Psychological Issues in Improving Adherence and Alliance

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The Patient–Doctor Relationship as a Determinant of Adherence to Treatment

From an intersubjective point of view, adherence to treatment can be defined as a multi-dimensional phenomenon [1] which occurs through the dynamic interaction of different variables which pertain both to the doctor (e.g., diagnosis, choice of medicines, prescription, therapeutic project, and goals of treatment) and to the patient (e.g., insight, attachment style, attitude toward the therapy, subjective well-being, and presence of a caregivers) (Fig. 1). All these factors, which are part of the therapeutic field built upon the relationship between doctor and patient, influence the therapeutic alliance. The phenomenon is multidimensional and this implies the necessity of taking into exam the greatest number of positive and negative factors involved. In psychiatry adherence represents one of the major current problems in the course of treatment. In fact, recent studies have shown that non adherence represents one of the most difficult issues in the treatment of schizophrenia [2] especially, and that a weak therapeutic alliance and low insight correlate with poor adherence [3]. The consequences of this phenomenon are quite obvious (e.g., scarce clinical improvement, chronicity, and relapses) and there are different factors which influence this.

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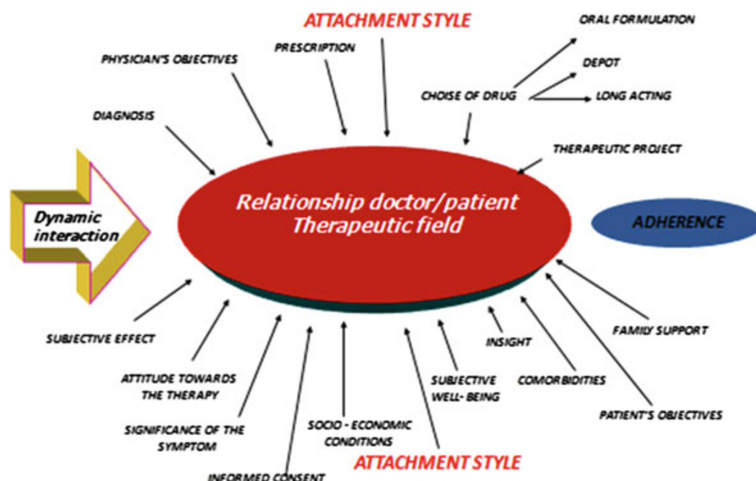

Fig. 1 Adherence: a multi-dimensional phenomenon (Niolu, Siracusano, 2005)

From Compliance to Adherence to the Alliance: Historical Notes

The concept of adherence is contiguous to that of compliance: compliance is defined as. "an amicable or serene agreement" and rather antithetical, as, "the act of giving in to pressure, demand, coercion... so servile.. accordance to satisfy formal requirements… promoted by official or legal authority". The adherence is defined as, "the act of forming a stable and trusting attachment (for a party, principle, cause)" [4].

From a semantic point of view, the two terms emphasize the fact that the subject is placed in a different position in relation to the agreement. The compliance presupposes the liabilities and the coercive characteristic of the action, induced by a hierarchically superordinate authority; however, adherence always seems to catch a glimpse of the assignment as a superordinate entity, but not experienced as coercive.

In the medical field these terms, in the course of time, have evolved from the point of view of the meaning and, consequently, also in the characteristics of their use: Sackett in 1976 defined the compliance as "the degree of coincidence of the behavior of a subject with the prescription" [5]; in 1986 Babiker spoke of "complex phenomenon that represents the subject's personal contribution to the management of their disease" [6]; Blackwell in 2000 speaks of "the degree to which the patient follows the doctor's prescription". In 1996, Hatcher, for the first time, combines the concept of *compliance* to that of the *therapeutic alliance*, calling it "a collaboration in which contribute, with varying degrees of activity, both the physician and the patient in an intersubjective dialogue", introducing the concept of *partnership* [7].

In 1991 [8], Probstfield used, for the first time, the terms *adherence* and *non-adherence* to refer to a therapeutic relationship in which the emphasis is shifted to the participation of the patient in the therapeutic choices. Focusing on the patient, the indexes of *subjective perceptions* and *patient satisfaction* are gaining greater value in the assessment of response to therapy and participation in treatment.

Subjective perceptions and patient satisfaction are elements that must be distinguished from the more general assessment of the drug's *effectiveness* on symptoms and the *side effects* objectively demonstrated. To confirm this observation there is the fact that, with the same effectiveness and incidence of side effects, many interruptions of treatment are to be related to low scores in ranges of *subjective well-being* and patient satisfaction [9]. A significant step forward was made with the introduction of informed consent, which is an instrument through which the patient expresses his desire to join the therapeutic program.

