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PHARMACOTHERAPY IN PERSONALITY DISORDER

Produced by :

P. Molavi

M.D. (PSYCH.)

Professor of psychiatry

General Principles of Treating Personality Disorder

- Individuals with PD do **not recognize** that they are **ill** and **seldom seek help** unless others people (such as a spouse or parents) are insistent.
- This usually happens when **maladaptive behaviors** create **marital, family, and job problems**, or when other **mental symptoms** (e.g., anxiety, depression, substance abuse), or **somatic symptoms** (e.g., obesity, heart disease, COPD), complicate their clinical picture.
- In general, patients with PD require a **multi-layered treatment** plan that often combines **psychotherapy and pharmacotherapy**.

- Psychotherapy and pharmacotherapy have a **bidirectional relationship**, as both modalities, in addition to their independent effects, also **interact in a positive feedback** manner.
- As the **first step**, pharmacotherapy stabilizes affects and ensures **safety** of the patient, which restricts with **psychotherapy**.

CHOICE OF MEDICATIONS FOR STABILIZATION.

- During the **initial stage** of treating patients with PDs, medications are often used to **target specific symptoms** of their disorders with the goals of **relieving** subjective **distress**,

- risky or self-destructive behaviors,
- and/or conflict with others,
- thereby preparing them for later stages of treatment that require calmness, safety, and non defensiveness to facilitate growth in selfawareness.
- One should keep in mind that the vast majority of affective symptoms of PDs (such as dysthymia, unstable affects among others), their chronic anxiety, and most of their behavior symptoms (e.g., impulsivity) are shared by all classified clinical subtypes.
- Hence, symptomatic pharmacotherapy is not focused on individual subtypes of PD but rather on the following four domains shared by all subtypes:
 - (i) Mood And Anxiety Dysregulation, related most strongly to Harm Avoidance,

- (ii) **Aggression And Impulse** control, related most strongly to **Novelty Seeking**,
- (iii) **Social And Emotional Detachment**, related most strongly to **Reward Dependence**, and
- (iv) **Psychotic Symptoms** and **cognitive distortions**, related most strongly to **intellectual reasoning** and **Persistence**.



Table 26–24.

Choice of Drugs According to Target Symptoms of Personality Disorders

Target Symptom	Drug/Treatment of Choice	Not Recommended
I. Mood dysregulation and anxiety		
Anxiety		
Chronic cognitive	PSYCHOTHERAPY SSRIs, SNRIs, MAOIs LOW-DOSE NOVEL PSYCHOTROPICS (aripiprazole, quetiapine) Valproates and other GABA analogs clonazepam, buspirone	Benzodiazepines and ethanol (risk of abuse/addiction)
Chronic somatic	MAOIs, SNRIs (duloxetine, milnacipran) Pregabalin and other GABA analogs TCAs, beta-blockers	If used—benzodiazepines with long half-life and short trials preferred
Obsessions	SSRIs, PSYCHOTROPICS (quetiapine) TCAs (clomipramine) Mild NMDA antagonists (riluzole, memantine)	
Acute and severe	MIRTAZAPINE, NOVEL PSYCHOTROPICS (quetiapine, aripiprazole, clozapine) TCAs, clonazepam, valproates, lithium	
Depression		
Atypical depression/dysphoria	MAOIs, SSRIs, SNRIs, ARIPIPRAZOLE Lurasidone, ziprasidone, quetiapine	TCAs
Classical depression	STANDARD ANTIDEPRESSANTS TCAs (males) SSRI (females) Atypical psychotropics (as monotherapy or augmentation)	



II. Behavior dyscontrol

Aggression/impulsivity

Affective aggression “Hot temper” with normal EEG	LITHIUM, SSRIs, ANTICONVULSANTS Low-dose novel psychotropics	Benzodiazepines (disinhibition)
Predatory aggression (cold blooded revenge/cruelty)	NO EFFECTIVE PHARMACOLOGICAL Tx Novel psychotropics, lithium, valproates, beta-blockers	BENZODIAZEPINES (disinhibition)
Organic-like aggression (traumatic brain injury)	BETA-BLOCKERS, VALPROATES, QUETIAPINE, CARBAMAZEPINE TCAs, cholinesterase inhibitors (donepezil)	BENZODIAZEPINES (disinhibition, delirium)
Ictal aggression (abnormal EEG)	CBMZ, DIPHENYLHYDANTOIN, VALPROATES Benzodiazepines (clonazepam)	TCAs LOW-POTENCY TYPICALS (both increase risk of seizures)



