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Lack of Insight in Bipolar Disorder: The Impact on Treatment Adherence, Adverse Clinical Outcomes and Quality of Life

Cătălina Angela Crișan

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Abstract

Insight is a multidimensional construct, defined as the awareness of having a mental disorder, of specific symptoms and their attribution to the disorder, the awareness of social consequences, and of need for treatment. Although insight has been studied specifically in schizophrenia and its study in mood disorders has traditionally received limited attention, the evaluation of this concept in mood disorders is also very important because of the impact on treatment compliance and outcome. In bipolar disorder (BD), clinical insight varies substantially over time. Most researchers observed that insight is more impaired during an illness episode than during remission, in mixed than in pure manic episodes, in bipolar II than in bipolar I patients, and in pure mania than in bipolar or unipolar depression. Lack of insight is a consistent factor of non-adherence to medication in bipolar patients, along with severity of BD, side effects of medication, effectiveness, and patient-related factors. Also, impaired insight into treatment and a great number of previous hospitalizations are associated with poorer clinical outcomes (psychiatric hospitalization, emergency room visits, violent or suicidal behavior) among the patients with bipolar I disorder. In the management of bipolar disorder, improving quality of life (QoL) and outcome should be one the most important goals.

Keywords: insight, bipolar disorder, adherence, quality of life, outcome

1. Introduction

In medicine, the concept of insight into madness seems to have started in early part of the nineteenth century when the clinical descriptions began to include observations about patients' awareness of their pathological state. In 1882, Pick used the term "Krankheitseinsicht" [1],

and in 1893, Krafft-Ebing used the term “insightlessness” (“in the later stages of insanity, where delusions have become organized or mental disintegration has ensued, the patient is completely insightless—(einsichtloss) about his disease state”) ([2], translated by [3]). In the history of this concept, there were differences in the approach of the most important French, German, and English authors. In the French view, Pinel (1801) referred to the patient’s “judgment” and to his capacity to correctly assess his state (“apprécie avec justesse son état”) [4]. Baillarger separated the patients into two categories (who were and who were not insane) using insight (the patients with hallucinations, who were convinced of the reality of their hallucinations, were truly mad; on the other hand, the patients with hallucinations who realized that these hallucinations were caused by some derangement in themselves, should not be considered truly mad) [5]. A major debate concerning awareness of mental illness (“la discussion sur les aliénés avec conscience de leur état”) and the responsibility of patients for criminal acts was held by the Société Médico-Psychologique in 1869–1870, and then in 1875 Billod observed that the number of patients who were aware about their state of madness was lower than those without the disease awareness [6]. He divided the patients into two categories:

1. Those who were not aware of their pathological state (they were aware of hallucinations and strange experiences but attributed those wrongly).
2. Those who were aware of their pathological state.
 - a. Patients with incomplete awareness (they were aware of their pathological state but, nevertheless, believed in the reality of their delusions and strange experiences).
 - b. Patients with complete awareness (they were aware of their pathological state and recognized the falseness of their abnormal experiences).

Billod also observed that insight is a good prognostic factor of the evolution of the disease and for illness recurrence.

Parant classified mentally ill patients, during an episode of illness, into five groups [7]:

1. Those who are aware of their acts and who can discern whether they are good or bad but are not aware of their morbid condition.
2. Those who are aware that they are in an abnormal state but do not understand or admit that this condition is a mental illness.
3. Those who are aware that their mental condition, their acts, and their ideas are the result of a mental illness, but they behave as if they would not do so (patients presenting hallucinations and delusions of persecution, being convinced by the reality of their symptoms, but who also consider themselves to be healthy).
4. Those who are aware of their condition and who understand that this condition is due to a mental illness, but who are incapable of taking an attitude in this regard.
5. Those who are aware of their condition and who understand that this condition is due to a mental illness, but who have committed or been forced to commit dangerous acts.

In the British view, Maudsley believes that the healthy man was incapable of accurately judging the behavior and the experiences of the mental ill; at the same time, the psychic patient could not judge with his healthy psychic functions the phenomenon produced by his psychically impaired functions [8]. Aubrey Lewis, in 1934, distinguished between the change in awareness and the change in judgment, both being mandatory components of the insight [9]. According to his opinion, the patient should be first aware of the change and then form an opinion, a judgment about it. Aubrey Lewis conceptualized the insight as a complex group of judgment types, based on different types of information. Lewis defined the insight as “an attitude adapted to an unhealthy change in itself, and ability to decentralize, and to give a personal judgment on one’s own state.”

