# Psychodynamic Psychopharmacology

*Addressing the Underlying Causes of Treatment Resistance*

by David Mintz, MD

During the past 2 decades, psychiatry has benefited from an increasingly evidence-based perspective and a proliferation of safer, more tolerable, and perhaps more effective treatments. Despite these advances, however, treatment outcomes are not substantially better than they were a quarter of a century ago.[1] Treatment resistance remains a serious problem across psychiatric diagnoses.[2] One likely reason that outcomes have not improved substantially is that as the pendulum has swung from a psychodynamic framework to a biological one, the impact of meaning (ie, the role of psychosocial factors in treatment-refractory illness) has been relatively neglected, and psychiatrists have lost some potent tools for working with the most troubled patients.

Psychodynamic psychopharmacology explicitly acknowledges and addresses the central role of meaning and interpersonal factors in pharmacological treatment.[3] This approach recognizes that many of the core discoveries of psychoanalysis (the unconscious, conflict, resistance, transference, defense) are powerful factors in the complex relationships between the patient, the illness, the doctor, and the medications. In many cases, these factors are largely concordant with treatment and do not need to be addressed in order for treatment to be effective. However, in patients who are treatment-resistant, it is likely that psychodynamic factors (that may well be unconscious) are deeply at odds with therapeutic goals.

## Dynamic factors in psychopharmacology

There is currently a small but impressive evidence base that shows that psychological and interpersonal factors play a pivotal role in pharmacological treatment responsiveness.

An analysis of the data from a large, NIMH-funded, multicenter, placebo-controlled trial of the treatment of depression found a provocative treater x medication effect.[4] While the most effective prescribers who provided active drug (antidepressant) had the best results, it was also true that the most effective one-third of prescribers had better outcomes with placebos than the least effective one-third of prescribers had with active drug. This suggests that *how* the doctor prescribes is actually more important than *what* the doctor prescribes!

A series of meta-analyses of FDA databases (examining an unbiased sample, including negative, unpublished studies) shows that although antidepressant medications are effective, the placebo effect accounts for between 76% and 81% of treatment effectiveness.[5-7] Placebo does not mean imaginary or untrue. Placebos produce real, clinically signifi-

cant, and objectively measurable improvements in a wide range of conditions, including psychiatric disorders.[8,9] And, placebo responses produce measurable changes in brain activity that largely overlap medication-induced improvements.[10] The patient's desire to change and a positive transference to the doctor and his or her medications can mobilize profound self-healing capacities—capacities that appear to be even more potent than the medication's active ingredient.

Although most of our patients ask us for help, many are conflicted about getting well if their illness has created some conscious or unconscious benefit. If a patient is not "ready to change," it is unlikely that a medication, however potent, will produce a therapeutic effect. Beitman and colleagues[11] found, in a placebo-controlled trial, that patients who received a benzodiazepine for anxiety and who were highly motivated to change had the most robust response. However, placebo recipients who were highly motivated to change had a greater reduction in anxiety than patients who took the active drug but were less ready to change. Readiness to change was found to be the single most powerful determinant of treatment effectiveness—even more potent than type of therapy (ie, active vs placebo).

In 1912, Freud[12] noted that the unobjectionable positive transference (consisting of such things as the patient's belief in the doctor's salutary intentions, the wish to use the doctor to get better, and the desire to win the doctor's love or esteem by genuinely trying to get better) was a key factor in the patient's ability to overcome symptoms. This unobjectionable positive transference, ie, the therapeutic alliance, is one of the most potent ingredients of treatment.[12,13] In a large, placebo-controlled, multicenter trial of treatments of depression, Krupnick and colleagues[14] showed that patients were most likely to respond when they received the active drug and had a strong therapeutic alliance. Those least likely to respond when given placebo had a poor therapeutic alliance. Patients who received placebo and who had a strong treatment alliance had a significantly more robust therapeutic response than patients who received an antidepressant but had a poor therapeutic alliance. Taken together, these studies examining the relative effectiveness of biologically and symbolically active aspects of the medication suggest that meaning effects in psychopharmacology are more potent than biological effects.[4-7,11,13,14]

Just as positive transferences to the doctor or drug lead to positive responses, negative transferences are likely to lead to negative responses. Patients who have been abused or neglected by caregivers in the past or those who otherwise feel vulnerable to authority figures (either because of social disadvantage or a propensity to acquiesce) are prone to nocebo responses.[15,16] The obverse of the placebo response, nocebo responses occur when patients expect (either consciously or unconsciously) to be harmed. Many patients who experience intolerable adverse effects to medications are nocebo responders. It comes as no surprise that these patients are likely to become treatment-resistant.

