference, thought block, pressure of thought), progressive depersonalization with intensified experience of thought spatialization, alienation, and/or autonomization of the interior dialogue (e.g, repeated inner self-instructions, self-comments, and/or self-conversations become progressively sonorized, automatized, and interfering), and loss of the ego boundaries, eventually culminating in omnipotent and omniscient alien voices and/or transitivistic experiences (93–95).

These basic alterations in the stream of thoughts, which might culminate in passivity delusions and/or AVHs, reveal a certain descriptive affinity and sometimes overlap with ego-dystonic intrusive thoughts characteristic of obsessive-compulsive disorder (OCD). Although in OCD the ego-dystonic and alien nature of such intrusion is generally related to their content rather than to their mode of presentation, the clinical overlap between OCD and SSDs is rather frequent and constitutes a challenge for early differential diagnosis. Notably, patients with OCD and their offspring present an increased risk for schizophrenia (96), obsessive-compulsive features are overrepresented in SSDs in comparison with the general population, and increased schizotypy is reported in OCD (97). This overlap may have a neurodevelopmental origin, hypothesized for SSDs (25) as for OCD (98); the neurodevelopmental account for OCD is suggested by neuroimaging (99,100) and

by the increased prevalence of perinatal risk factors also in OCD (101), representing possible triggers of an altered neurodevelopment. Indeed, considering neurological soft signs as a proxy of an altered neurodevelopment, they are meta-analytically reported with higher rates in OCD in comparison with healthy control subjects (102), especially in domains such as motor coordination and sensory integration that are particularly dependent on the integrity of CD mechanisms. Interestingly, poor fine motor abilities during childhood predict the persistence of early OCD symptoms during adulthood (103), and the severity of comorbid schizotypy in patients with OCD is associated with velocity gain in a smooth pursuit task (104), where performance is also based on CD mechanisms (46).

In sum, motor impairment in OCD could be considered of probable neurodevelopmental origin and in an intermediate position in a gradient of clinical severity from healthy subjects to the schizophrenia spectrum, in which motor impairment is more pronounced and worsening along clinical staging (57); this pattern could indirectly suggest an alteration of CD mechanisms in OCD, although with milder severity in comparison with SSDs. This hypothesis was preliminarily confirmed in an electroencephalographic study on patients with OCD (105). The authors measured suppression of the N1 component of the event-related potential during active generation and passive observation of visual feedback in patients with OCD, reporting significantly reduced N1 suppression to actively generated feedback as compared with passively observed feedback in comparison with control subjects; moreover, in patients with OCD, the N1 was not modulated by additional predictive motor cues as observed in control subjects. Overall, the findings showed a failure of patients with OCD in the sensory prediction of consequences of their own actions not accompanied by a sensory attenuation, suggesting a possible alteration of CD mechanisms in this clinical population. Further recent studies empirically confirmed a reduced implicit feeling of agency through the IB paradigm (106) and on intrusive thoughts (107) in patients with OCD.

Therefore, it is possible to hypothesize that a fraction of the co-occurrence of SSD and OCD features may rely on a common low-level ground of altered sensorimotor prediction of inner mental phenomena, from performed actions to generated thoughts. The experiential correlates of such alterations may be subjectively felt as a gradient of lack of control, fading sense of mineness (i.e., the intrinsic sense of ownership of one's own experience), and increasing passivity; milder alteration of sensorimotor predictions may lead to feelings of passivity and lack of subjective control of thoughts, which in turn may be experienced as intrusive, alien, and ego dystonic-dystonic. The failure of sensorimotor prediction and its further exacerbation in terms of external misattribution of self-generated stimuli to the environment may ultimately lead to more severe manifestations (e.g., AVHs, passivity delusions) (108).

CONCLUSIONS

In previous sections, we collected multilevel (neurodevelopmental, phenomenological, and clinical) evidence that could be integrated in a unitary view. We hypothesize a

possible developmental cascade starting from early childhood alterations of CD mechanisms, expressed in the endophenotype as difficulties of sensorimotor integration and delay of motor development; the persistence of altered CD mechanisms may concur to a progressive fading of the feeling of agency. This in turn could interfere with the ontogenesis of the embodied self, progressively distorting lived experience and resulting in self-disorders (i.e., traitlike anomalies of subjective experience specifically indexing vulnerability to SSDs). A reduced feeling of agency could be clearly central to the development of self-disorders and, in more severe cases, could contribute to the progressive emergence of attenuated psychotic symptoms, ultimately giving rise to passivity delusions and AVHs (see Figure 1B).