Within the informed consent, the terms adhesion and adherence must a fortiori be distinguished. The adhesion is, as has been said, a general acceptance a priori of the treatment proposed, before it has started, while *adherence* refers to a contract in which patients, after having experienced the effects of the treatment, express their intention to continue it.

Through the expression of informed consent, the evaluation of *subjective perceptions* of patients and the expression of their *satisfaction* for the ongoing treatment, it establishes a *negotiation* and *dialogue* between *informed patient* and *caregiver*, that is the person who takes care of the patient (e.g., relative, assistant, medical-nursing staff).: This involves the active involvement of the subject in establishing treatment goals, and therefore, the establishment of a *therapeutic alliance* (see Table 1).

The interaction is called dynamic because each of the factors listed may vary over time within the therapeutic relationship. Examples of this include the introduction of a new drug, suspension and/or reduction of the previous treatment, the decision to start psychotherapy in the course of a drug in a psychological relationship.

Table 1 Niolu e Siracusano, 2005

Period	Type of relationship	Role of Doctor/Patient
Early twentieth century	Hierarchical relationship	Doctor: role of taxation Patient: passive role
Fifties	Hierarchical relationship	Doctor: paternalistic role Patient: passive role
Nineties	Collaborative relationship	Intersubjective dialogue
Two thousand years	Shared decision making model	Therapeutic choice shared

Subjective Well-Being

Satisfaction and well-being are subjective experiences: the way patients experience drugs and sensations that patients experience when taking psychopharmacological therapy appears to be an essential clinical data for both the overall understanding of the patient's attitude towards therapy and for predicting the adherence to treatment [10]. In addition to the factors previously considered, these feelings have a significant impact in maintaining adherence. The patient's attitude towards the drug by psychopathological conditions, clinical severity of the subject and the side effects.

As neuroleptics were introduced into clinical practice, patients, in the position of influencing the selection of therapy, have now spoken of the "unpleasantness". The side effects that mostey affect adherence in a negative way are: extrapyramidal symptoms (akathisia in particular), weight gain, sexual dysfunction and, more generally, the negative sensations related to the treatment [11–14]. In fact, despite the side effects of drugs are a cause of discontinuation of therapy, response and subjective well-being to treatment with antipsychotics are the most important predictors for adherence [12, 13, 15].

In this regard, it is useful to remember that the line between side effects and subjective effect is very thin, and is difficult to detect in the patient's report; however, it is important that in the clinical interview is thoroughly investigated, because frequently, patients tolerate serious side effects well if they do not identify their subjective feelings as particularly unpleasant. The subjective experience is often found in the patient's idea of his or her illness and what is the idea of recovery or, more simply, to "be better". The most frequent unpleasant sensations reported by patients taking psychiatric drugs recall "feeling strange and drawn, without feelings, difficulty thinking" [12, 15]. In summary, it is believed that some unpleasant sensations that arise during treatment represent a specific element in its own right, usable in order to provide nonadherence, and then to implement strategies which limit the interruption of therapy. The clinical importance of the study of subjective responses lies, no doubt, in the ability to accurately predict sufficient adherence to treatment in patients with schizophrenia, as well as, according to Dworkin, to recognize subjective feelings to treatment as an indicator of initial symptomatic response [16]. The earliest evidence dates back to the end of the 1990s; Singh and Smith in 1973 reported that patients with dysphoria during treatment with haloperidol had a negative outcome over time [17]. More recent studies have confirmed that the occurrence of negative feelings after 24 to 48 hours of treatment with neuroleptics significantly correlated with poor adherence within 3 weeks or less in response to treatment [12]. Another study conducted on a fairly large sample of patients (150 subjects) with a diagnosis of chronic schizophrenia showed that slightly more than half of the participants did not follow the therapy. Among them, the patients did not differ by sex, age, and total time of hospitalization, but a significant negative correlation was observed between subjective experiences (assessed with the Drug Attitude Inventory-DAI) and poor adherence;

also almost all patients (80 %) within the sample had a *pattern* of adherence in accordance with the type of subjective response reported [12]. Recently, other experiences have allowed us to observe that the attitude and feelings of the patient toward medication, assessed with specific scales such as the *Drug Attitude Inventory* (DAI), *Subjective Well-Being under Neuroleptic Scale* (SWN), and *Rating of Medication Influences* (ROMI) are not explained by the overall severity of positive or negative symptoms: not necessarily in sicker patients observed an approach to the treatment worse than those with milder symptoms and it always show that the feelings related to the treatment and the way in which the subject experiences the relationship with the drug are something autonomous, not closely related neither to the state of the disease nor to side effects. This data is very important and should be constantly kept in mind: an improvement of psycho-pathological picture, in fact, is not always associated with a similar improvement in subjective well-being, or to a greater adherence to therapy by patients.

