Clinical Neuropsychiatry (2021) 18, 6, 293-295

EDITORIAL

BEFORE SCHIZOPHRENIA: SCHIZOPHRENIC VULNERABILITY IN DEVELOPMENTAL AGE AND ITS DETECTION

Michele Poletti, Andrea Raballo

Michele Poletti: Department of Mental Health and Pathological Addiction, Child and Adolescent Neuropsychiatry Service, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy.

Andrea Raballo: Section of Psychiatry, Clinical Psychology and Rehabilitation, Department of Medicine, University of Perugia, Perugia, Italy.

Citation: Poletti, M., Raballo, A. (2021). Before schizophrenia: schizophrenic vulnerability in developmental age and its detection. *Clinical Neuropsychiatry, 18*(6), 293-295.

doi.org/10.36131/cnfioritieditore20210602

Funding: None.

Competing interests: None.

Corresponding author

Michele Poletti
Department of Mental Health and Pathological Addiction, Child and Adolescent Neuropsychiatry Service, Azienda USL-IRCCS di Reggio Emilia
Via Amendola 2
Reggio Emilia, Italy
Phone: +390522335540
E-mail: michele.poletti@ausl.re.it

In the field of psychiatry and mental health, early intervention is one of the hottest issues of the last decades. This increasing attention to early manifestations of risk for mental illness is due to heightened awareness on the fact that the clinical onset of many severe mental illnesses in adolescence or early adulthood is preceded by a period of progressive structuration and manifestation of psychopathological vulnerabilities (Raballo & Poletti, 2020). Along this perspective, apart from acute psychopathological reactions to extreme life-events, severe mental illnesses do not come out of the blue, but rather represent a progressive quantitative and qualitative symptomatic progression accompanied by a progressive functional impairment, with subjective severity signaled by help-seeking. Broadly considered as the period of transition from childhood to adulthood, adolescence is the key developmental stage in which such a vulnerability to psychopathology (the so called '*p*' factor, Caspi & Moffitt, 2018) begins to be progressively overt (Allegrini et al., 2020), as documented by the epidemiological peak of clinical onset of several mental disorders (Paus et al., 2008).

As younger is the manifestation as more transdiagnostic or pluripotent appears the longitudinal psychopathological risk, with many heterotypic directions that can be traced from similar starting points. Indeed, the early detection paradigm has been originally conceived in the field of psychosis, especially schizophrenic psychosis, supported by the clinical staging model of psychosis (McGorry et al., 2006), but subsequently shifted to a transdiagnostic update (McGorry et al., 2018) and other mental disorders, as bipolar disorder (Saraf et al., 2021; Vieta et al., 2018), obsessive compulsive disorder (Fineberg et al., 2019; Preti et al., 2022) and eating disorder (Treasure & Russell, 2011).

Before schizophrenia

In the perspective of an early detection of psychopathological risk, schizophrenia remains one of the most interesting severe mental illnesses, being more characterized in the comparison with other illnesses by evident putative premorbid and prodromal features (Parellada et al., 2017). While prodromal features of schizophrenic psychosis are now well characterized by clinical descriptors of Clinical High Risk for Psychosis (CHR-P) subgroups (Fusar-Poli et al., 2013), putative premorbid features indexing a schizophrenic vulnerability are more elusive, although early manifest and progressively impacting on functioning, so that the clinical stage of schizophrenia in terms of first episode of psychosis is now considered a rather late stage of an altered neurodevelopment (Insel, 2010). As regards the neurodevelopmental trajectory headed to schizophrenia, while early genetic and environmental risk factors (Birnbaum & Weinberger, 2017; Stilo & Murray, 2019) as well as late prodromal features (Fusar-Poli et al., 2013) are well described, intermediate longitudinal dynamics between early triggers and late prodromes are poorly characterized. This divergent cross-eyed view let paradoxically neglected the longest period of schizophrenic vulnerability structuration, i.e., the putative premorbid stage of schizophrenia, in which instead many (endo)phenotypic features in multiple domains can be described and profiled (Poletti & Raballo, 2020; Poletti, 2021). Among these features, childhood motor impairment and intersubjective difficulties are of particular salience for the aim of an early detection of schizophrenic risk and their developmental dynamics are briefly sketched.