The long-term effects of this developmental cascade starting from altered sensorimotor predictions is unlikely to be an all-or-none phenomenon. Indeed, while the severe failure of sensorimotor prediction by conditioning the development of an altered feeling of agency represents a substrate for the progressive buildout of some psychotic symptoms, milder alterations of sensorimotor predictions (and related milder attenuation of feeling of agency) may represent an enabling condition for the development of milder clinical conditions. Current data suggest that at least intrusive thoughts, passively felt as perturbing the normal flow of thoughts in OCD, could be interpreted in light of this hypothesized (neurodevelopmental and phenomenological) gradient and such gradient may contribute to explain the overlap between SSDs and OCD in terms of both partial symptom affinity and comorbidity (108).

In light of this hypothesis, alterations of CD mechanisms and their potential subjective resonance (at least for the feeling of agency) should be further investigated also outside the SSDs. This investigation should consider in particular clinical conditions characterized by a motor impairment of neurodevelopmental origin (109) and especially impairments in domains of sensorimotor integration and motor coordination that could reveal alterations of CD mechanisms. In this perspective, it is interesting to report a study that applied the IB paradigm in adults with autism spectrum disorder, reporting a reduced IB effect and a reduced feeling of agency in comparison with control subjects (110), providing a preliminary empirical basis to discuss the potential role of SoA as a precursor of social impairment in this clinical population (111), characterized since childhood by motor difficulties (112).

Finally, it must be highlighted that in addition to this hypothesized developmental cascade starting from altered CD mechanisms, a multitude of other co-occurrent pathophysiological mechanisms, such as early life events and social deprivation, exposure to xenobiotics (e.g., cannabis), and/or dopaminergic systems' dysregulation (113), might intervene in the longitudinal construction of psychotic symptoms. Nonetheless, altered CD mechanisms may specifically contribute to such trajectory by interfering with the development of the embodied self in its implicit prereflective levels of experience. This constitutes the experiential substrate on which other pathophysiological mechanisms could intervene incrementally, accelerating the longitudinal development of psychotic manifestations.

Therefore, this framework has potential clinical implications. The presence of motor impairment should be more systematically investigated through standardized instruments in clinical practice, and once it is detected, clinicians should be aware that this may be accompanied by alterations at the subjective level (as reduced agency and anomalous self-experience of disembodiment) and may represent a substrate for psychopathological manifestations of passivity ranging from intrusive thoughts to psychotic symptoms. This is particularly relevant in children and adolescents presenting with putatively premorbid or prodromal stages of psychosis because detecting early alterations at the subjective level before the development of full-blown psychotic symptoms could radically modify the risk trajectory. In this respect, alterations of CD mechanisms at this phase might still be modified by early rehabilitative motor interventions. In fact, these interventions may also have beneficial effects on the subjective level, promoting a better embodiment of lived experience and reducing perspectival psychopathological risk.

ACKNOWLEDGMENTS AND DISCLOSURES

ARTICLE INFORMATION

From the Department of Mental Health (MP), Azienda Unità Sanitaria Locale–IRCSS di Reggio Emilia, Reggio Emilia, Department of Medicine (AT, AR), Division of Psychiatry, Clinical Psychology and Rehabilitation, University of Perugia, and Center for Translational, Phenomenological and Developmental Psychopathology (AR), Perugia University Hospital, Perugia, Italy.

MP and AR contributed equally to this work.

Address correspondence to Andrea Raballo, M.D., Section of Psychiatry, Clinical Psychology and Rehabilitation, Department of Medicine, University of Perugia, Piazzale Lucio Severi 1, IT-06132 Perugia, Italy; E-mail: andrea.raballo@unipg.it.