The relationship between doctor and patient, fundamental in all branches of medicine, is in psychiatry, the *core* of the therapeutic program and ensures the therapeutic continuity. The therapeutic relationship between doctor and patient was found to be significant for adherence to treatment in all psychiatric conditions. The therapeutic relationship was investigated as it was emphasized by Freud. He wrote that, "The first aim of treatment consists of fixing [the patient] for the treatment and the person of the physician". A discontinuity in treatment does not merely indicate an interruption in the assumption of drugs, but represents an important signal that something in the doctor–patient relationship has changed or is changing. This relationship is peculiar, and as a matter of fact, even in a doctor-patient relationship that is primarily based on psychopharmacological prescription, the simple drug prescription has the value of "relational act" and necessarily involves the construction of a relationship that takes into account the drug use, giving to therapist and patient roles that turn around this central element. Therefore, in choosing a therapeutic program the primary target to be achieved (if the diagnosis is correct and the chosen drug effective) is to ensure the appropriate therapy intake, at the right doses and for the prescribed time, which in turn, affects response, remission, relapse, recurrence and the possible development of resistance and / or chronicity, which will shape the course of the disorder. In fact, neither the accuracy of diagnosis, nor the right medication can provide sufficient guarantees about therapeutic adherence. The ability to predict, within certain limits, adherence to treatment can occur only if the physician has a thorough knowledge of his/her patient: he/she must have much information about his/her previous history, personality traits, capacity of insight, his attitude toward drugs in general, and psychiatric ones in particular, his illness idea: the nature of it and the extent to which it has changed his life, what he means by his idea of getting better, the family and social network, how they establish and maintain, if this happens, significant emotional ties (attachment style). To pursue this objective, the *interview* is the spatial, temporal, and mental location, to collect all the elements and to lay the foundations for the creation of a therapeutic field. As mentioned above, in psychiatry any type of doctor–patient counseling, and in particular the first

interview, is already a relational and therapeutic act. In order to achieve this objective, *the interview* represents the spatial, temporal, and mental place to collect all of the elements in play and to lay the foundation for the creation of a therapeutic field.

As mentioned above, in psychiatry any type of doctor–patient meeting, even and especially the first interview, is already an act and relational therapy.

The points on which the therapist must focus during the first interview are:

- Active listening (processing of biological, psychological, and motivational meaning of the symptoms, “mapping” of the patient)
- Setting up a dialogue and a therapeutic relationship based on clarity in some areas:
  - on his own idea about drugs,
  - on the idea of the patient about medication and its previous experiences,
  - on the manner of *prescription*,
  - on the reasons for choice of the drug,
  - on the outcome expectations,
  - on the expectations of side effects;
  - on the involvement of the patient and underscoring his or her role in monitoring and reporting therapeutic and side effects, and;
  - on the involvement of the family network in the construction of the covenant: evaluation of the real possibility of taking the prescribed treatment, detection and prompt reporting of symptoms “sentinel” of relapse and practical help in taking the drug daily.

The follow-up interviews are meant to the monitoring of drug treatment and to strengthen the collaborative approach established in the first interview, through the following steps:

- the verification of the patient’s reactions to the drug prescribed;
- the verification of the difficulties encountered in following the prescription;
- emphasizing the importance of the point of view of the patient, his subjective perception;
- the verification of the degree of adherence as compared to the predictions made in the first interview;
- evaluating the efficacy and tolerability of treatment (side effects);
- dosage adjustment, and
- feedback from the family.

The *prescription* is at the same time the official start of drug therapy and the endpoint of a path that has developed through the execution of all previous diagnostic and therapeutic acts, from which now, largely depends on the outcome of the prescription. The context where the prescription happens is a relationship between doctor and patient which is human and dynamic and goes beyond the symptoms to shape the “therapeutic field”, an area of intersubjectivity, which is the result of this dynamic interaction between factors that belong to the patient and the therapist, and influence, in various measure, the achievement of an adequate therapeutic alliance. This latest is defined as the relational base on which a therapeutic project is built, a relationship of trust and cooperation with mutual sharing

of skills, objectives, and methods, that has a crucial effect on adherence to pharmacological or psychotherapeutic treatment, issues which areas fundamental as they are problematic for all medicine and for psychiatry in particular.

Alliance and Psychodynamic Issues

The therapeutic alliance is also defined as a relationship to which both doctor and patient contribute, with varying degrees of activity. It is the relational collaboration established between the physician and the patient with the aim of building a relationship of trust and mutual cooperation. On this relational base, a treatment plan is built, and allows the patient and the physician to plan together the course of treatment articulated in the time and manner necessary to address the specific disorder.