Submitted December 2021, December 2021

From childhood motor impairment to disembodiment

Childhood motor impairment is associated with both early genetic and environmental risk factors for schizophrenia and is predictive of subsequent schizophrenic psychosis in offspring of schizophrenic patients (Burton et al., 2016, 2017). Interestingly, impairments in corollary discharge mechanisms may represent a common pathophysiological correlate of both childhood motor impairment (Poletti et al., 2019a) and psychotic symptoms as hallucinations and passivity phenomena (Feinberg, 1978), with the latter developed through intermediate alteration of the Sense of Agency (Poletti et al., 2017, 2019b). Impairments in corollary discharges and their effects on sensory-motor integration and motor coordination in children may represent the schizotaxic (i.e., neurobiological) basis of vulnerability to schizophrenia that has been hypothesized since seminal conceptualizations of schizotypy proposed by Rado (1960) and Meehl (1962). The childhood motor impairment evident at the phenotypic level may be associated, at the subjective phenomenological level, with the structuration of a progressive alteration of embodiment resulting in the adult schizophrenic disembodiment, i.e., the lack of an immediate and implicit attunement between the Self and the body. This pathological detachment from the bodily side of the Self has been described in various prototypical forms, e.g., deanimated body (that is a body deprived of the possibility of living personal experience as its own) or disembodied spirit (that is a sort of abstract entity which contemplates its own existence from outside, in a third-perspective rather than in a first-perspective) (Stanghellini, 2009)

From intersubjective impairment to social anhedonia

In premorbid phases of schizophrenic vulnerability, childhood intersubjective difficulties in the implicit attunement with peers may gradually evolve at the subjective level towards interpersonal oversensitivity to feelings, intermittent sensations of exposure and self-reference, and perceived negative attitudes of others. Such experiences in the social domain may facilitate a gradual loss of spontaneity in the way of relating to others, as well as the developmental of social hypohedonia, alterations of intersubjective resonance, propensity to de-socializing and solipsistic modes of experience (Raballo & Krueger, 2011), up to schizophrenic autism in most severe cases (Parnas et al., 2002). This trajectory is coherent with narratives of adult schizophrenic patients that often allocate a sense of quasi-ontological awareness of interhuman alterity in their childhood. Such a sense of irreducible alterity and alienation is not reduced to common psychological reasons that usually accompany thoughts of loneliness, shyness and normal interpersonal frustrations in children and adolescents. By contrast, in childhood memories of schizophrenic patients, the feeling of alterity and alienation from peers is more subtle, radical and intimate at the same time, and often hard to properly verbalize, so that it can be expressed through the appearance of childhood fantasies (Parnas & Henriksen, 2014).

From the schizotaxic Self to clinical symptoms

Full-blown psychotic symptoms in the schizophrenic spectrum does not generally emerge suddenly, but rather reflect a prolonged developmental trajectory facilitated by progressive anomalies of subjective experience, defined as Self-disorders. Self-disorders are trait-like, non-psychotic anomalies of subjectivity that have been recursively and meta-analytically corroborated as schizophrenia-spectrum disorders vulnerability phenotypes (Raballo et al., 2021). 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 his own actions. In the previous sections, two possible developmental trajectories from childhood features to subsequent trait-like anomalous subjective experiences (as disembodiment and social anhedonia) have been outlined, suggesting that Self-disorders may reflect at the subjective experiential level that neurobiological vulnerability associated with early genetic and environmental risk factors and triggering an altered neurodevelopment. These abnormal subjective experiences can constitute the schizotaxic Self (Raballo & Parnas, 2011) of patients within the schizophrenia spectrum disorders, and the interaction of such trait-like basis with risk and protective factors as well as with life-events, might produce a different degree of symptomatic expression towards the negative and the positive dimensions.

Conclusions: early detection of risk is possible

An early detection of features indexing a possible psychotic and schizophrenic longitudinal risk is possible and feasible not only from a neurodevelopmentally late period as the prodromal stage described by CHR-P criteria. Although unspecific and not deterministic as regards their prognostic power, some endophenotypic features of risk may be observed and profiled since childhood premorbid stages, as for example in the motor and in the social domains, progressively focusing on their subjective resonance. Further studies are needed to refine such profiles of risk in the premorbid period as regards the schizophrenia spectrum, as well further studies are needed to profile possible premorbid and prodromal features of other severe mental illnesses in the perspective of their early detection.