REFERENCES

1. Friston KJ, Kiebel S (2019): Predictive coding under the free-energy principle. Philos Trans R Soc Lond B Biol Sci 364:1211–1221.
2. Levy DJ, Glimcher PW (2012): The root of all value: A neural common currency for choice. Curr Opin Neurobiol 22:1027–1038.
3. Aitchison L, Lengyel M (2017): With or without you: Predictive coding and Bayesian inference in the brain. Curr Opin Neurobiol 46:219–227.
4. Wolpert DM, Ghahramani Z, Jordan MI (1995): An internal model for sensorimotor integration. Science 269:1880–1882.
5. Crapse TB, Sommer MA (2008): Corollary discharge across the animal kingdom. Nat Rev Neurosci 9:587–600.
6. Sober SJ, Sabes PN (2003): Multisensory integration during motor planning. J Neurosci 23:6982–6992.
7. Straka H, Simmers J, Chagnaud BP (2018): A new perspective on predictive motor signaling. Curr Biol 28:R232–R243.
8. van der Weiden A, Prikken M, van Haren NE (2015): Self-other integration and distinction in schizophrenia: A theoretical analysis and a review of the evidence. Neurosci Biobehav Rev 57:220–237.
9. Feinberg I (1978): Efference copy and corollary discharge: Implications for thinking and its disorders. Schizophr Bull 4:636–640.
10. Feinberg I, Guazzelli M (1999): Schizophrenia—A disorder of the corollary discharge systems that integrate the motor systems with the sensory systems of consciousness. Br J Psychiatry 174:196–204.

11. Ford JM, Mathalon DH, Heinks T, Kalba S, Faustman WO, Roth WT (2001): Neurophysiological evidence of corollary discharge dysfunction in schizophrenia. Am J Psychiatry 158:2069–2071.

12. Shergill SS, White TP, Joyce DW, Bays PM, Wolpert DM, Frith CD (2014): Functional magnetic resonance imaging of impaired sensory prediction in schizophrenia. JAMA Psychiatry 71:28–35.

13. Griffin JD, Fletcher PC (2017): Predictive processing, source monitoring, and psychosis. Annu Rev Clin Psychol 13:265–289.

14. Blakemore SJ, Smith J, Steel R, Johnstone CE, Frith CD (2000): The perception of self-produced sensory stimuli in patients with auditory hallucinations and passivity experiences: Evidence for a breakdown in self-monitoring. Psychol Med 30:1131–1139.

15. Frith CD (2005): The self in action: Lessons from delusions of control. Conscious Cogn 14:752–770.

16. Shergill SS, Brammer MJ, Fukuda R, Bullmore E, Amaro E Jr, Murray RM, McGuire PK (2002): Modulation of activity in temporal cortex during generation of inner speech. Hum Brain Mapp 16:219–227.

17. Scott M (2013): Corollary discharge provides the sensory content of inner speech. Psychol Sci 24:1824–1830.

18. Frith CD, Done DJ (1988): Towards a neuropsychology of schizophrenia. Br J Psychiatry 153:437–443.

19. Allen P, Larøi F, McGuire PK, Aleman A (2008): The hallucinating brain: A review of structural and functional neuroimaging studies of hallucinations. Neurosci Biobehav Rev 32:175–191.

20. Moseley P, Fernyhough C, Ellison A (2013): Auditory verbal hallucinations as atypical inner speech monitoring, and the potential of neurostimulation as a treatment option. Neurosci Biobehav Rev 37:2794–2805.

21. Pienkos E, Giersch A, Hansen M, Humpston C, McCarthy-Jones S, Mishara A, et al. (2019): Hallucinations beyond voices: A conceptual review of the phenomenology of altered perception in psychosis. Schizophr Bull 45(suppl 1):S67–S77.

22. Blakemore SJ, Wolpert DM, Frith CD (1998): Central cancellation of self-produced tickle sensation. Nat Neurosci 1:635–640.

23. Rochat P, Hespos SJ (1997): Differential rooting response by neonates: Evidence of an early sense of self. Early Dev Parent 6:105–112.

24. Rochat P (1998): Self-perception and action in infancy. Exp Brain Res 123:102–109.

25. Fatemi SH, Folsom TD (2009): The neurodevelopmental hypothesis of schizophrenia, revisited. Schizophr Bull 35:528–548.

26. McGorry PD, Killackey E, Yung A (2008): Early intervention in psychosis: Concepts, evidence and future directions. World Psychiatry 7:148–156.

27. Gomez A, Sirigu A (2015): Developmental coordination disorder: Core sensori-motor deficits, neurobiology and etiology. Neuropsychologia 79:272–287.

28. Wilson PH, Ruddock S, Smits-Engelsman B, Polatajko H, Blank R (2013): Understanding performance deficits in developmental coordination disorders: A meta-analysis of recent research. Dev Med Child Neurol 55:217–228.