There are two different types of therapeutic alliance. In the first type, called "*helping alliance*", the patient perceives the therapist as "warm, helpful and supportive", in this case it may run the risk of reducing the relationship in terms of "demand-response", whereby the patient "asks" and the doctor, colluding, "provides" the drug. In this case it is important to insist on engaging the patient in a reciprocal relationship, in which he must take the most active and proactive attitudes, even with respect to dose adjustments and decisions on drug. The second type of alliance, called "*working alliance*", is based on a sense of common work, that targets the containment of the discomfort that hinders the patient. Key points of this type of alliance are the sharing of similar interpretations of the etiology and for the reasons of hardship by the therapist and patient, combined with the feeling of a positive evolution in the ability of cooperation of the patient in the treatment program, through the acquisition of therapeutic tools borrowed from the progress of the relationship with the therapist.

It is possible to foresee a third type of alliance, which in successive stages, is found to shift from a *helping to a working* alliance during the gradual, but steady, development of the therapeutic relationship [8]. The "*intersubjective alliance*" [18, 19] is a new concept derived from psychotherapy, later adapted to the pharmacological therapeutic relationship. To develop an effective and appropriate patient–physician relationship, the psychiatrist must always be aware of working with a people who have their own personality, feelings, sensitivity and intelligence, apart from symptoms and illness. Psychoanalytic theories suggest that the quality of the therapeutic relationship is linked training to interpersonal relationship training of unconscious reactions such as transfert and controtransfert. Since the beginning of his studies, Freud had understood that the work of revelation, which is essential for the success of psychoanalysis, required a collaborative attitude and cooperation between patient and therapist. Placing inside the "irrepressible positive transfert" (conscious positive feelings toward the analyst, who helps the patient to overcome the resistance), Freud used the term "rapport" to refer to this important aspect of patient–therapist relationship and called it the

"vehicle for the success" [20]. Transfert is defined as the shift of thoughts, feelings, desires, and behaviors of the patient, originally facing significant characters of his childhood world, on the therapist. Through this shift, the patient turns the memories into present life: in the analysis space. However, the controtransfert is, however, the wide range of reactions that the doctor may have toward the ill. It may take the form of positive or negative feelings (e.g., a doctor who has feelings of anger, hostility, antipathy toward the patient, tends to assume a destructive and ineffective attitude in the relationship) [21]. According to Freud, the conditions for withdrawal of the setting (opacity, silence) create frustrating situations for pulses so that they win the obstacle of resistance, actualized in the analytic relationship. In contrast, in the cognitive model, the conditions of interpersonal security, offered by the therapeutic relationship, promote the awareness and development of autoriflessive more heuristics activities. The experience of a positive relationship with the therapist can change the negative forecasts of the patient's interpersonal patterns. Such corrective interpersonal experiences concern the affective and cognitive side and the disposition of the action. Looking at the therapist the patient can assimilate ways of acting more useful than those usually adopted. The therapeutic outcome is most significantly correlated with the therapeutic relationship rather than the different psychotherapeutic techniques [22].

In this complex model of prescription, focused on relationship, the attachment styles emerge as central points. As the therapist and the drug represent attachment figures and the patient is a caregiving figure, each of them enters the relationship with their Internal Working Models (IWM) and behavioral patterns, which must be taken into account in the construction of a prescription to optimize adherence. Attachment theory also contributes to the understanding of working alliance by providing a framework to conceptualize the way in which therapist and client factors interact in determining the quality of the relationships. There is empirical evidence to suggest that therapist attachment style is influential in the development of a therapeutic relationship [23].

The attachment system has its basis in the innate propensity of human beings to form strong emotional bonds with their figures of reference, which Bowlby calls "particular others" [24, 25]. The evolutionary purpose of the attachment system is to find a caregiving figure that the subject perceives as strong and reliable. This attachment system is established according to the different qualities of the mother-child relationship, resulting in several "attachment styles", with varying characteristics depending on different dynamic and circular patterns of demand (attachment) and answer (caregiving). Attachment style is the way in which each individual assumes the innate propensity to form affectionate bonds with others. The attachment developed within the infant-caregiver relationship is thought to form the "secure basis" of future relational dynamics.

Research by developmental psychologist Mary Ainsworth in the 1960s and 1970s, through the protocol of the Strange Situation, reinforced the basic concepts and introduced the concept of the "secure basis". As such, she developed a theory which included a number of attachment patterns in infants: secure attachment, insecure-anxious avoidant attachment and insecure-anxious ambivalent attachment.

Infants who are "securely attached" use their caregiver as a secure basis while exploring new surroundings; such infants seek contact with, and are comforted by, caregivers after separation. Infants described as "anxious-ambivalent" have difficulty using the caregiver as a secure base; these infants seek, then resist, contact with caregivers after separation. Finally, infants with an "avoidant attachment" style do not exhibit distress upon separation and do not seek contact after the caregiver's return.