## Pharmacological treatment resistance

From a psychodynamic perspective, patients may be seen as resistant *to* medication or resistant *from* medication. These 2 broad categories of pharmacological treatment resistance tend to have different underlying dynamics and may require different kinds of interventions.

Patients who are resistant *to* medications have conscious or unconscious factors that interfere with the desired effect of medications. Often, resistance in this category takes the form of nonadherence but also includes patients who repeatedly experience adverse responses to medications (ie, nocebo responders).

In contrast, patients who are resistant *from* medications more typically are eager to receive the medication or some benefit that the patient ascribes to the medication. For such patients, pills may appear to relieve symptoms, but they do not contribute to an improvement in the patient's quality of life. Resistance *to* medications and resistance *from* medications are not mutually exclusive, and some patients present with both dynamics.

In 1905, Freud[17] described the psychodynamic concept of resistance and concluded that many patients were unconsciously reluctant to relinquish their symptoms or were unwittingly driven, for transference reasons, to resist the doctor. These same dynamics may apply in pharmacotherapy. Although suffering greatly, patients may find good uses for their symptoms. Patients who derive significant secondary gains from their symptoms (eg, they are relieved from various burdens, or they receive care rather than neglect as a result of their illness) can be deeply conflicted about getting better, which may manifest as treatment resistance.

Patients who need their symptoms to communicate something that they cannot put into words will be similarly ambivalent.[2] When symptoms constitute an important defense mechanism, patients are also likely to resist medication effects until they have developed more mature defenses or more effective ways of coping.[3]

Patients who are not resistant to symptom reduction may nonetheless be motivated to resist the doctor on the basis of a transference experience of the doctor as untrustworthy or even dangerous. Such patients often painstakingly negotiate the medication, dosing, and timing of medications (so as not to feel under the control of the malevolently experienced doctor) or surreptitiously manage their own regimen (by taking more or less than the prescribed dose). Needless to say, if they are not taking a therapeutic dose, they lessen their chances of a therapeutic response. As noted, if these patients cannot resist the doctor's orders, then their bodies may unconsciously do the resisting for them, which leads to nocebo effects.

Patients who are treatment-resistant *from* medication typically present as hungry for medications. Although they take the medications and may report symptom reduction, these patients do not function better with pharmacotherapy; in fact, some seem to get worse. A psychodynamic psychopharmacologist is mindful that there are countless ways these medications may serve countertherapeutic and/or defensive aims.

Patients may use pills defensively to disavow responsibility for their feelings and actions.[18] This commonly occurs in the case of primitively organized and character-disordered patients who rely on splitting and projective dynamics. Such patients tend to see things strictly in black and white and frequently defend against feeling intolerably and completely bad by displacing all of the "badness" onto the "other" in a relationship.

After receiving a prescription for mood stabilizers for bipolar disorder, a patient prone to splitting as a defense will often experience an immediate reduction in dysphoria. A psychopharmacologist who is inclined

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to think both psychodynamically and biologically will recognize that the reduction in dysphoria may be occurring not because of the medication but because it allows the patient to create a stable split within which he can remain good while all badness is located in "my bipolar."

While patients may feel better, they actually do worse. No longer feeling personally responsible for symptomatic behavior, they give their worst instincts free rein, exacerbating personal and interpersonal chaos. It is important not to collude unwittingly with these legally competent patients whose treatment resistance relates to defensive use of medications. Rather, it is crucial to empathically help them understand that although they are ill, they remain responsible for their choices.

Medications can be used defensively in myriad ways. Patients who experience people as dangerous and unreliable may attempt to replace people with pills. Still other patients may feel that any "negative" feeling is pathological and should be extinguished. If accepted at face value, this can lead a well-meaning psychiatrist toward an ever more complex and burdensome medication regimen that actually contravenes healthy developmental aims.

When pills are used to manage developmentally appropriate feelings, such as loneliness, disappointment, sadness, frustration, or anger, patients lose important opportunities that might lead to improved internal controls and increased affective or interpersonal competence. Patienthood may be reinforced.