In the German view, Pick argued that for the most part of the mental illnesses (mania, melancholia, obsessive–compulsive disorder, psychosis, dementia, alcohol abuse), the patients were somewhat aware of their affection [1]. He noted that the patients with progressive onset had a better insight time wise, unlike those for whom the disease suddenly started. Pick subdivided the concept of the disease awareness (“Krankheitsbewußtsein”) into the awareness of the phenomenon of being sick (“Krankheitsgefühl”) and the disease insight (“Krankheitseinsicht”).

Unlike Kraepelin and Bleuler, who did not approach the concept of the insight, Jaspers was the one who studied it for a long time and the one who brought many new elements [10]. He considered that not only the patients become conscious and develop a judgment regarding the symptoms of their illness but also the expression of their illness’ symptoms is affected by the patients’ awareness and judgment. Jaspers noticed that in the early stages of psychosis, the patients were uncomfortable and embarrassed, having a meaningful reaction to the lived experiences. With the disease progression, the patients tried to make sense of their own experiences, and they elaborated a delusional system. When the disease produced changes in personality, the patient’s attitude to the illness was less and less understood.

Even if the concept of insight is widely used, there are important differences between authors regarding its components. In 1989, Greenfeld et al. proposed a model of insight consisting of five distinct and independent dimensions [11]: (1) views about symptoms, (2) views about the existence of an illness, (3) speculations about etiologia, (4) views about the risk of recurrence, and (5) opinions about the opportunity of treatment. This approach is focused more on patients’ understanding of what is happening to them and what individual sense they are making of their experiences.

David described three distinct dimensions of insight: (1) the recognition of the presence of a mental illness, (2) the compliance with treatment, and (3) the ability to relabel psychotic symptoms (delusions and hallucinations) as pathological [12].

A more complex multidimensional model of insight is proposed by Amador et al. and consists of the following elements: (1) awareness of the signs, symptoms, and consequences of illness, (2) general attribution about illness and specific attribution about symptoms and their consequences, (3) self-concept formation, and (4) psychological defensiveness [13].

Trying to give a more practical description of the concept, Amador and Strauss proposed two important components: (1) awareness of illness and (2) attribution regarding the illness [14].

Marková [3] summarized in her monography the following components of insight: (1) an attribution of the change to pathology [10, 12, 13], (2) social consequences of illness [13], (3) views concerning etiologia and likely recurrence [11], (4) perception of changes in the self and one's interaction with the world [15], (5) need for medical treatment [12, 13, 16], (6) attitudes toward experiences [17], (7) comparison with the previous function [18], (8) predictions of performance on specific tests [19, 20], and (9) resemblance of own experiences to hypothetical cases [21].

Most studies about insight were conducted with patients suffering from schizophrenia and other psychotic disorders, neglecting patients with mood disorders. However, in the last few years, there has been an increase in interest about insight in patients with bipolar disorder [22]. The awareness of illness can be quite impaired in mania, second only to schizophrenia, even in the absence of psychosis [23].

Given the importance of insight to diagnosis, treatment adherence, and psychosocial outcome, we considered that it is appropriate to pay attention to this phenomenon. This chapter presents few remarks about the history of the concept, different models of insight, the most important psychometric tools in assessing insight and clinical implications of poor insight in patients diagnosed with bipolar disorder. Taking into account that clinical insight varies substantially over time in bipolar patients, the relationship of insight to episode subtypes and symptom dimensions is analyzed in detail. Than other important themes are addressed: the impact of unawareness of illness on non-adherence to medication, on outcome, and quality of life (QoL).