In 1985 M. Main identified, along with the attachment styles delineated by Ainsworth, a fourth attachment style in children, that she called "disorganized" [26–29].

The "disorganized" style, evaluated as a risk factor for the onset of a series of psychological disorders, can be characterized by the absence of a coherent organized behavioral strategy, to cope with the stresses that the child receives during the Strange Situation. Mary Main, based on the Strange Situation for children, designed by Mary Ainsworth, created the Adult Attachment Interview (AAI), a semistructured interview assessing attachment style in adults. According to these measures adults have four attachment styles: secure, anxious–preoccupied, dismissive–avoidant, and fearful–avoidant. The secure attachment style in adults corresponds to the secure attachment style in children. The anxious–preoccupied attachment style in adults corresponds to the anxious–ambivalent attachment style in children. However, the dismissing–avoidant attachment style and the fearful–avoidant attachment style, which are distinct in adults, correspond to a single avoidant attachment style in children. Another pattern of adult attachment style is the one proposed by Bartholomew and Horowitz. These authors focused on a pattern of attachment related to Internal Working Models (IWM) of self and others. For IWM we refer to the mode in which subjects define themselves and others in terms of intimate relationships. Bartholomew and Horowitz delineated four different patterns of attachment (see Table 2) and developed the Relationship Questionnaire (RQ) [30], which highlights the subjective perception of the interpersonal relationship relative to each of the attachment styles. Integrating data regarding attachment in adults with data on the different meaning of emotions of attachment in mother/ child relationships [28, 31, 32], we strived to extrapolate

Table 2 Attachment styles and internal working models IWM[a]. Copyright © 1991 by the American psychological association. Reproduced with permission [30]

	I.W.M.of other Positive	I.W.M.of other Negative
I.W.M.of self Positive	Secure	Avoidant/Dismissng
I.W.M.of self Negative	Anxious/Preoccupied	Avoidant/Fearful

[a] Internal working model: Modality with which subjects define themselves and others on the basis of interpersonal relationships

hypotheses about the role of attachment style in the doctor-patient relationship and adherence to treatment. In the fearful and preoccupied attachment styles, ambivalent emotions of attachment itself prevail, assessment of ambivalent emotions of attachment itself, while in others, the person would doubt the effectiveness of these emotions by evoking a coherent response. Individuals with preoccupied attachment styles would have more positive beliefs about help-seeking, but may still be relatively ineffective in regulating distress through seeking support or methods of self-regulation. This is reflected in the therapeutic relationship where adherence sometimes is inconsistent, sometimes exaggerated, and sporadic. In avoidant attachment, emotions are classified by subjects as a source of irritation moreover as a sign of personal inadequacy for themselves. It should be obvious that the identification of the attachment style of the patient must be supported by an equally clear understanding of the therapist's own attachment style. This aspect, necessary in a psychotherapeutic relationship, must also be considered as fundamental in the psychopharmacological relationship, where the drug itself is an attachment figure [33]. Identifying the patient's attachment style can be useful to the physician to build a good therapeutic alliance and to predict adherence to treatment. With particular attention on case managers of patients suffering from severe and persistent mental health problems, *Dozier and colleagues* found that physicians with secure attachment style, assessed with the AAI, were less likely to develop a therapeutic alliance with patients with dismissing or preoccupied attachment style [34]. Instead, another study showed that patients with opposite attachment style compared to their doctor established a stronger therapeutic alliance [35].

Attachment style, therapeutic relationship, and adherence in schizophrenia

In schizophrenic patients with avoidant attachment style there is a greater tendency to develop positive symptoms and a lower adherence to pharmacological therapy that, in contrast, is higher in patients with anxious attachment. Individuals with avoidant attachment style will tend to show avoidance coping styles which are associated with poorer outcomes because they have negative expectations about help-seeking; in contrast, patients with preoccupied attachment style develop more positive lived experiences about help-seeking but may still be relatively ineffective in regulating distress through seeking support or methods of self-regulation [36]. In disorganized attachment style the emotions in the relationship are often multiple and dissociated, and then reflected in an interpersonal relationship of this type. The clearest example concerns the therapeutic relationship with patients with borderline personality disorder or dissociative disorder patients [28].

To date there is limited research investigating attachment theory relevance to psychosis. The starting point is the finding of high levels of insecure attachment in patients suffering from psychosis. Cognitive models of psychosis emphasize the importance of self and other schemata in the development and maintenance of psychosis and according to these theories, early life events, such as trauma related to the breakdown of meaningful interpersonal relationships, can lead to a vulnerability to perceive others as a threat and this could contribute to the development of psychotic symptoms in adulthood [37]. The attachment theory emphasizes the importance of interpersonal events and trauma in psychotic *social cognition* [38].

