

Beyond the Usual Suspects: Positive Attitudes Towards Positive Symptoms Is Associated With Medication Noncompliance in Psychosis

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Antipsychotic medication represents the treatment of choice in psychosis according to clinical guidelines. Nevertheless, studies show that half to almost three-quarter of all patients discontinue medication with antipsychotics after some time, a fact which is traditionally ascribed to side-effects, mistrust against the clinician and poor illness insight. The present study investigated whether positive attitudes toward psychotic symptoms (ie, gain from illness) represent a further factor for medication noncompliance. An anonymous online survey was set up in order to prevent conservative response biases that likely emerge in a clinical setting. Following an iterative selection process, data from a total of 113 patients with a likely diagnosis of schizophrenia and a history of antipsychotic treatment were retained for the final analyses (80%). While side-effect profile and mistrust emerged as the most frequent reasons for drug discontinuation, 28% of the sample reported gain from illness (eg, missing voices, feeling of power) as a motive for noncompliance. At least every fourth patient reported the following reasons: stigma (31%), mistrust against the physician/therapist (31%), and rejection of medication in general (28%). Approximately every fifth patient had discontinued antipsychotic treatment because of forgetfulness. On average, patients provided 4 different explanations for noncompliance. Ambivalence toward symptoms and treatment should thoroughly be considered when planning treatment in psychosis. While antipsychotic medication represents the evidence-based cornerstone of the current treatment in schizophrenia, further research is needed on nonpharmacological interventions for noncompliant patients who are willing to undergo intervention but refuse pharmacotherapy.

Key words: schizophrenia/psychosis/neuroleptics/antipsychotics/compliance/adherence

Introduction

Whereas antipsychotic agents, especially atypical neuroleptics, represent the treatment of choice in schizophrenia according to most clinical guidelines, recent meta-analyses indicate that effect sizes for their efficacy are only moderate.¹ In addition, a significant number of patients have incomplete or poor response to antipsychotics.^{2,3} Not surprisingly, treatment noncompliance is common in patients, even with the newer antipsychotic drugs: half to up to three-quarter of patients do not take their medication as prescribed.^{4,5}

A solid literature has identified major factors promoting noncompliance with antipsychotics: side-effects, poor therapeutic alliance (particularly mistrust against the prescriber) and lack of illness insight.^{5,6} Fear of stigma and negative attitudes of peers or family members toward medication additionally exert a detrimental effect on medication compliance. Another factor for noncompliance relates to forgetfulness, which emerged as a reason for drug discontinuation in 32% of patients with psychotic disorders in a recent anonymous internet survey.⁷ Findings on neurocognition and medication adherence are mixed,^{8,9} however, putatively reflecting methodological limitations: standard memory tests tap into retrospective memory, whereas medication intake is a prospective memory function. While specific interventions (eg, pill containers) have been developed to address adherence-related cognitive problems, these are rarely used in practice.

Beyond these “usual suspects,” the present study was concerned with a potentially underrecognized reason for drug discontinuation: “gain from illness” (We use the term gain from illness in a noncausal descriptive way to denote that the symptom is appraised in an at least partially positive way and is not necessarily perceived as a problem by the patient per se.). The postulation

of gain from illness, an originally psychodynamic concept, is obviously in stark contrast to the known short- and long-term consequences of schizophrenia, such as anxiety, depression, and low functional outcome.¹⁰ On the other hand, an emerging literature suggests that patients exhibit at least some ambivalence toward their symptoms,¹¹ particularly their positive symptoms. Notwithstanding the fact that psychosis is often perceived as frightening, patients sometimes refer to it as a fascinating experience and often attach not only negative but also positive meanings to their symptoms.¹²

In a number of studies, Morrison and colleagues demonstrated that hallucinations are associated with both positive and negative beliefs.^{13,14,15} For example, patients hearing voices report associated benefits, such as companionship or comfort,^{14,16} and paranoia is often reported to be a subjective survival strategy.¹⁷ Some patients appraise voice hearing as a pleasurable experience.^{18,19} Interestingly, this rate seems to be higher for voice-hearers not using the mental health system.²⁰ In accordance with these studies, it has also been shown that patients with schizophrenia regard negative and disorganization symptoms as most troubling, whereas clinicians lay the therapeutic focus on the amelioration of positive symptoms.²¹