2. Measurement of insight

Over the past 15 years, semi-structured interviews with systematized scoring systems and proven psychometric strengths have been devised to measure insight. The first such measure to be used widely was The Insight and Treatment Attitudes Questionnaire (ITAQ) developed by McEvoy et al. [24]. The ITAQ has been used in large samples of patients with schizophrenia and has been shown to be reliable and valid. The questionnaire comprises 11 items designed to assess patients' recognition of illness and the need for treatment. The response of the patient is scored as 2 = good insight, 1 = partial insight, and 0 = no insight. The ITAQ employs a narrow definition of insight and does not assess many of the psychological domains that are believed to comprise insight into illness more generally.

David's Schedule for the Assessment of Insight (SAI) assesses insight based on a patient's recognition of having a mental illness, compliance with treatment, and ability to label unusual events, such as delusions and hallucinations, as pathological [12]. The Schedule for the Assessment of Insight explores insight beyond the acknowledgment of illness and the need for treatment. This measure does not, however, consider how insight may vary from symptom to symptom, nor does it consider differences between current and retrospective insight into illness.

Similarly, the Insight Scale (IS) devised by Birchwood et al. is an alternative direct translation from David's three-dimensional model of **insight, but in this case**, the empirical form is presented as a self-report measure (scoring 0–4 on each dimension, maximum: 12) [25].

Kemp and David, back in 1995, developed The Schedule for Assessment of Insight—Expanded version (SAI-E) [26], a three-dimensional scale designed to measure insight into mental illness. The questionnaire contains 10 items on three apparently separated but actually overlapped extents, as follows: the first three questions evaluate the awareness of the illness, questions 4–7 measure the capacity to relabel psychotic experiences as abnormal and the awareness of symptoms, while the latter questions rank the treatment compliance of the evaluated patient. The clinician conducts the survey by asking the patient a set of questions and then calculates the result: a higher-attained score indicates an increased level of insight.

Amador and Strauss developed the Scale to assess Unawareness of Mental Disorder (SUMD) [27], which distinguishes current and retrospective awareness of (1) having a mental disorder, (2) the effects of medication, (3) the consequences of mental disorder, and (4) the specific signs and symptoms. Since its development, this scale has gained widespread acceptance as a multidimensional measure of insight and has been validated and studied on a range of clinical samples. SUMD consists of 20 items: the first three evaluate general aspects, such as awareness of the mental disorder, of the attained effects of medication, and of the social consequences of having a mental disorder, while the latter inquire more specific topics: hallucinations, delusions, thought disorder, inappropriate affect, unusual appearance and eye contact, stereotypic or ritualistic behavior, poor social judgment and relationships, poor control of aggressive and sexual impulses, poverty of speech, flat or blunt affect, avolition, apathy, presence of anhedonia, diminished attention, and confusion-disorientation. The survey is administered by the clinician or by a trained reviewer and it can take up to 40 min. Evaluation is performed through a five-level Likert scale, a value of 0 showing intact insight.

In 1992, Carsky et al. developed Patient's Experience of Hospitalization (PEH), an 18-item self-report scale, which reflects predominantly views about being in hospital [28]. The instrument is focused on a narrow definition of denial, specifically limiting this to a failure to acknowledge: (1) having an illness or that the illness has a name or a cause, (2) any need for hospitalization, and (3) that the illness has personal impact. Each item is rated on a four-point scale of severity or level of agreement with a higher total score indicating greater denial.

Using the same concept, Marks et al. developed the Self-Appraisal of Illness Questionnaire (SAIQ) based closely on the PEH but designed for use in community settings. SAIQ is a 17-item self-report scale following the format of the PEH but substituting items about hospitalization with similar items about the need for treatment [29]. Olaya et al. developed a multidimensional scale, the Insight Scale for Affective Disorders (ISAD), a hetero-evaluation instrument for patients with mood disorders [30]. The scale evaluates dimensions like insight into illness, treatment needs, and social consequences [31]. The instrument, based on the Scale to Assess Unawareness in Mental Disorders (SUMD) [27], consists of 17 items. Scores may range from 1 (absence of symptom or full insight) to 5 (no insight) for each item, meaning

that any score above 1 indicates insight alteration for that item. This scale allows for a more complex assessment of insight, addressing BD in a comprehensive manner.