Particularly, this theory is fundamental to understanding specific symptoms associated with psychosis (e.g., voice hearing, paranoia, and negative symptoms). There are indications that specific types of insecure attachment predispose individuals to the development of different symptom profiles associated with psychosis or once developed be a key factor involved in their maintenance. In this regard, an example is the theory that distinguishes between the two types of paranoia: "poor me" paranoia, related to high self-esteem ("I'm persecuted because they envy me") and "bad me" paranoia, related to low self-esteem ("I'm persecuted because I'm guilty"). In terms of attachment style, the two types of paranoia can be related to the dismissing and fearful styles, associated with negative beliefs about others, but which differ in terms of self-view. Particularly, clinical studies show that there is a correlation between dismissing attachment and "poor me" paranoia and fearful attachment and "bad me" paranoia [39]. Research with nonclinical samples has supported this theory by finding an association between avoidant attachment style and negative schizotypy and anxious attachment style and experience of nonclinical paranoia and voices [40, 41]. A key factor in the outcome of psychosis is the quality of the therapeutic relationship and moreover, an important element is the attachment style of these patients. Several studies have shown that a key factor for the therapeutic treatment compliance is the development of a secure attachment style. Individuals diagnosed with schizophrenia and with a dismissing attachment style have a greater tendency to beware of the physician, a lower tendency to assume drugs and less self-disclosure; on the contrary patients with preoccupied attachment style show a greater tendency to require attention from the doctor, although they also have poor compliance [42]. In addition, the avoidant attachment style, is linked to a poorer adherence to treatment, while anxious attachment is associated with better therapeutic alliance [43]. Insecure attachment as a while leads to poor adherence to treatment and poor engagement in psychiatric services [44–46].

Individuals with psychosis of multiple constructs may potentially influence medication adherence or engagement in services: symptoms, insight, personality traits, alliance, childhood trauma, substance abuse, social functioning, and sociodemographics. More positive symptoms, having witnessed violence as a child and high agreeableness as a personality trait predict poor medication adherence; physical abuse as a child, lack of knowledge regarding consumer rights, difficulties in building an alliance, low neuroticism, high agreeableness predict poor service engagement [47]. Comorbid depressive symptoms may lead to less involvement in care services, and patients with insecure attachment style and greater severity of depressive symptoms show a lower adherence regardless of the presence or absence of psychotic symptoms. Patients with severe depressive symptoms and insecure attachment style may difficulties attending to regular services. Individuals with anxious attachment style, requiring external approval to increase their self-esteem, may refuse treatment if they feel that the staff is unable to respond immediately to their own needs and requests. Finally, patients with avoidant attachment style tend to deny the importance of close relationships and tend to not engage in important and helpful relationships [48].

Moreover, the attachment theory allows us to make assumptions about the way in which attachment style can be modified on the basis of the therapeutic relationship [49].

Toward the Concept of Concordance of the Therapeutic Project

The therapeutic intervention in schizophrenia is a complex procedure, which requires a variety of approaches. The pharmacological approach is still the mainstay of treatment in patients with schizophrenia. Despite the introduction of atypical antipsychotic with a good tolerability profile and with fewer side effects, the main problem of the treatment of schizophrenic patients is medication nonadherence. Therefore, strategies to improve adherence must be based on a multidisciplinary approach. The WHO stresses the importance of increasing interventions aimed at skipping the factors "related" to the patient. Strategies to improve adherence in patients are articulated through various levels, ranging from educational programs that include family, to cognitive behavioral psychotherapy. On the pharmacological point of view, one should choose the pharmaceutical medications according to the clinical characteristics and medical history of the patient, monitor the possible side effects, ensure that the patient understands the regimen and promote family and social support that encourages the regular intake.

Therefore, one should integrate psychosocial, pharmacological and planning interventions for an effective strategy to improve adherence [50, 51]. A good doctor–patient relationship is important in the construction of adherence, as it provides the patient with a framework in which he or she can handle needs and anxieties linked either to the pathology or to the treatment. Patients should feel free to show their doctors their concepts of illness and health, and to discuss and gather information on the effectiveness of therapies and possible side effects. Patients should, always, have the perception that the therapist is interested in them as people and not only from a medical–technical point of view [52].