The impact of gain from illness on medication noncompliance has not been widely investigated, and causal inferences are often based on correlational data. The topic is not new, however. Van Putten²² noted decades ago that “some schizophrenics may prefer an ego-syntonic grandiose psychosis to a relative drug-induced normality” (p. 1443). This observation has been validated in clinical studies indicating that the presence of delusions of grandiosity predicts lower compliance during inpatient treatment^{23,24} or, conversely, that fewer depressive symptoms are associated with lower illness insight and lower perceived medication efficacy.²⁵ Concerning auditory hallucinations, Copolov et al²⁶ hypothesized that “... not wanting to lose positive Ahs [ie, auditory hallucinations] may be one reason underlying noncompliance with treatment” (p. 169). Chadwick and Birchwood have shown that depression is most severe with malevolent but not benevolent voices.²⁷ Patients with malevolent voices tend to resist to the voices, whereas patients with benevolent voices are likely to engage with them.^{28,29} Recently, Favrod et al³⁰ found a negative relationship between engagement with benevolent voices and compliance in a small sample of 29 subjects. In a prior study of our group,⁷ 11% of patients with schizophrenia admitted noncompliance because they missed their acoustic hallucinations and an even greater number reported noncompliance because they longed for the feeling of power imparted by psychosis.

The present study assessed motives for noncompliance for both less frequently investigated (eg, gain from illness and forgetfulness) as well as traditionally described factors

(eg, side-effects). The present study was an anonymous online trial without expert ratings. This particular setup was deemed more informative, since many patients with paranoia do not trust mental health professionals.

Methods

Setting and Procedures

Invitations for participation were posted on several moderated German online discussion forums specialized on psychosis, as we solely aimed to attract and recruit patients with psychotic disorders. A web link provided access to the internet questionnaire.

In an introductory part, data on sociodemographic and background information (age, gender, and occupational status) and medical history (eg, overall number of treatments) were collected. We also questioned participants regarding diagnoses determined during treatment. Participants were then asked if they were receiving medication and, if so, to specify the type and dose of medication. Participation was anonymous in order to ensure unbiased responses. Cookies prevented multiple access attempts from the same computer.

Materials

Community Assessment of Psychic Experiences Scale and Insight Scale. Respondents were requested to complete the Community Assessment of Psychic Experiences scale (CAPE³¹) tapping psychotic, negative, and depressive symptoms. We added 4 lie scale items encompassing common misconceptions of psychosis: (a) seeing tiny objects like white mice (indicating delirium rather than psychosis), (b) alien abduction (rare but highly publicized symptom), (c) being a famous historical personality (rare but highly publicized symptom), and (d) mental lapses during which one becomes another person (split personality; rare/implausible but highly publicized [cliché] symptom). The questionnaire proceeded with the 8-item self-report Insight Scale.³²

Noncompliance and its Reasons. Then, attitudes toward antipsychotic medication were assessed on a 5-point scale (ie, “refuse intake” [no compliance] to “medication helps me and I take them on a regular basis” [full compliance]). Subsequently, patients were asked whether they had ever discontinued their medication or not taken it as prescribed. If noncompliance was affirmed, the patient was requested to specify the reasons (see table 2 for response options).

Participants. A total of 383 individuals accessed the web survey. Data from 113 participants (30%) were eventually retained for the final analyses following a conservative iterative exclusion procedure. Reasons for exclusion (a priori criteria) were as follows: failure to

Table 1. Background Characteristics, Psychopathology, and Insight

Variable	Psychosis, (<i>N</i> = 113)
Background and medical history	
Age	37.15 (9.55)
Gender (male/female)	39/74
Number of hospitalizations	4.66 (1.78)
Number of positive voices	2.34 (2.16)
Number of negative voices	3.52 (3.18)
Community Assessment of Psychic Experiences (CAPE)	
Positive	1.72 (0.45)
Negative	2.28 (0.53)
Depressive	2.28 (0.50)
Insight scale	
Awareness of symptoms	3.07 (1.11)
Awareness of illness	2.97 (1.40)
Need for treatment	4.84 (1.56)

Note: Means and SDs.

complete the questionnaire (*n* = 176), no diagnosis of schizophrenia (*n* = 6), either providing no answer or providing the name of a nonantipsychotic drug (eg, SSRI or benzodiazepine) when asked about the prescribed antipsychotic agent (*n* = 82), and admitting to not having provided truthful answers (*n* = 3). We also deleted 3 subjects who achieved more than 8 of 16 possible points on the 4 lie scale items. Moreover, it was a priori determined that at least 15% of a subject's individual item scores on the CAPE should deviate from the most frequent (modal) score. This criterion led to the exclusion of one subject.