3. Clinical implications of poor insight in bipolar disorder

3.1. The relationship of insight to episode subtypes and symptom dimensions

Even if the researcher's attention was focused mainly on patients diagnosed with schizophrenia, and there is far less research on insight in bipolar disorder, a number of studies have shown that individuals with bipolar disorder frequently experience impairments in insight [32–36]. While in schizophrenia insight is viewed as more of a stable trait [37], in bipolar disorder it has been conceptualized as more of a state-dependent construct, with alterations dependent on illness phases [38–40].

Results are mixed when comparing insight of patients with schizophrenia and of bipolar patients. Some studies show that schizophrenic patients have less insight than those suffering of psychotic or mixed mania [41], while other researches show that schizophrenic patients have a similar insight deficit with patients who have been diagnosed with acute-phased bipolar disorder [32, 42–44] and to bipolar disorder with psychotic features [23, 45, 46]. The reason for the mixed results is not very clear, but one of the possible explanations could be that these studies have not taken comorbid alcohol use disorder into consideration.

Peralta and Cuesta reported in their study that the presence of psychotic features did not significantly affect insight level in manic patients at discharge from the acute ward [47]. However, Yen et al., comparing insight in-patients with schizophrenia and bipolar disorder in remission, reported that bipolar patients with psychotic features had lower levels of insight than those without psychotic features [48].

In another study, Yen et al. analyzed a cohort of 65 patients with type-I bipolar disorder and observed them over a 2-year period [49]. During this period, patients received six follow-up assessments. SAI-E was used for establishing their insight levels, along with the Young Mania Rating Scale (YMRS) and the Hamilton Rating Scale for Depression (HAM-D), for determining affective tendencies. It was observed that insight was constant during the 2-years period in continuously-stable patients. A decreased insight could be associated with the presence of the manic phase, in both single manic and repeated manic episodes. The insight returned to the pre-episodic level for patients with a single manic episode, but it remained altered in most of patients with multiple manic episodes. Depressive episodes have shown no change of insight, regardless of the number of episodes.

In 2010, Cassidy examined lack of insight in 156 bipolar patients in all phases of the illness. A total of 86 patients were evaluated during pure manic episodes, 29 during mixed manic episodes, 14 during bipolar depressed episodes, and 27 in remission [38]. The purely manic group scored a mean (SD) lack of insight of 2.39 (1.62), the bipolar depressed group had a score of 0.57 (0.85) ($p < 0.001$), while the euthymic group has shown a mean of 0.444 (0.934) ($p < 0.001$).

Differences between the mixed-manic, bipolar-depressed, and euthymic groups were null. The author findings (84.9% subjects during pure mania had scores of 1 or greater) indicated at least a moderate denial of illness in manic patients. Psychomotor agitation and irritability, both core features of mania, were predictive of lack of insight during acute episodes.

De Assis da Silva et al. included in their study from 2015 95 patients with bipolar disorder and divided them into two different groups according to the mood state presented during assessment (i.e., euthymia, mania, and depression) [36]. Insight was evaluated using the hetero-evaluation questionnaire ISAD developed by Olaya et al. [30]. Patients with bipolar disorder in mania show less insight about their condition than patients in depression or euthymia, and less insight about their symptoms than patients with depression, with the exception of awareness of weight change. The advantage of this study is that the scale used to assess insight (ISAD) is a specific scale tailored to mood disorders, which allowed the authors to conduct a detailed evaluation of insight into specific symptoms of mood disorders.

There are some longitudinal studies of insight in the acute depressive episode [23, 44, 47, 50]. These studies suggest that insight is not very impaired in the acute non-psychotic depressive episode, and that insight may increase as depression worsens. However, insight is moderately impaired in psychotic depression [23]. Insight appears to improve markedly upon acute recovery from psychotic depression.

The relationship between insight and suicidality is complex. Amador et al. [51] and Schwartz and Petersen [52] found in their studies an association between intact insight and increased risk of suicide in patients diagnosed with schizophrenia. The results are not similar when analyzing patients with mood disorders.