Currently, the majority of psychotherapy research focuses on the attempt to bring together method and the relationship. There is greater emphasis on the emerging dynamic process rather than the therapeutic technique. The quality of the therapeutic relationship seems to be the main element of care, more than other techniques. The aim is to increase the therapeutic efficacy and the adherence to treatments. Dworkin use a "relational lense" [53] through which there is a focus on the real relationship, different from the phenomena of transference and countertransference, on the development and maintenance of collaborative working alliance, and empathic attunement with the patient. The Author specifically refers to the treatment for trauma spectrum disorder Eye Movement Desensitization and Reprocessing (EMDR) and speaks of "relational imperative": a working alliance that will allow therapist and patient not only to work side by side for the achievement of a goal (symptom) but also to be one (face-to-face) in a relationship. Authors from different theoretical settings refer to the same phenomenon

using different terminology and descriptions. A Boston group named "The Boston Change Process Study Group," in the wake of evolutionistic cognitive psychology, proposed some conceptual changes in the quality of interventions. They focused the concepts of implicit relational knowledge and on the idea that change happens in "meeting moments", through changes in "ways of staying with", meaning the change is given by the therapeutic relationship itself. In the therapeutic relationship something new is built that changes the intersubjective environment. The past experience is recontextualized in the present, so that the subject comes to act with a different mental landscape, which produces new behaviors and new experiences in the present and in the future. The implicit relational knowledge is, therefore, obtained through interactive and intersubjective processes, which alter the relational field in the context of the shared implicit relationship [54].

According to this approach, a meeting between therapist and patient is preceded by a set of "present moments" in which one moves subjectively to each other. When a present moment takes a strong affective valence, it becomes relevant in the therapeutic process, and is defined as "the moment now". In the event that it is recognized and accepted by both partners during the therapeutic relationship, it would lead to mutual harmony: a true moment of encounter and emotional understanding. The "moments of meeting" are the focal events that act within the "shared implicit relationship" and are able to change it by changing the implicit knowledge, both intrapsychic and interpersonal.

The key concepts of this change are the nature of dyadic adapting and directionality, sloppiness, and vitalizing of the therapeutic process. The therapeutic relationship is an ongoing process between therapist and patient, which directly creates a change and therefore a so-called dyadic process. The process connection is directional: searching and finding a direction leads to repetitions, errors, many attempts, and exploration. These movements are called sloppiness of directional flow. The vitalizing of the therapeutic process is given its own contribution to the adapted interactions. The mutual adjustment is the vitalizing. The quality of relationships depends on how the therapist or the patients advance forward and expand the shared therapeutic field. The quality can not be separated from the directionality of the process; it is given by the direction of research and adaptation, and by the attempts to expand the range of emotionally charged experiences that can be brought into the therapeutic relationship. To the extent that these processes are understood dyadic should emerge in the therapeutic relationship, a relationship of trust and mutual vitalizing. These dynamic processes when activated move in the direction of increasing integration, consistency, and smoothness in the patient's ability to make a balance in significant trade with others. The Boston group proposed a change in the classical psychoanalytic theory and also of current theory. Traditional psychoanalysis emphasizes the fact that the patient is contributing to the therapeutic relationship and the therapist is an "intervention" as if he were speaking from the outside. The current theory proposes a reconceptualization of the alliance as the "continuous process of intersubjective negotiation". For the Boston group, the core process in treatment is instead, trading the combined direction. The change of the dyadic state is unrelated to the emergence of the

"meeting point" between the two interacting subjects. Much of the environment comes from intersubjective implicit relational knowledge, which is reconstructed in the course of therapy. The process of change takes place during the re-enactment of the shared implicit relationship during "moments of meeting", thus opening new and fruitful perspectives for therapeutic change.

This emphasis on the intersubjective relationship is what is also proposed by the Value-Based Practice (VBP) also proposed, providing specific tools that allow us to carry out more patient-centered scientific work. VBP is the theory and skills for effective healthcare decision-making, where different (patient's and therapist's) are involved (and potentially conflicting). Good process in VBP, as shown, is based on 10 key indicators. The starting point for good process in VBP is the careful attention to the individual patient. Where the values are in conflict, however, the VBP seeks to achieve a balanced approach to clinical decision-making by drawing on a range of different perspectives of value, represented in this case by the multidisciplinary team. Achieving a balance of value perspectives in turn depends on four key clinical skills: raising awareness, reasoning skills, cognitive abilities and communication skills. Approaches based on values and those based on evidence, are complementary [55]. In particular, as David Sackett (one of the greatest exponents of the practice of the evidence) pointed out, they are both essential to create concrete collaboration between professionals, patients, and patients' families. This aspect of the smooth running of the VBP is reflected in the model of the Participatory Decision-Making System.

The therapist must be aware of his or her own values consider that these will enter into the relationship with his patient, and that he or she will face the patient's values. An "alliance in values" is one of the best pathways to therapeutic alliance and adherence to treatment.