Results

Sample Characteristics

Table 1 summarizes the background and illness-related variables. The sample consisted of rather chronically ill patients with more than 4 admissions on average. The CAPE scores were largely in line with previously reported values.⁷

Noncompliance with Antipsychotic Medication

A total of 72 patients (64%) reported having discontinued antipsychotic medication before and were subsequently questioned on the underlying reasons (see table 2). On average, patients provided 3.83 (SD = 1.97) different explanations for noncompliance (maximum score: 16). Table 2 shows the percentages of each reason (multiple reasons could be provided so that the percentages amount to over 100%). The most often provided reason was side-effects (80%), followed by a subjective lack of need (58%). The following reasons were endorsed by at

Table 2. Reasons for Discontinuation of Antipsychotic Medication (Sorted in Descending Frequency for the Present Study, Multiple Endorsements Were Allowed)

Variable	Present Study
1. Too many side-effects	80%
2. Did not need antipsychotics in my view	58%
3. Medication intake amounts to stigma as being ill	31%
4. I distrust my physician/therapist	31%
5. I had the feeling that taking medication was the same as acknowledging that all I have experienced was untrue (although this is not the case)	28%
6. I reject medication in general	28%
7. Forgot intake	21%
8. Friends/relatives advised me not to take it	20%
9. During psychosis, I had a feeling of importance and power which I did not want to miss	18%
10. During my illness, I become another person and for this reason I need this state from time to time	18%
11. Do not work for me	16%
12. I falsely assumed that I should only take them when having acute symptoms	15%
13. Medication is too expensive for long-term treatment	8%
14. I missed the voices	7%
15. I had fears that acquaintances might detect medication boxes	3%
16. Intake was too complicated	2%

least one-fifth of patients: stigma (31%), mistrust against the physician/therapist (31%), attributing medication intake as a negation of the validity of personal experience (28%), rejection of medication in general (28%), forgetfulness (21%), and advice against medication intake by friends/relatives (20%). Cumulatively assessed over 3 items (items #9 [importance and power: 18%], #10 [becoming another person: 18%], and #14 [missing voices: 7%] on table 2), gain from illness was provided as a reason for drug discontinuation in 28% of patients (ie, at least 1 of the 3 items had to be endorsed).

A logistic regression model was computed with compliance as the dependent variable (ie, no/partial compliance vs noncompliance) and age, gender, number of hospitalizations, and questionnaire scores (CAPE, Insight) as predictors. The total score of the Insight Scale (Wald index = 10.81, *P* = .001) and the CAPE positive subscale (Wald for = 8.12, *P* = .004) emerged as the strongest predictors for noncompliance.

Discussion

Research has traditionally emphasized the burden that schizophrenia inflicts on patients,³ whereas gain from illness, particularly the positive appraisal of psychotic symptoms, has been an area of neglect until very recently. As many patients are stuck in ambivalence toward their

symptoms, there is an urgent need to shed more light on the possible relationship between gain from illness and low compliance in schizophrenia.

Almost two-thirds (64%) of the sample acknowledged at least one incident of noncompliance in the course of their illness. Significant predictors of noncompliance included low illness insight and high current level of positive symptoms. The most frequent reasons for drug discontinuation were as follows: side-effects (80%), a subjective lack of need for medication (58%), stigma (31%), and mistrust against the physician/therapist (31%). However, apart from the usual suspects (eg, side-effects), less frequently studied factors, such as missing positive illness effects and forgetfulness, were revealed as causes of noncompliance.