In 2017, throughout the year, de Assis da Silva et al. [53] followed a group of 165 bipolar patients, 53 of whom had depressive episodes according to DSM-5 criteria. Insight was evaluated through the Insight Scale for Affective Disorder (ISAD). ISAD total scores and sub-scores based on the four factors of the scale (insight into symptoms, the condition itself, self-esteem, and social relationship) were generated for the analysis. Worse total insight correlated with suicide attempt/ideation. An altered self-esteem insight was associated not only with suicidal ideation or suicide attempt but also with activity reduction and psychomotor retardation. Altered symptom-related insight correlated also with psychomotor retardation. It was shown that a better insight into having an affective disorder determines more intense hypochondriac symptoms. Worse insight into having an illness was associated with psychotic episodes. The study concluded by exposing that symptoms other than psychosis, that is, suicidal ideation, psychomotor retardation, and reduction of activity, correlate with insight impairment in bipolar depression.

Focusing on the correlation between insight level and suicidal behavior/ideation in bipolar depression, de Assis da Silva et al. [54] observed in the same group of 165 patients who were followed during one year that a history of suicidal attempts was associated with worse insight in 60 patients with one episode of bipolar depression. No correlation between current suicidal ideation and insight level was found. The results of this study suggest that a history of suicide attempts may correlate with higher impairment of insight in bipolar depression.

3.2. The impact of insight on non-adherence

One of the greatest problems clinicians face when dealing with chronic illnesses is the effectiveness of treatment. This is influenced by different factors such as patient tolerance of the drug, the appropriateness of the regimen [55], and adherence to treatment. Studies demonstrated that antipsychotic medication reduces the severity of serious mental illness and improves patient outcomes if medicines are taken as prescribed. Medication adherence previously known as compliance [56], is a process of collaboration between the physician and the patient (if during the compliance, the physician is omniscient, the patient must strictly follow the medical prescription; in case of adherence, the patient has an active role in decision-making regarding the type of agreed medication, the way of administration, and the therapy duration). In this case, the patient may refuse to check-in for appointments or may begin to discontinue his medication. Such behavior has a negative impact on the outcome and leads to higher rates of recurrence and hospitalization [57]. The non-adherence may be deliberate (the patient reduces or stops deliberately the medication, being convinced that he does not need medication for feel good and the medication is harmful for him due to possible side effects) or unintentionally (the patient skips some medication doses, either by forgetting them or because they do not check-in in time for a new recipe).

Medication adherence is a dynamic behavior, influenced by multiple factors [58]: factors related to patients (adverse effects of medication, lack of insight), their social relationships (family support and therapeutic alliance), cognitive problems (impaired memory or attention) [59], and the system for providing health services [60]. Rates of low adherence have been reported to be as high as two-thirds in patients with schizophrenia [61]. Bipolar patients have also low rates of adherence [62–64].

In their review about adherence to antipsychotic medication in two serious psychiatric disorders, bipolar disorder and schizophrenia, Garcia et al. systematized (**Table 1**) factors common for both pathologies and specific factors by diagnosis [65].

Lack of insight seems to be the most crucial factor impacting adherence [66]. Lack of awareness may fluctuate from complete denial of illness and full rejection of the diagnosis to minimization and rationalization of symptoms along with disapproval of medication's beneficial effects, such as treating specific symptoms and minimizing the relapse risk. A considerable number of patients with schizophrenia exhibit a diminished or completely absent insight into their ailment, being more likely to completely reject their need for treatment, therefore being sustainably noncompliant. Hence, it is essential to assess patients' insight on a continuum and not just to rate it as "good" or "poor." Is the patient aware of the disease, its nature, its symptoms, and the need of undergoing antipsychotic treatment for both acute and maintenance treatment? Lacks in the capability of recognizing the presence of a mental illness and the beneficial effect of antipsychotic medication would definitely increase the likelihood of altered compliance. Also, insight has a beneficial impact over the therapeutic relationship [67].