Intersubjectivity is the central fulcrum on which converge the efforts of different psychotherapeutic approaches and therapy in a broad sense. Intersubjectivity is a tool for the consolidation of the therapeutic alliance that is not only aimed at achieving the therapeutic objective (psychotherapeutic, pharmacological or combined) but also at building a new relational model, which allows changes in the different modes of the patient is relational style. One of the most significant aspects of the relationship between attachment and intersubjectivity, referring to the ability to relate with each other, is the different role they occupy in the scale of human development, both as development of the species (evolution) and personal growth of each individual. These are marked by the overlapping of different more advanced systems, more and more advanced, which regulate the transition from the stage of exclusively biological evolution and development, common to other primates, to more specifically human, characterized by symbolic language. The upper level is represented evolutionarily by intersubjectivity, characterized by symbolic language, and the ability to build, through this, meanings shared by members of our species. The link between less advanced level of report/motivation and the latter is the ability to enter a peer relationship with each other through the ability of joint shared attention on the same object, such as happens in the social game and in affiliation to a group. According to recent studies, this ability to

"perceive the other human being as fundamentally similar to himself intentionality" begins to develop in children as early as the 9th month of life in all human cultures, so it should be considered as a further step in the Darwinian adaptation of Homo sapiens [56, 57]. This step is certainly crucial in marking the passage, the ability to relate to the child's personal identity through the fusion mechanisms of imitative gestures of a "similar" but perceived as "other."

So the transition to intersubjectivity as independence from the driver would be an exclusively "human" feature. All other behavior, as we have seen are determined by motives evolutionarily determined and aimed at survival. Intersubjectivity, according to most studies of evolutionary anthropology, would be independent for a very specific reason. The behaviors of affiliation and cooperation, also present in primates, however, are determined by the aim of strengthening the forces to achieve a goal, such as to escape a predator or to reach a prey [58]; therefore, they are always based on the interest of the individual, which is motivated to obtain a specific advantage in the report. In the intersubjective relation, mother–child exchanges are accompanied by expressions of "joy" that have no match with personal benefits that are unrelated to the exchange itself (reciprocity). The "purpose" of the exchange seems to be the exchange itself, namely the report, in the absence of more benefit to the individual [59].

Close to this is the concept of "intersubjective consciousness" [60–62], uniquely human, too. It is the ability to have a continuous dialogue with a foreign interlocutor internalized interlocutor: Intersubjectivity is like an ever running that does not need external stimuli (motivation) to be turned on, but that is always running as long as we are awake. It is important to note that this game system, governed by precise reasons partly innate and partly learned in relation to the environment, is mostly done initially using preverbal signals, implicit, characterized by different emotions. The emotion has an immediacy of impact on both individuals who come into contact, making it clear to both what is the meaning and motivation of the report, without conscious and rational reprocessing. Everything that happens in an intersubjective dimension is primarily mediated by emotion; the ability (or inability) to recognize and match the emotion of the other determines the quality of the relationship: secure, insecure, disorganized, and the subsequent ability of sharing with each other jointly ("joy of sharing"). Empathy is the key emotion of intersubjectivity.

In conclusion, adherence is a complex phenomenon and the drug's intake represents the culmination of a series of aware evaluations of and by the patient. Elements that appear to play significant role are many, but a good patient–physician relationship is essential for the development of therapeutic approaches that address the individual problems interfering with adherence. A positive influence on adherence is possible if professionals focus on positive aspects of drugs on a better insight and on the promotion of a positive therapeutic relationship with patients and their caregivers. A key role plays also played by the so-called subjective well-being, which is defined as the subjective sensations under neuroleptic treatment, to be distinguished from side effect of drugs and which assesses the physical and mental subjective feelings the patient experiences. These feelings having to do with body and mind image and sensations, very often lead

the patient to feel "altered" and "detached from self", and for this reason, much more than side effects lead to treatment discontinuation [63].

Another hot point is quality of life, as "functioning" is becoming more and more one of the most important key and ambitions goals of treatment. Finally, going back to our initial definition of adherence as a multi- dimensional issue, we could say that the concept of concordance of the therapeutic project overlaps with the concepts of doctor–patient relationship, therapeutic field and intersubjective alliance. Factors belonging to the physician, such as diagnosis, prescription, choice of drug, physician's objectives, attachment style, therapeutic project, meet with factors belonging to the patient and his caregivers, subjective effect, attitude toward the therapy, insight, attachment style, subjective well-being, socio economic conditions, informed consensus, significance, family support, patient's objective, in a dynamic therapeutic field represented by the doctor–patient relationship.

This meeting becomes concordance only when the physician succeeds in matching his face of the coin with the patient's one, for every single factor, through an intersubjective and dynamic balance which goes along with illness course but, moreover, with patient's lifespan and life events.

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