III. Social and emotional detachment

Chronic asociality and disinterest	LOW-DOSE PSYCHOTROPICS (aripiprazole, olanzapine, low-dose
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Blunted affect clozapine, sulpiride)



IV. Cognitive-perceptual distortions/psychotic symptoms

Acute and brief psychotic episodes	NOVEL PSYCHOTROPICS (Risperdal, olanzapine) Typical neuroleptics (for the duration of psychosis)
Chronic and low-level psychotic-like symptoms	NOVEL PSYCHOTROPICS

- (i) Symptom domain of mood dysregulation and anxiety This symptom domain includes:
 - typical and atypical depression and/or dysphoria (dysphoria and dysthymia are used here as synonymous terms—Latin and Greek for low mood), and
 - chronic cognitive and somatic anxiety.
 - Emotional instability and mood swings

- Emotional instability and mood swings are usually responsive to
- lithium or valproates (for patients with frequent episodes of euphoria) or
- lamotrigine (for patients with more frequent depressive episodes).
- Lowdose atypical psychotropics may be used to stabilize mood or improve depression as the second-line medications.
- TCAs, sometimes increase impulsivity and anger in emotionally unstable patients (e.g., borderline, narcissistic, histrionic, dependent).

- This paradoxical effect caused by the so-called “catecholamine stress,” that is, a dramatic increase in catecholamine levels during TCA treatment.
- As a general rule, antidepressants may cause an episode of mania if not combined with mood stabilizers in persons with emotional lability or cyclothymia.
- TCAs are extremely dangerous in an overdose, so these drugs should to be used with caution in patients with PD.
- Atypical depression and dysphoria are very frequently observed in patients with any subtype of PD.

- The “first-line” medications used here are (SSRIs), (SNRIs), (MAOIs),
- or low-dose atypical psychotropics, such as aripiprazole, ziprasidone, lurasidone, or clozapine.
- TCAs are not recommended as at least half of the PD subjects suffering from atypical depression worsen on TCAs.
- Again, antipsychotics are used only after careful consideration of the risk–benefit ratio in voluntary patients.
- Typical depression, including Major Depression may complicate any PD.

- These syndromes are treated with antidepressants, including heterocyclics, in doses suggested for primary major depression.

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- Patients with PD often present with both :
 - cognitive anxiety (anticipatory worry)
 - somatic anxiety (concerns about bodily pains and psychophysiological reactions).
- Treatment of choice for chronic cognitive anxiety is psychotherapy, especially various forms of CBT.
- With respect to pharmacotherapy, chronic cognitive anxiety is most responsive to SSRIs, MAOIs, SNRIs, GABA analogues (such as



valproates, pregabalin, gabapentin), and (with caution) long half-life benzodiazepines.

- Chronic somatic anxiety is more responsive to MAOIs, SNRIs (e.g., venlafaxine or duloxetine), and buspirone.
- Low doses of TCAs are very effective for somatic anxiety in some patients, but MAOIs are more often effective if the required dietary regimen can be followed.
- Avoidant traits can be also effectively treated with either SSRIs or MAOIs.

- Some components of somatic anxiety, such as sweating, palpitations, diarrhea, and tremor, can be treated with betablockers.
- Severe, psychotic-like anxiety responds to low-dose neuroleptics, (e.g., quetiapine).
- Despite relative safety of novel atypical drugs, caution about prolonged use is necessary, as noted earlier, because there is still substantial risk of serious side effects (e.g., for risperidone, tardive dyskinesia sudden cardiac death, neuroleptic malignant syndrome).

- Therefore, the risk of some serious and irreversible side effects is about 1 percent per person per year and requires careful consideration of risk–benefit ratio with voluntary informed consent.

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(ii) Aggression

- It is useful, though sometimes difficult, to distinguish different types of aggression.
- However, diagnosis of different types of aggressive behaviors has important diagnostic consequences as well as essential guidelines for pharmacotherapy.



II. Behavior dyscontrol

Aggression/impulsivity



Affective aggression
“Hot temper” with
normal EEG

LITHIUM, SSRIs, ANTICONVULSANTS
Low-dose novel psychotropics

Benzodiazepines (disinhibition)



Predatory aggression
(cold blooded
revenge/cruelty)

NO EFFECTIVE PHARMACOLOGICAL Tx
Novel psychotropics, lithium,
valproates, beta-blockers

BENZODIAZEPINES (disinhibition)



Organic-like aggression
(traumatic brain
injury)

BETA-BLOCKERS, VALPROATES,
QUETIAPINE, CARBAMAZEPINE
TCAs, cholinesterase inhibitors
(donepezil)

BENZODIAZEPINES (disinhibition,
delirium)



Ictal aggression
(abnormal EEG)