There are several studies which proved the importance of insight (as patient-related factor) on adherence in patients diagnosed with bipolar disorder. González-Pinto et al. [68], analyzing 1831 patients with bipolar disorder (in the EMBLEM Project), found that the following

SCHIZOPHRENIA	COMMON FACTORS	BIPOLAR DISORDER
<ul style="list-style-type: none"> • positive symptoms • highly-severe depression at baseline • early dysphoric response • brief illness duration • presence of adverse effects (extrapyramidal syndrome, neuroleptic-induced dysphoria, akathisia, sexual impairment, weight gain) • poor therapeutic response or tolerance development • early treatment cessation rate • hostility to treatment 	<ul style="list-style-type: none"> • low levels of education • young age • cognitive impairment • high intensity of delusional symptoms and suspiciousness • substance abuse/dependence • minority ethnicity • poor insight • poor therapeutic alliance • low socioeconomic status • barriers to treatment, bad patient experience of admission 	<ul style="list-style-type: none"> • psychotic symptoms • highly-severe depressive episodes • presence of rapid-cycling • increased affective morbidity • comorbidities (anxiety, obsessive-compulsive disorder) • adverse effects: weight gain, cognitive impairment • longer duration of suicide attempts episodes

Table 1. Factors influencing adherence to antipsychotic medication in bipolar disorder and schizophrenia [65].

factors were significantly positively associated with good adherence: good illness awareness (good adherence from the start of treatment) and a short duration of episodes. In contrast, high scores in the Clinical Global Impressions hallucinations/delusions scale at baseline and depressive symptoms during mania were related to poor adherence.

An observational study, conducted in Europe by Novick et al. [69], included 903 patients, out of which 612 were diagnosed with schizophrenia and 291 with bipolar disorder. Its design was meant to evaluate the outcome of patients treated with two oral formulations of olanzapine over a 1-year period through several evaluation tools, as follows: Clinical Global Impression (CGI), Global assessment of Functioning (GAF), Scale to Assess Unawareness of Mental Disorder (SUMD), Medication Adherence Rating Scale (MARS), and Working Alliance Inventory (WAI). The results have shown that medication adherence had higher levels in bipolar patients (mean MARS score (SD) 6.5 (2.8)) versus schizophrenic patients (mean MARS score (SD) 5.8 (2.7)) ($p < 0.0001$). An increased insight was associated with a better treatment adherence. Higher levels of insight were related to a powerful therapeutic alliance (SCC ranging from 0.38 to 0.48, $p < 0.0001$). The research has also shown that, 1 year after the follow-up, the improvement of patients' awareness of their mental disorder (gain of insight) or an improvement in the patient-physician relationship was directly associated with a better medication adherence, an improvement of the overall functioning, and a better outcome.

Copeland et al. [70] conducted a cross-sectional survey of patients recruited into the Continuous Improvement for Veterans in Care-Mood Disorders, assessing therapeutic insight and two measures of medication adherence: the Morisky scale of interpersonal barriers and missing any doses the previous four days. A total of 435 patients were included. Greater insight into medication was negatively associated with both measures of poor adherence. Poor adherence was increased for women, African Americans, mania, and hazardous drinking. Moon et al. investigated dropout patterns and their associated factors in 275 patients with bipolar disorders who were prospectively examined for 3 years [71]. The authors observed that the dropout rates increased rapidly during the first three months and slowed after 12 months. Past psychotic symptoms, longer illness duration, past psychiatric diagnoses, and a past history of dropouts significantly influenced the time to dropout in bipolar patients. The main reasons for dropout were denial of therapeutic need and lack of treatment efficacy.

A cross-sectional study, conducted by Medina et al. [72] in five Spanish mental health community centers, was aimed to establish the various attitudes toward antipsychotics at the moment of discharge in both patients with schizophrenia and bipolar disorder and, as a secondary aim, to analyze the connection between patients' attitude and sociodemographic and clinical data. A total of 86 patients (45 with a diagnosis of schizophrenia and 41 with bipolar disorder) were initially included in the study. Patients' attitude toward treatment was assessed with the 10-item Drug Attitude Inventory (DAI-10) [73], aspects of treatment adherence with Rating of Medication Influences (ROMI) scale [74], insight with SUMD scale [27]. A total of 26% of the patients presented a negative attitude toward antipsychotic treatment (mean DAI-10 score of -4.7 , SD 2.7). Most of them were diagnosed with schizophrenia. Patients with a negative attitude obtained insight scores at discharge indicative of poorer disease awareness ($r = -0.31$, $P = 0.0039$) and had a greater number of previous acute episodes.