Noncompliance due to gain from illness expressed as a composite parameter consisting of 3 items tapping positive attitudes toward positive symptoms, was a reason for drug discontinuation in 28% of the sample. These results are largely in line with our hypothesis that gain from illness should be added to the known risk factors for medication noncompliance. The subjective illness concept, specifically the question whether a mental condition is considered an illness or a partly desired state seems very relevant to treatment-seeking behavior and compliance. This question has so far been often neglected in studies of medication compliance in schizophrenia, presumably due to the fact that the disadvantages of psychosis largely overshadow any subjective advantages (eg, being important) in patients seeking psychiatric treatment. Thus, manifestations of fear and despair in many patients at hospital admission may inflate the clinical impression that psychotic symptoms are solely experienced as negative.

A large subgroup of patients rejected medication in general (28%) or noted advice against medication intake by friends/relatives (20%) as a further reason for noncompliance, a finding that mirrors common preconceptions in the general population against medication in general and antipsychotics in particular.³³ Studies on patients with nonpsychotic disturbances receiving antipsychotic medication, eg, patients with obsessive-compulsive disorder, also report relatively high rates of noncompliance (43%) in spite of better illness insight in these patient groups, a finding that indicates that noncompliance is thus not always due to lack of insight and that antipsychotic agents might be unpopular per se.⁷

A significant percentage of patients (28%) affirmed that taking medication would feel the same as acknowledging that all they had experienced was untrue.⁷ Many patients with schizophrenia have endured negative life events such as neglect and abuse.³⁴ For these patients, a medication prescription without complementary psychotherapeutic assistance may create the impression that these incidences are deemed irrelevant. In a similar vein, Klapheck et al¹² argue that “psychotic patients do have a strong need to give a subjective meaning to their psychosis” (p. 9). If this subjective meaning of illness is

overlooked by clinicians, nonadherence to medication might be a consequence.

Hence, the treatment of psychotic symptoms should optimally address the (idiosyncratic) benefits of certain symptoms and their obvious costs. Psychological treatments such as cognitive behavioral therapy may help carefully counter such assumptions without invalidating the experience of the patient. Such treatments may help patients to regard medication as one building block of treatment rather than as a means of silencing them. At this point, it should be stressed that, on average, patients provided almost 4 reasons for drug discontinuation in our study. Clinicians should therefore keep in mind that noncompliance has to be addressed on several levels.

The present study faces a number of limitations. First, patients were recruited over the internet. While we adopted a number of precautions and strict inclusion criteria to ensure validity of diagnoses, we have to acknowledge that no formal diagnosis of schizophrenia was established. Thus, the representativeness of our sample cannot be fully verified, nor can the possibility be excluded that some questions may have been too complex for patients with cognitive deficits. Secondly, noncompliance rested on self-report only. However, the elimination of these limitations through inclusion of a clinically defined sample and use of standardized assessments would be accompanied by several important disadvantages. Clinical samples are not representative of the entire population, as treatment-seeking patients markedly differ from patients not seeking treatment on a number of dimensions across different psychiatric disorders.^{20,35} Moreover, patients in clinical settings may not respond openly because of fear of negative consequences when disclosing noncompliance and its particular reasons (eg, distrust against clinician due to the experience of the loss of civil rights in closed wards¹⁵). Thus, an anonymous internet survey might help to obtain a more complete less biased picture of the motives of noncompliance. Finally, it might have been interesting to discern among different side-effects (eg, weight gain, extrapyramidal symptoms) as causes of noncompliance, by including multiple items rather than just one.

To conclude, noncompliance remains a serious and multidimensional problem, even in the era of second-generation antipsychotics. While side-effects pose the biggest challenge, they are not the only obstacle, and patients in this study reported approximately 4 out of 16 possible reasons for drug discontinuation on average. Our findings suggest that greater consideration of the possible positive effects of psychotic symptoms and the subjective illness model of the patient is needed in order to formulate an optimal hierarchy of target symptoms. Psychotherapy and psychoeducation might be of particular importance in challenging dysfunctional beliefs about the disorder and its treatment, while cognitive remediation might be useful for tackling forgetfulness as a reason for noncompliance.

Even though antipsychotic medication currently represents the treatment-of-choice in psychosis, studies are warranted that investigate psychotherapeutic approaches for treatment-resistant patients as well as alternative treatments for patients who refuse medication. Promising steps in this direction have already been taken.³⁶

Acknowledgments

The Authors have declared that there are no conflicts of interest in relation to the subject of this study.

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