29. Wilson PH, Smits-Engelsman B, Caeyenberghs K, Steenbergen B, Sugden D, Clark J, et al. (2017): Cognitive and neuroimaging findings in developmental coordination disorder: New insights from a systematic review of recent research. Dev Med Child Neurol 59:1117–1129.

30. Smits-Engelsman B, Wilson PH (2013): Noise, variability, and motor performance in developmental coordination disorder. Dev Med Child Neurol 55(suppl 4):69–72.

31. Katschmarsky S, Cainery S, Maruff P, Wilson PH, Currie J (2001): The ability to execute saccades on the basis of efference copy: Impairments in double step saccade performance in children with developmental coordination disorder. Exp Brain Res 136:73–78.

32. Adams JL, Lust JK, Wilson PH, Steenbergen B (2014): Compromised motor control n children with DCD: A deficit in the internal model?—A systematic review. Neurosci Biobehav Rev 47:225–244.

33. Blank R, Barnett AL, Cairney J, Green D, Kirby A, Polatajko H, et al. (2019): International clinical practice recommendations on the definition, diagnosis, assessment, intervention, and psychosocial aspects of developmental coordination disorder. Dev Med Child Neurol 61:242–285.

34. Schiffman J, Sorensen HJ, Maeda J, Mortensen EL, Victoroff J, Hayashi K, et al. (2009): Childhood motor coordination and adult schizophrenia spectrum disorders. Am J Psychiatry 166:1041–1047.

35. Burton BK, Hjorthoj C, Jepsen JR, Thorup A, Nordentoft M, Plessen KJ (2016): Research Review: Do motor deficits during development represent an endophenotype for schizophrenia? A meta-analysis. J Child Psychol Psychiatry 57:446–456.

36. Filatova S, Koivumaa-Honkanen H, Khandaker GM, Lowry E, Nordstrom T, Hurtig T, et al. (2018): Early motor milestones and schizotypy in the Northern Finland Birth Cohort Study 1966. Schizophr Bull 44:1151–1158.

37. Jones P, Rodgers B, Murray R, Marmot M (1994): Child development risk factors for adult schizophrenia in the British 1946 Birth Cohort. Lancet 344:398–402.

38. Hjriak D, Meyer-Lindenberg A, Kubera KM, Thomann PA, Wolf RC (2018): Motor dysfunction as research domain in the period preceding manifest schizophrenia: A systematic review. Neurosci Biobehav Rev 87:87–105.

39. Walker EF, Savoie T, Davis D (1994): Neuromotor precursors of schizophrenia. Schizophr Bull 20:441–451.

40. Cavanaugh J, Berman RA, Joiner WM, Wurtz RH (2016): Saccadic corollary discharge underlies stable visual perception. J Neurosci 36:31–42.

41. Robert MP, Ingster-Moati I, Albuisson E, Cabrol D, Golse B, Vaivre-Douret L (2014): Vertical and horizontal smooth pursuit eye movements in children with developmental coordination disorder. Dev Med Child Neurol 56:595–600.

42. Lencer R, Sprenger A, Reilly JL, McDowell JE, Rubin LH, Badner JA, et al. (2015): Pursuit eye movements as an intermediate phenotype across psychotic disorders: Evidence from the B-SNIP study. Schizophr Res 169:326–333.

43. van Tricht MJ, Nieman DH, Bour LJ, Boerée T, Koelman JH, de Haan L, et al. (2010): Increased saccadic rate during smooth pursuit eye movements in patients at ultra high risk for developing a psychosis. Brain Cogn 73:215–221.

44. Thakkar KN, Schall JD, Logan GD, Park S (2015): Response inhibition and response monitoring in a saccadic double-step task in schizophrenia. Brain Cogn 95:90–98.

45. Thakkar KN, Schall JD, Heckers S, Park S (2015): Disrupted saccadic corollary discharge in schizophrenia. J Neurosci 35:9935–9945.

46. Bansal S, Ford JM, Spering M (2018): The function and failure of sensory predictions [published online ahead of print Apr 23]. Ann N Y Acad Sci.

47. Thakkar KN, Diwadkar VA, Rolfs M (2017): Oculomotor prediction: A window into the psychotic mind. Trends Cogn Sci 21:344–356.