The determinant reasons of non-adherence to medication in patients with serious mental illness were evaluated by Velligan et al. through a systematic literature review [75]. Intentional and unintentional adherence was evaluated through several indicators for each category, as follows: poor insight, disavowal toward medication, distressful effects of medication, family or social support, access to mental health-care providers, poor therapeutic alliance, and stigma for the first category and substance abuse, cognitive impairment, depression, family and social support, access to mental health care, and social functioning for the second category. A total of 20 insight-related studies (11 prospective and 9 cross-sectional) analyzed the relationship between insight and adherence. Several prospective studies have shown that a better insight, evaluated through three insight scores, was associated with an improved adherence in both schizophrenic and bipolar patients [69]. Patients with bipolar disorder presented poor awareness of their disease after acute mania treatment, associating a higher probability of non-adherence during the maintenance therapy [68]. Cross-sectional studies have shown that, in patients over 50 years old diagnosed with bipolar disorder, a poor insight is associated with non-adherence [76]. Poor insight was identified as a cause for non-adherence in more than half of the studies, followed by substance abuse, a negative attitude toward medication, side effects, and cognitive impairments. Having a negative attitude toward medication is a determinant factor of intentional non-adherence, being considered to mediate effects of insight and of the therapeutic alliance.

Taking into account the major impact that adherence to medication has on the outcome of bipolar patients and the strong correlation between three factors—awareness of illness, adherence to medication and therapeutic alliance—García et al. [65] summarize in their systematic review the potential areas for intervention to improve adherence:

- *factors associated with patients*
 - early intervention programs for young patients.
 - treatment for different dependencies (on alcohol or other drugs), encouraging cessation.
 - increase awareness of the illness and of the benefits of antipsychotic treatment through psycho-education and psychotherapy interventions.
 - prevent or minimize adverse effects of antipsychotics, personalized treatment.
 - programs and/or technical devices to support treatment adherence for patients with cognitive dysfunctions.
 - assess patient education and quality of life.
 - analyze the symptoms at onset and during the course of illness.
 - consider patient ethnicity as a potential risk factor for non-adherence
- *factors associated with pharmacological treatment*
 - explanation about treatment plan.
 - simple posology
- *factors associated with social relationships*
 - improve the patient-physician relationship.
 - involve the family in the illness of the patient
- *factors associated with the service provision system*
 - avoid patients' first contact with the health system being a traumatic experience.
 - facilitate the access to treatment and health centers.

3.3. Quality of life and its association with insight in bipolar patients.

It is important to note that the impact of insight on quality of life may be subtle during remission and may be more substantially affected in full-blown manic symptoms. Impaired insight into treatment and a greater number of previous admissions significantly increased the risk of adverse clinical outcomes with bipolar disorder.

Dias et al. evaluated in their study the relationship between insight, quality of life, and cognition in bipolar disorder [77]. A neuropsychological battery assessing attention, mental control, perceptual-motor skills, executive functions, verbal fluency, abstraction and visuospatial

attention was administered to 70 remitted bipolar patients and 50 healthy controls. No differences in quality of life and cognitive performance were observed between bipolar patients with impaired and preserved insight. Insight was found to be correlated with poorer psychological and environmental quality of life.

Gazalle et al. [78] studied 120 type-I bipolar patients (40 manic, 40 depressed, 40 euthymic), and 40 matched controls. Manic patients presented the lowest GAF measures but reported same overall QoL as euthymic patients and controls, and better QoL than depressed patients. Authors suggested that this mismatch between objective and subjective measures during acute mania may be associated with a lack of insight or awareness of their own illness.

Quality-of-life levels were compared by Yen et al. among two groups: remissive schizophrenic and bipolar patients and healthy control subjects. The impact of insight, adverse effects of medication, and use of atypical antipsychotics over the quality of life was analyzed [79]. A total of 96 subjects with bipolar disorder in remission, 96 subjects with schizophrenia in remission, and 106 healthy control subjects were included in the study. The results demonstrated that the subjects with bipolar disorder in remission had similarly poor levels of quality of life in all four domains as those with schizophrenia in remission, and both groups had poorer quality of life than subjects in control group. Insight was negatively associated with quality of life on the physical domain in schizophrenia and bipolar patients in remission. The results indicate that subjects with bipolar disorder are dissatisfied with their quality of life, even when they are in remitted state.