References

Allegrini, A. G., Cheesman, R., Rimfeld, K., Selzam, S., Pingault, J. B., Eley, T. C., & Plomin, R. (2020). The p factor: genetic analyses support a general dimension of psychopathology in childhood and adolescence. *Journal of Child Psychology and Psychiatry, 61*(1), 30-39. https://doi.org/10.1111/jcpp.13113

Birnbaum, R., & Weinberger, D. R. (2017). Genetic insights into the neurodevelopmental origins of schizophrenia. *Nature Reviews. Neuroscience, 18*(12), 727-740. https://doi.org/10.1038/nrn.2017.125

Burton, B. K., Hjorthøj, C., Jepsen, J. R., Thorup, A., Nordentoft, M., & Plessen, K. J. (2016). Research Review: Do motor deficits during development represent an endophenotype for schizophrenia? A meta-analysis. *Journal of Child Psychology and Psychiatry, 57*(4), 446-456. https://doi.org/10.1111/jcpp.12479

Burton, B. K., Thorup, A., Jepsen, J. R., Poulsen, G., Ellersgaard, D., Spang, K. S., Christiani, C. J., Hemager, N., Gantriis, D., Greve, A., Mors, O., Nordentoft, M., & Plessen, K. J. (2017). Impairments of motor function among children with a familial risk of schizophrenia or bipolar disorder at 7 years old in Denmark: an observational cohort study.

Lancet Psychiatry, 4(5), 400-408. https://doi.org/10.1016/S2215-0366(17)30103-7

Caspi, A., & Moffitt, T. E. (2018). All for one and one for all: mental disorders in one dimension. *American Journal of Psychiatry, 175*(9), 831-844. https://doi.org/10.1176/appi.ajp.2018.17121383

Feinberg, I. (1978). Efference copy and corollary discharge: implications for thinking and its disorders. *Schizophrenia Bulletin, 4*(4), 636-640. https://doi.org/10.1093/schbul/4.4.636

Fineberg, N. A., Dell'Osso, B., Albert, U., Maina, G., Geller, D., Carmi, L., Sireau, N., Walitza, S., Grassi, G., Pallanti, S., Hollander, E., Brakoulias, V., Menchon, J. M., Marazziti, D., Ioannidis, K., Apergis-Schoute, A., Stein, D. J., Cath, D. C., Veltman, D. J., Van Ameringen, M., … Zohar, J. (2019). Early intervention for obsessive compulsive disorder: An expert consensus statement. *European Neuropsychopharmacology, 29*(4), 549-565. https://doi.org/10.1016/j.euroneuro.2019.02.002

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., Keshavan, M., Wood, S., Ruhrmann, S., Seidman, L. J., Valmaggia, L., Cannon, T., Velthorst, E., De Haan, L., Cornblatt, B., Bonoldi, I., Birchwood, M., McGlashan, T., Carpenter, W., McGorry, P., … Yung, A. (2013). The psychosis high-risk state: a comprehensive state-of-the-art review. *JAMA Psychiatry, 70*(1), 107-120. https://doi.org/10.1001/jamapsychiatry.2013.269

Insel, T. R. (2010). Rethinking schizophrenia. *Nature, 468*(7321), 187-193. https://doi.org/10.1038/nature09552

McGorry, P. D., Hickie, I. B., Yung, A. R., Pantelis, C., & Jackson, H. J. (2006). Clinical staging of psychiatric disorders: a heuristic framework for choosing earlier, safer and more effective interventions. *Australian and New Zealand Journal of Psychiatry, 40*(8), 616-622. https://doi.org/10.1080/j.1440-1614.2006.01860.x

McGorry, P. D., Hartmann, J. A., Spooner, R., & Nelson, B. (2018). Beyond the "at risk mental state" concept: transitioning to transdiagnostic psychiatry. *World Psychiatry, 17*(2), 133-142. https://doi.org/10.1002/wps.20514

Meehl, P.E. (1962). Schizotaxia, schizotipy, schizophrenia. *American Psychologist, 17*, 827-838.

Parellada, M., Gomez-Vallejo, S., Burdeus, M., & Arango, C. (2017). Developmental differences between Schizophrenia and Bipolar Disorder. *Schizophrenia Bulletin, 43*(6), 1176-1189. https://doi.org/10.1093/schbul/sbx126

Parnas, J., Bovet, P., & Zahavi, D. (2002). Schizophrenic autism: clinical phenomenology and pathogenetic implications. *World Psychiatry, 1*(3), 131–136.

Parnas, J., & Henriksen, M. G. (2014). Disordered self in the schizophrenia spectrum: a clinical and research perspective. *Harvard Review of Psychiatry, 22*(5), 251-265. https://doi.org/10.1097/HRP.0000000000000040

Paus, T., Keshavan, M., & Giedd, J. N. (2008). Why do many psychiatric disorders emerge during adolescence? *Nature Reviews. Neuroscience, 9*(12), 947-957. https://doi.org/10.1038/nrn2513

Poletti, M. (2021). *Prima della schizofrenia. la vulnerabilità schizofrenica in età evolutiva: esperienze, fenotipi, traiettorie*. Giovanni Fioriti Editore, Roma.