48. Hameed MA, Lewis AJ (2016): Offspring of parents with schizophrenia: A systematic review of developmental features across childhood. Harv Rev Psychiatry 24:104–117.

49. Gamma F, Goldstein JM, Seidman LJ, Fitzmaurice GM, Tsuang MT, Buka SL (2014): Early intermodal integration in offspring of parents with psychosis. Schizophr Bull 40:992–1000.

50. Goldman D (2017): Polygenic risk scores in psychiatry. Biol Psychiatry 82:698–699.

51. Bogdan R, Baranger DAA, Agrawal A (2018): Polygenic risk scores in clinical psychology: Bridging genomic risk to individual differences. Annu Rev Clin Psychol 14:119–157.

52. Poletti M, Raballo A (2018): Editorial perspective: From schizophrenia polygenic risk score to vulnerability (endo-)phenotypes: Translational pathways in child and adolescent mental health. J Child Psychol Psychiatry 59:822–825.

53. Serdarevic F, Jansen PR, Ghassabian A, White T, Jaddoe VWV, Posthuma D, et al. (2018): Association of genetic risk for schizophrenia and bipolar disorder with infant neuromotor development. JAMA Psychiatry 75:96–98.

54. Perez VB, Woods SW, Roach BJ, Ford JM, McGlashan TH, Shirhari VH, et al. (2014): Automatic auditory processing deficits in

schizophrenia and clinical high-risk patients: Forecasting psychosis risk with mismatch negativity. Biol Psychiatry 75:459–469.

55. Mathalon DH, Roach BJ, Ferri JM, Loewy RL, Stuart BK, Perez VB, et al. (2019): Deficient auditory predictive coding during vocalization in the psychosis risk syndrome and in early illness schizophrenia: The final expanded sample. Psychol Med 49:1897–1904.

56. Oestreich LK, Mifsud NG, Ford JM, Roach BJ, Mathalon DH, Whitford TJ (2016): Cortical suppression to delayed self-initiated auditory stimuli in schizotypy: Neurophysiological evidence for a continuum of psychosis. Clin EEG Neurosci 47:3–10.

57. Peralta V, Cuesta MJ (2017): Motor abnormalities: From neuro-developmental to neurodegenerative through "functional" (neuro) psychiatric disorders. Schizophr Bull 43:956–971.

58. Poletti M, Gebhardt E, Kvande MN, Ford JM, Raballo A (2018): Motor impairment and developmental psychotic risk: Connecting the dots and narrowing the pathophysiological gap [published online ahead of print Jul 11]. Schizophr Bull.

59. Gallagher S (2000): Philosophical conceptions of the self: Implications for cognitive science. Trends Cogn Sci 4:14–21.

60. Haggard P (2017): Sense of agency in the human brain. Nat Rev Neurosci 18:196–207.

61. Braun N, Debener S, Spychala N, Bongartz E, Sörös P, Müller HHO, et al. (2018): The senses of agency and ownership: A review. Front Psychol 9:535.

62. Tsakiris M (2010): My body in the brain: A neurocognitive model of body ownership. Neuropsychologia 48:703–712.

63. Metzinger, T. (2003). Being No One: The Self-model Theory of Subjectivity, vol. 7. Cambridge, MA: MIT Press.

64. Metzinger T (2007): Empirical perspectives from the self-model theory of subjectivity: A brief summary with examples. Prog Brain Res 168:215–245.

65. Synofzik M, Vosgerau G, Newen A (2008): Beyond the comparator model: A multifactorial two-step account of agency. Conscious Cogn 17:219–239.

66. Moore JW, Obhi SS (2012): Intentional binding and the sense of agency: A review. Conscious Cogn 21:546–561.

67. Gentsch A, Weber A, Synofzik M, Vosgerau G, Schutz-Bosbach S (2016): Towards a common framework for grounded action cognition: Relating motor control, perception and cognition. Cognition 146:81–89.

68. Carruthers G (2012): The case for the comparator model as an explanation of the sense of agency and its breakdowns. Conscious Cogn 21:30–45.

69. David N, Newen A, Vogeley K (2008): The "sense of agency" and its underlying cognitive and neural mechanisms. Conscious Cogn 17:523–534.

70. Frith CD, Blakemore SJ, Wolpert DM (2000): Abnormalities in the awareness and control of action. Philos Trans R Soc Lond B Biol Sci 355:1771–1788.

