

## Commentary: “Exploring the “Insight Paradox” in Treatment Resistant Schizophrenia: Correlations Between Dimensions of Insight and Depressive Symptoms in Patients Receiving Clozapine”

Insight into the symptoms of almost all mental illnesses is a cornerstone directly related to adherence to therapy and treatment outcome. The critical awareness or non-awareness of the mental illness is a reason to take into account the guidelines for carrying out therapeutic interventions for individual patients. One fundamental concern is whether we should consider insight as a qualitative phenomenon or as a phenomenon in the continuum? On the other hand, insight in patients with mental disorders in general is an approach that can be questioned in the context of Freud's concept: “The ego is not master of its own house”.<sup>1</sup> This view calls into question whether we are critical of our own experiences and behavior at all.

In patients with schizophrenia as well as in patients with bipolar depression, insight is impaired.<sup>2</sup> Previous research indicates that during the life cycle it is U-shaped. In the early years or at first psychotic episode, it is mostly absent, improving over time until it worsens again with advancing age.<sup>1</sup> This form can be explained on the one hand as a gradient dynamic of adaptation of patients to life with psychotic symptoms and on the other hand as an attempt to adapt to the social environment. Dönmezler and associates confirm this trend in their research. Their research may also indirectly explain adaptation to the environment with compliance to treatment as associated with patient functioning.<sup>2</sup>

Other research suggests that patients with schizophrenia who have better understanding of their illness are more likely to experience depressive symptoms. It may well be explained with the disease insight which leads to greater awareness of the negative consequences of the disease, such as social isolation, stigma, and reduced quality of life<sup>3,4</sup>

In addition, there have been reported better insight in patients with schizophrenia who are more likely to recognize and report symptoms of depression. Most probably illness insight contributes to the ability to recognize changes in mood and behavior.<sup>5,6,7</sup> Disruption of insight in schizophrenia can hardly be comprehended as a single-component phenomenon, since schizophrenia is a complex heterogeneous disorder with its individual evolution and pathoplastic development, whereby the assessment of impaired insight as a gradual phenomenon should also be considered.<sup>8</sup>

Depressive symptoms on one hand may be associated with the corresponding psychological reaction and development of affective symptoms, and on the other hand, the change in neuromediation itself as a result of the pharmacological therapy with antipsychotic drugs could also cause depressive episodes.<sup>9</sup> The relationship between depression and insight is regarded to be influenced by the stigma associated with the disease.<sup>9,10</sup> In this respect, the results of Dönmezler and associates are completely in line with the natural course of disease and treatment.<sup>11</sup> Since schizophrenia is not a linear disorder, treatment resistance regardless to applied resistance criteria, is also not a uniform and homogeneous construct either. This means that, taking into account the degree of the insight, individual patients will be positioned differently in this scale with various degrees of manifestation of depressive symptoms.



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Studies have demonstrated that up to 50% of individuals with a history of psychosis will experience a depressive episode within the first year of remission from the psychotic episode.<sup>12</sup> Another study found that the incidence of depression in the first year after a first episode of psychosis was about 30%<sup>13</sup>

For the evaluation of insight, we are guided by the narrative of the patient, which is not reliable as introspective and subjective reflection. In resistant schizophrenia, it should be noted that the patients achieve some balance between the mental disorder and the common sense “realities” and sometimes adjust within the framework of the patient role. This is also the reason why the level of depressive symptoms is found to be higher in resistant patients as compared to treatment responders that do not report clinically significant depressive scores.<sup>14</sup>

Dönmezler and coauthors do not find relationship between adherence to treatment, and depressive complaints which is consistent with the above findings since depressive symptoms are ego-dystonic. In this perspective, the patient would be expected to avoid provocation of symptoms leading to discomfort, which would in turn affect compliance with therapy. On the other hand, the overall functioning of the patients is dependent on the clinically manifested combination of psychotic, affective and anxiety complaints as well as on the social environment. Dönmezler and associates (2023) address a critical concern from a clinical point of view. It is to establish the relationship between the dimensions of insight and depressive symptoms. The presence of depression is clinically significant in patients with schizophrenia. On one hand, in the treatment of patients with schizophrenia, post-psychotic depression is observed in a large proportion of patients, and usually the presence of these symptoms is related to the severe course of the disease and the development of possible resistance. From pharmacological perspective it is not possible to observe the fully manifested depressive state in post-psychotic episode because there is no post-psychotic episode in treatment resistant schizophrenia, but the persistence of psychotic symptoms with varying degrees of expression and fluctuation. Other authors found a higher level of depressive complaints in patients with resistant schizophrenia, but this relationship can be interpreted as depressive complaints associated with the presence of a certain reduction of psychotic output without reaching its complete resolution.<sup>14</sup> The analysis of depressive symptoms is essentially an analysis of ego-dystonic symptoms, i.e. symptoms that are reported by the patient as discomfort. This raises a question whether insight paradox should be interpreted as a paradox indeed or rather as expected phenomenon that we observe in resistant patients in terms of dynamics and course of the disease.

It should be noted as well that resistant schizophrenia is also characterized by various interwoven markers in the course and clinical presentation. Some early markers such as the effect of the first antipsychotic medication, high comorbidity with ACS, cognitive disorders, functional lateralization, high degree of dissociation, changes in accepted social roles are observed in her.<sup>15-21</sup>

The results of Dönmezler and associates show that there is generally some insight breakthrough in treatment-resistant patients. The question that remains opened is how insight will change over time in patients with treatment resistance if changed at all? Future studies

showing what the insight curve would be in patients with resistant schizophrenia would allow for a better assessment of long-term prognosis.

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