### Elements of psychodynamic psychopharmacology

Psychodynamic psychopharmacology represents an integration of biological psychiatry and psychodynamic insights and techniques. Psychodynamic psychopharmacology provides little guidance about what to prescribe; instead, it helps prescribers know how to prescribe to improve outcomes.

There are 6 principles for psychodynamically informed pharmacological practice with treatment-resistant patients[3]:

- Avoid a mind-body split
- Know your patient
- Attend to the patient's ambivalence about the loss of symptoms
- Address negative transferences and resistance to medications
- Be aware of countertherapeutic uses of medications (resistance *from* medications)
- Identify and contain countertransference involving prescribing[19]

*Avoid a mind-body split.* A psychodynamic psychopharmacologist recognizes that a rigid mind-body dualism is a fantasy. Experiences, feelings, ideas, and relationships change the structure and function of the brain just as the state of the brain influences experience. A psychodynamic psychopharmacologist considers that a positive or negative medication response may be a direct action of the pill or may be mediated by the meanings the patient attaches to the pill.

Mind-body integration also means that psychotherapy and psychopharmacology will need to be well-integrated so that psychopharmacological interventions facilitate the psychotherapy and so that the therapy helps the patient become conscious of psychological sources of pharmacological treatment resistance. Effective psychopharmacological interventions to treatment nonresponse might include an increase in frequency of appointments rather than an increase in medication dosage.[20]

*Know your patient.* Sir William Osler, the father of modern medicine, remarked that "it is much more important to know what sort of patient has a disease than to know what sort of disease a patient has." This is a central tenet of psychodynamic psychopharmacology. Practically, this means that the pharmacologist should get a thorough developmental and social history to make reasonable hypotheses about the psychosocial origins of the patient's treatment resistance. The prescriber should also directly assess the patient's attitudes about medications (fears of dependency, worries about being "turned into a zombie," and so on). This not only helps assess potential sources of resistance, but it also lets the patient know the prescriber is interested in him as a person, which may enhance the alliance.

*Attend to ambivalence about loss of symptoms.* Identify potential sources of ambivalence about symptoms, such as secondary gains, and communicative or defensive value of symptoms. It may be helpful at the point of intake to ask the patient what he would stand to lose if treatment was successful. (The same question posed in the middle of a treatment may be colored by the doctor's frustration and is more likely to produce a negative response.)

*Address negative transferences and resistance to medications.* Once potential sources of resistance to the medication or the doctor are understood, they must be addressed. If they are clear at the outset, they must be addressed preemptively. In this way, an alliance is made with the patient before massive resistance is sparked. Negative transferences must be identified and worked through. Empathic interpretation of nocebo responses can resolve adverse effects.[21]

*Be aware of countertherapeutic uses of medications (resistance* from *medications).* Countertherapeutic uses of medications should also be interpreted. As a prescriber, you might tolerate some irrational use of medications if the patient is working through an issue that interferes with a healthier use of those medications. There comes a time, however, when discontinuation of a countertherapeutic medication may become a condition of continued pharmacological treatment.

*Identify and contain countertransference in prescribing.* When patients struggle with overwhelming dysphoric affects, they often evoke corresponding effects in their prescribers.[2] It seems likely that a medication regimen made up of, for example, 3 antidepressants, 4 mood stabilizers, 3 antipsychotics, and 1 or 2 anxiolytics, has in part been shaped by countertransference. Such a regimen is unlikely to be effective and is perhaps aimed at treating the doctor's anxiety rather than the patient's; the patient is not the only source of treatment resistance. A psychodynamic psychopharmacologist recognizes that the psychiatric relationship is an encounter between a big mess and an even bigger mess. An attitude of humility along with periodic consultation about difficult cases helps manage irrational prescribing.

### Conclusion

There are many sources of pharmacological treatment resistance. When treatment resistance arises from the level of meaning, interventions are not likely to be successful unless they address problems at the level of meaning. Psychiatric care providers who operate from either a dogmatic psychotherapeutic paradigm or a psychopharmacological paradigm are hobbled by having access to only half the patient. Psychodynamic psychopharmacology combines rational prescribing with tools to identify and address irrational interferences with healthy and effective use of medications. We should not neglect psychodynamic contributions that enhance the integration of meaning and biology. It is the capacity to integrate and understand complex situations that more than anything else lends its particular power to our discipline and gives us skills for working with particularly troubled patients.

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