71. Kalckert A, Ehrsson HH (2012): Moving a rubber hand that feels like your own: A dissociation of ownership and agency. Front Hum Neurosci 6:40.

72. Hubl D, Schneider RC, Kottlow M, Kindler J, Strik W, Dierks T, et al. (2014): Agency and ownership are independent components of "sensing the self" in the auditory-verbal domain. Brain Topogr 27:672–682.

73. Jeannerod M (2009): The sense of agency and its disturbances in schizophrenia: A reappraisal. Exp Brain Res 192:527–532.

74. Klaver M, Dijkerman HC (2016): Bodily experience in schizophrenia: Factors underlying a disturbed sense of body ownership. Front Hum Neurosci 10:305.

75. Shaqiri A, Roinishvili M, Kaliuzhna M, Favrod O, Chkonia E, Herzog MH, et al. (2018): Rethinking body ownership in schizophrenia: Experimental and meta-analytical approaches show no evidence for deficits. Schizophr Bull 44:643–652.

76. Poletti M, Gebhardt E, Raballo A (2017): Corollary discharge, self-agency and the neurodevelopment of the psychotic mind. JAMA Psychiatry 74:1169–1170.

77. Parnas J, Handest P (2003): Phenomenology of anomalous self-experiences in early schizophrenia. Compr Psychiatry 44:121–134.

78. Raballo A, Sæbye D, Parnas J (2011): Looking at the schizophrenia spectrum through the prism of self-disorders: An empirical study. Schizophr Bull 37:344–351.

79. Raballo A, Parnas J (2011): The silent side of the spectrum: Schizotipy and the schizotaxic self. Schizophr Bull 37:1017–1026.

80. Parnas J, Henriksen MG (2014): Disordered self in the schizophrenia spectrum: A clinical and research perspective. Harv Rev Psychiatry 22:251–265.

81. Stern D (1985): The Interpersonal World of the Infant: A View From Psychoanalysis and Developmental Psychology. New York: Basic Books.

82. Rochat P (2003): Five levels of self-awareness as they unfold early in life. Conscious Cogn 12:717–731.

83. Rochat P (2015): Layers of awareness in development. Dev Rev 38:122–145.

84. Parnas J, Bovet P, Innocenti GM (1996): Schizophrenic trait features, binding, and corticocortical connectivity: A neurodevelopmental pathogenetic hypothesis. Neurol Psychiatry Brain Res 4:185–196.

85. Postmes I, Sno HN, Goedhart S, van der Stel J, Heering HD, de Haan L (2014): Schizophrenia as a self-disorder due to perceptual incoherence. Schizophr Res 152:41–50.

86. Sass L, Borda JP, Madeira L, Pienkos E, Nelson B (2018): Varieties of self disorder: A bio-pheno-social model of schizophrenia. Schizophr Bull 44:720–727.

87. Stanghellini G (2009): Embodiment and schizophrenia. World Psychiatry 8:56–59.

88. Schnell K, Heekeren K, Daumann J, Schnell T, Schnitker R, Möller-Hartmann W (2008): Correlation of passivity symptoms and dysfunctional visuomotor action monitoring in psychosis. Brain 131:2783–2797.

89. Graham-Schmidt KT, Martin-Iverson MT, Waters FAV (2018): Self- and other-agency in people with passivity (first rank) symptoms in schizophrenia. Schizophr Res 192:75–81.

90. Taylor MA, Heiser JF (1971): Phenomenology: An alternative approach to diagnosis of mental disease. Compr Psychiatry 12:480–486.

91. Koehler K (1979): First rank symptoms of schizophrenia: Questions concerning clinical boundaries. Br J Psychiatry 134:236–248.

92. Ebel H, Gross G, Klosterkotter J, Huber G (1989): Basic symptoms in schizophrenic and affective psychosis. Psychopathology 50:165–170.

93. Henriksen MG, Raballo A, Parnas J (2015): The pathogenesis of auditory verbal hallucinations in schizophrenia: A clinical-phenomenological account. Philos Psychiatry Psychol 3:165–181.

94. Raballo A (2017): From perception to thought: A phenomenological approach to hallucinatory experience. Schizophr Bull 43:18–20.

95. Raballo A, Poletti M, Henriksen MG (2018): Hallucinatory symptom-atology in major psychoses (schizophrenia and bipolar disorders). In: Brambilla P, Altamura CA, Mauri P, editors. Hallucinations in Psychoses and Affective Disorders. Cham, Switzerland: Springer International, 85–97.