CBMZ, DIPHENYLHYDANTOIN,
VALPROATES
Benzodiazepines (clonazepam)

TCAs
LOW-POTENCY TYPICALS (both
increase risk of seizures)

III. Social and emotional detachment

Chronic asociality and
disinterest

LOW-DOSE PSYCHOTROPICS
(aripiprazole, olanzapine, low-dose

Blunted affect

clozapine, sulpiride)

IV. Cognitive-perceptual distortions/psychotic symptoms

Acute and brief
psychotic episodes

NOVEL PSYCHOTROPICS (Risperdal,
olanzapine)
Typical neuroleptics (for the duration
of psychosis)

Chronic and low-level
psychotic-like
symptoms

NOVEL PSYCHOTROPICS

- “Affective aggression” :
- The most common form of aggression occurs when a quick-tempered person is motivated by frustration or threats.
- Here, the very act of aggression does not have a obvious long-term goal or secondary gain.
- This is often called “affective aggression” and is frequent in Cluster B impulsive-aggressive individuals who are high in novelty seeking and low in harm avoidance.

- **Predatory aggression** or “**cruelty**” is also known as “**organized aggression**” because it involves **planning, social motives, and/or secondary gains**.
- This type of aggression involves **hostile revengefulness** and taking **pleasure** in **victimizing** others, usually with **intact impulse control**.
- most frequent in individuals who are **very low in cooperativeness** and who are also **emotionally dissociated** and **disengaged**, such as **Antisocial** and **Schizoid** PD.
- “**Organic-like**” aggression is often accompanied by **poor social judgment** and **disinhibition**; it is best distinguished from other by

prominent distractibility, inattention, and emotional lability, all characteristic of patients with frontal lobe lesions and traumatic brain injury.

- “Ictal aggression” : aggression that appears to be unprovoked sometimes occurs in patients with cerebral instability documented by an abnormal (EEG) and is often called “ictal aggression” regardless of any associated personality traits.
- Multiple double-blind trials have shown efficacy of lithium carbonate in the treatment of affective aggression.

- Lithium salts help impulsive–aggressive individuals to be more **reflective**, that is, to **think about consequences** before acting on impulse.
- **To a lesser extent**, it may be helpful in **reducing cruelty** and **lack of cooperativeness**, but this may be an indirect result of reducing impulsivity, which often is a predisposing influence in the development of hostility and revengefulness.
- Also, **low-dose atypical neuroleptics** may be useful in setting the stage for the patient to modify old habits and assist him or her in **reducing affective aggression**.

- The **decisions** to use **long-term neuroleptics** requires consideration of potential **side effects**, such as **tardive dyskinesia**, and should be made with carefully **informed consent** of the patient.
- **Double-blind** trials have shown that **psycho stimulants** and catecholamine agonists, such as **methylphenidate**, are often **beneficial** in the treatment of **inattentive** and **hyperactive** adults who are **impulsive** and **aggressive**, especially when the **symptoms** have begun **in early childhood**.
- In accord with **postulated serotonergic mechanisms** in aggressive behaviors, **antidepressants** (particularly **SSRIs** and **SNRIs**) are

considered by many to be beneficial for certain subtypes of impulsive PD (e.g., **borderline, histrionic**).

- Finally, **MAOIs** are effective in some **dysphoric** states with **somatic anxiety** and **hostility**.
- There is **no effective pharmacotherapy** for **predatory**, premeditated, and **cold-blooded** aggression.
- One treatment with **some chances of success** is psychotherapy, usually **CBT**.

- Low-dose traditional neuroleptics (haloperidol) or low-dose novel psychotropics (Risperdal, quetiapine) may help tone down predatory aggression.
- Of note, antipsychotic-level doses have not been shown more effective here and are not recommended.
- When accompanied by impulsivity, predatory aggression may improve if treated with beta-blockers.

There are some relative contraindications for the aforementioned listed drugs.





Lithium should not be given to antisocial persons without aggression and impulsivity because it does not diminish non aggressive antisocial behaviors (such as lying, cheating, and stealing) and is poorly tolerated by anxious schizoid individuals

- Thus, lithium exposes such patients to risk of neurological, renal, and thyroid toxicity without providing much benefit.
- Likewise, benzodiazepines and alcohol have disinhibiting effects on violence, reduce conditioned avoidance behavior (“loosen inhibitions”), and further impair passive avoidance learning in impulsive antisocial persons.