Poletti, M., Gebhardt, E., & Raballo, A. (2017). Corollary discharge, self-agency, and the neurodevelopment of the psychotic mind. *JAMA Psychiatry, 74*(11), 1169-1170. https://doi.org/10.1001/jamapsychiatry.2017.2824

Poletti, M., Gebhardt, E., Kvande, M. N., Ford, J., & Raballo, A. (2019a). Motor impairment and developmental psychotic risk: connecting the dots and narrowing the pathophysiological gap. *Schizophrenia Bulletin, 45*(3), 503-508. https://doi.org/10.1093/schbul/sby100

Poletti, M., & Raballo, A. (2020). Developmental Psychotic Risk: toward a neurodevelopmentally informed staging of vulnerability to psychosis. *Harvard Review of Psychiatry, 28*(4), 271-278. https://doi.org/10.1097/HRP.0000000000000266

Poletti, M., Tortorella, A., & Raballo, A. (2019b). Impaired corollary discharge in psychosis and at-risk states: integrating neurodevelopmental, phenomenological, and clinical perspectives. *Biological Psychiatry Cognitive Neuroscience and Neuroimaging, 4*(9), 832-841. https://doi.org/10.1016/j.bpsc.2019.05.008

Preti, A., Meneghelli, A., Poletti, M., & Raballo, A. (2022). Through the prism of comorbidity: A strategic rethinking of early intervention in obsessive-compulsive disorder. *Schizophrenia Research, 239*, 128-133. https://doi.org/10.1016/j.schres.2021.11.038

Raballo, A., & Krueger, J. (2011). Phenomenology of the social self in the prodrome of psychosis: from perceived negative attitude of others to heightened interpersonal sensitivity. *European Psychiatry, 26*(8), 532-533. https://doi.org/10.1016/j.eurpsy.2011.03.003

Raballo, A., & Parnas, J. (2011). The silent side of the spectrum: schizotypy and the schizotaxic self. *Schizophrenia Bulletin, 37*(5), 1017-1026. https://doi.org/10.1093/schbul/sbq008

Raballo, A., & Poletti, M. (2020). Advances in early identification of children and adolescents at risk for psychiatric illness. *Current Opinion in Psychiatry, 33*(6), 611-617. https://doi.org/10.1097/YCO.0000000000000652

Raballo, A., Poletti, M., Preti, A., & Parnas, J. (2021). The Self in the spectrum: a meta-analysis of the evidence linking basic Self-disorders and schizophrenia. *Schizophrenia Bulletin, 47*(4), 1007-1017. https://doi.org/10.1093/schbul/sbaa201

Rado, S. (1960). Theory and therapy: the theory of schizotypal organization and its application to the treatment of decompensated schizotypal behavior. In: S.C. Scher, H.R. Davism (Eds.) *The Outpatient Treatment of Schizophrenia*. New York, NY: Grune and Stratton, pp. 87-101.

Saraf, G., Moazen-Zadeh, E., Pinto, J. V., Ziafat, K., Torres, I. J., Kesavan, M., & Yatham, L. N. (2021). Early intervention for people at high risk of developing bipolar disorder: a systematic review of clinical trials. *Lancet Psychiatry, 8*(1), 64-75. https://doi.org/10.1016/S2215-0366(20)30188-7

Stanghellini, G. (2009). Embodiment and schizophrenia. *World Psychiatry, 8*(1), 56-59. https://doi.org/10.1002/j.2051-5545.2009.tb00212.x

Stilo, S. A., & Murray, R. M. (2019). Non-Genetic Factors in Schizophrenia. *Current Psychiatry Reports, 21*(10), 100. https://doi.org/10.1007/s11920-019-1091-3

Treasure, J., & Russell, G. (2011). The case for early intervention in anorexia nervosa: theoretical exploration of maintaining factors. *British Journal of Psychiatry, 199*(1), 5-7. https://doi.org/10.1192/bjp.bp.110.087585

Vieta, E., Salagre, E., Grande, I., Carvalho, A. F., Fernandes, B. S., Berk, M., Birmaher, B., Tohen, M., & Suppes, T. (2018). Early Intervention in Bipolar Disorder. *American Journal of Psychiatry, 175*(5), 411-426. https://doi.org/10.1176/appi.ajp.2017.17090972