96. Meier SM, Petersen L, Pedersen MG, Arendt MC, Nielsen PR, Mattheisen M, et al. (2014): Obsessive-compulsive disorder as a risk factor for schizophrenia: A nationwide study. JAMA Psychiatry 71:1215–1221.

97. Poyurovsky M, Koran LM (2005): Obsessive-compulsive disorder (OCD) with schizotypy vs. schizophrenia with OCD: Diagnostic dilemma and therapeutic implications. J Psychiatr Res 39:399–408.

98. Rosenberg AE, Keshavan MS (1998): Toward a neurodevelopmental model of obsessive-compulsive disorder. Biol Psychiatry 43:623–640.

99. Rus OG, Reess TJ, Wagner G, Zaudig M, Zimmer C, Koch K (2017): Hypogyrification in obsessive compulsive disorder. Psychol Med 47:1053–1061.

100. Reess TJ, Rus OG, Gursel DA, Schmitz-Koeb B, Wagner G, Berberich G, Koch K (2018): Network-based decoupling of local

gyrification in obsessive compulsive disorder. Hum Brain Mapp 39:3216–3226.

101. Brander G, Rydell M, Kuja-Halkola R, Fernandez de la Cruz L, Lichtestein P, Serlachius E, et al. (2016): Association of perinatal risk factors with obsessive-compulsive disorder: A population-based birth cohort, sibling control study. JAMA Psychiatry 73:1135–1144.

102. Jaafari N, Fernandez de la Cruz L, Grau M, Knowles E, Radua J, Wooderson S, et al. (2013): Neurological soft signs in obsessive-compulsive disorder: Two empirical studies and meta-analysis. Psychol Med 43:1069–1079.

103. Bloch MH, Sukhodolsky DG, Dombrowski PA, Panza KE, Craiglow BG, Landeros-Weisenberger A, et al. (2011): Poor fine-motor and visuospatial skills predict persistence of pediatric-onset obsessive-compulsive disorder into adulthood. J Child Psychol Psychiatry 52:974–983.

104. Bey K, Meyhöfer I, Lennertz L, Grützmann R, Heinzel S, Kaufmann C, et al. (2019): Schizotypy and smooth pursuit eye movements as potential endophenotypes of obsessive-compulsive disorder. Eur Arch Psychiatry Clin Neurosci 269:235–243.

105. Gentsch A, Schutz-Bosbach S, Endrass T, Kathmann N (2012): Dysfunctional forward model mechanisms and aberrant sense of agency in obsessive-compulsive disorder. Biol Psychiatry 71:652–659.

106. Oren E, Eitam B, Dar R (2019): Intentional binding and obsessive-compulsive tendencies: A dissociation between indirect and direct measures of the sense of agency. J Obsessive Compuls Relat Disord 20:59–65.

107. Fradkin I, Eitam B, Strauss AY, Huppert JD (2018): Thoughts as unexpected intruders: Context, obsessive-compulsive symptoms, and the sense of agency over thoughts. Clin Psychol Sci 7:162–180.

108. Poletti M, Raballo A (2019): Intruding thoughts: Between obsessions and hallucinations [published online ahead of print Mar 26]. Clin Psychol Sci.

109. Hirjak D, Meyer-Lindenberg A, Fritze S, Sambataro F, Kubera KM, Wolf RC (2018): Motor dysfunction as research domain across bipolar, obsessive-compulsive and neurodevelopmental disorders. Neurosci Biobehav Rev 95:315–335.

110. Sperduti M, Pieron M, Leboyer M, Zalla T (2014): Altered pre-reflective sense of agency in autism spectrum disorders as revealed by reduced intentional binding. J Autism Dev Disord 44:343–352.

111. Zalla T, Sperduti M (2015): The sense of agency in autism spectrum disorders: A dissociation between prospective and retrospective mechanisms? Front Psychol 6:1278.

112. West KL (2018): Infant motor development in autism spectrum disorder: A synthesis and meta-analysis [published online ahead of print May 15]. Child Dev.

113. Howes OD, McCutcheon R, Owen MJ, Murray RM (2017): The role of genes, stress, and dopamine in the development of schizophrenia. Biol Psychiatry 81:9–20.