3.4. Insight and outcome in bipolar disorder

Research has revealed that a lack of insight is associated with poorer clinical outcomes in both schizophrenia and bipolar disorder.

Ghaemi et al. performed a study to assess the relationship between impairment in insight and long-term outcomes in affective and anxiety disorders [80]. They included 101 patients and the mean follow-up period was 3.9 months. Initial impairment in insight did not correlate with poor outcome. However, improvement in insight correlated with good outcome, particularly in bipolar disorder type I ($r = 0.56-0.67$, $P = 0.0005$).

Yen et al. followed 65 remitted bipolar I disorder patients over a 2-year period. Assessments were performed at 3, 6, 9, 12, 18, and 24 months to detect the adverse clinical outcomes defined by the incidence of bipolar-related psychiatric hospitalization, emergency room visits, and violent or suicidal behavior. Impaired insight into treatment and a greater number of previous hospitalizations significantly increased the risk for adverse clinical outcomes. However, insight into recognition of the illness and relabeling of psychotic phenomena did not have any significant effect on adverse clinical outcomes. Bipolar patients' insight into treatment is an independent predictor of adverse clinical outcomes [81].

It was shown that, in order to target a better patient outcome, treatment-related insight should be improved. The Health Belief Model, a proposed psychological model, aims to explain and predict health behaviors by focusing on individuals' attitudes and beliefs that may influence

adherence [82]. The aforementioned model stipulates that two behaviors are playing an essential role in medication acceptance, that is, patients' awareness of their condition and patients' acknowledgement of the benefits provided by their treatment adherence.

Psycho-education became a common practice in mental health settings, especially for patients diagnosed with bipolar disorder. Its aim is to increase patients' ability of managing their life during a long-term illness. Specifically designed psychological interventions for relapse prevention, associated with mood stabilizers, are useful in patients with bipolar disorder.

Most recently published psychotherapy studies describe positive maintenance results as an add-on treatment, with efficiency in the treatment of depressive episodes. Interestingly, several groups from all over the world described similar results and reached similar conclusions; almost all tested interventions contain psycho-educative tools for compliance enhancement and early identification of prodromal signs, stating the importance of a regular lifestyle, and exploring patients' health beliefs and the awareness of illness [83].

4. Conclusions

In bipolar disorder, awareness of illness is not the same in manic, mixed, or depressive episodes. In acute mania, patients lack insight, while depression, viewed either syndrome wise or dimensionally, appears to preserve insight during acute episodes. Thus, insight impairment is less severe in bipolar depression than in mania. However, psychotic depression, compared to nonpsychotic depression, is associated with a worsened insight. Evidence shows that depression-related insight might be augmented by the severity of the depressive symptoms, possibly approving the depressive realism hypothesis. Insight of remissive bipolar patients seems to be recovered. Therefore, lack of insight in bipolar disorder appears to be a mood range-related phenomenon, unlike schizophrenia.

Poor insight is associated with non-adherence. Insight impacts on the therapeutic alliance with mental health professionals (this association may be bidirectional: while insight may influence therapeutic relationship, therapeutic relationship may also influence insight). Insight, therapeutic alliance with the treating psychiatrist, and medication adherence are highly correlated in bipolar patients as in patients diagnosed with schizophrenia. The three factors covary during the course of illness and an improvement in one leads to improvements in the others. Patient's insight into treatment is a significant predictor of adverse clinical outcomes. It may be essential to include that improving insight into treatment might be a promising objective for final outcome.

At present, the usefulness of psychotherapy (family-focused therapy, interpersonal and social rhythm therapy, cognitive-behavioral therapy) for improving treatment adherence and clinical outcome of bipolar patients is unquestionable, and future treatment guidelines should promote its regular use among clinicians. As clinicians, we are responsible to offer the best treatment available to our patients, and this includes both evidence-based psycho-education programs and newer pharmacological agents.

Conflict of interest

The authors declare that they have no conflict of interest.

Author details

Cătălina Angela Crișan^{1,2*}

*Address all correspondence to: ccrisan2004@yahoo.com

1 Department of Neurosciences, Discipline of Psychiatry and Pediatric Psychiatry, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

2 Psychiatric Clinic I, Emergency County Hospital, Cluj-Napoca, Romania

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