- The use of benzodiazepines seems appropriate only in nonaggressive asocial behaviors, for example, patients with schizoid PD.
- As a general rule, typical and novel psychotropics are used with extreme caution, and the patient is closely monitored, so that early signs of complications and adverse effects are recognized and prevented, usually by terminating the offending agent.
- Anticonvulsants, such as valproates, lamotrigine, carbamazepine, and oxcarbazepine (to mention only those most frequently used), reduce both the intensity and the frequency of unprovoked angry outbursts in many patients regardless of normality of their EEG.

II. Behavior dyscontrol

Aggression/impulsivity

	Affective aggression "Hot temper" with normal EEG	LITHIUM, SSRIs, ANTICONVULSANTS Low-dose novel psychotropics	Benzodiazepines (disinhibition)
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III. Social and emotional detachment

Chronic asociality and disinterest	LOW-DOSE PSYCHOTROPICS (aripiprazole, olanzapine, low-dose
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Blunted affect clozapine, sulpiride)

IV. Cognitive-perceptual distortions/psychotic symptoms

Acute and brief psychotic episodes	NOVEL PSYCHOTROPICS (Risperdal, olanzapine) Typical neuroleptics (for the duration of psychosis)
Chronic and low-level psychotic-like symptoms	NOVEL PSYCHOTROPICS

- (iii) Symptom domain of **social** and **emotional detachment**
- Emotional detachment, **cold** and **aloof emotions**, and **disinterest** in social relations (“**chronic asociality**”) are most frequently observed with **schizoid** and **paranoid** PD and, to a lesser extent, with **antisocial** PD.
- In **some** cases, emotional detachment or disinterest may respond to novel **psychotropics**, such as **aripiprazole**, **risperidone**, **quetiapine**, **clozapine**, **olanzapine**, or **ziprasidone**

- These medications may help reduce social withdrawal and other features of “aloof” PDs with less risk of extrapyramidal.
- However, dose adjustment is crucial to maintain compliance because patients with PD often have little tolerance for side effects.
- In cases in which emotional disinterest reflects an underlying depression, antidepressants frequently help.
- One should be cautious with TCAs in schizotypal PD, because they may worsen and/or trigger psychosis.
- (iv) Cognitive-perceptual distortions; psychotic symptoms

- distortions observed in patient with PD primarily include
- mild cognitive symptoms, such as bizarre fantasies, eccentric attitudes, suspiciousness, egocentric perception of reality (“everything revolves around me”),
- nonpsychotic thought disorder (such as ideas of reference and magical thinking), unusual perceptual experiences (such as illusions), and eccentric and bizarre behaviors, among many others.
- Dissociative phenomena are also frequently observed, such as déjà vu, depersonalization, and derealization.

- These and similar symptoms can be occasionally observed with **all subtypes of PDs** but are more frequent in **Cluster A** and to a lesser extent **in Cluster B PDs**.
- These **chronic**, low-level, **psychosis-like** but essentially **nonpsychotic** symptoms **may improve** indirectly, after **pharmacological stabilization** of **disturbing affects**, and/or after **psycho** **therapeutical** correction of cognitive underlying beliefs, and/or after **reduction** of realistic external **stress**.
- For example, a **narcissistic** person can be “**paranoid**” that other people have conspired to **prevent** his or her **success**.

- **Psychotherapy** is the **treatment of choice** for this kind of nonpsychotic paranoia.
- In cases in which these symptoms **persist** and **interfere** with everyday functioning despite psychotherapy, medications are occasionally needed, usually **novel atypical psychotropics** (such as **aripiprazole**, **quetiapine**).
- **Some chronic cognitive disturbances**, such as **mild ideas of reference** or **suspiciousness**, tend to subside when the **background emotional tension is reduced**.

- For example, **alprazolam** has been found to be **beneficial** in patients with **borderline personality**, particularly those with a **history of drug abuse** and **suspiciousness**.
- However, **long-term use** of **benzodiazepines** is associated with **high risk of drug dependence**, and should be prescribed **only** after **careful consideration** of the **risk–benefit** ratio.
- Chronic cognitive and behavior **oddities**, such as **eccentric attitudes**, **bizarre behavior**, **odd beliefs**, or extrasensory perceptions are seen with **Schizotypal PD**.

■ There is **substantial empirical evidence** that **Schizotypal** symptoms should to be classified among other **Schizophrenia Spectrum Disorders**.

■ **Acute, brief reactive psychoses** may complicate **most subtypes of PD**. ■ These are **treated symptomatically**, according to accepted pharmacological practices, most frequently with **second-generation** atypical psychotropics due to much better **safety** and **tolerability**.

- Again, acute psychotic symptoms requiring medication may subside when environmental stressors are brought under control; thus one should be ready to lower the dose or discontinue the medication.

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Aggression/impulsivity

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Thank
you



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