

PSYCHOPHARMACOLOGY OF PERSONALITY DISORDERS

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Pre-Lecture Exam

Question 1

1. Which of these issues does psychopharmacologic treatment of people with personality disorders not characteristically pose?
 - A. Adherence to prescribed medication regimen
 - B. Low tolerance for side-effects
 - C. Altered liver metabolism of medication
 - D. Inconsistent reporting of missed doses and side-effects

Question 2

- 2. Low doses of atypical antipsychotic medications may be useful in the treatment of the following symptoms in people with SPD except?**
- A. Ideas of reference**
 - B. Persistent auditory hallucinations**
 - C. Social isolation**
 - D. Transient psychotic-like symptoms**

Question 3

- 3. Which medication could usually be contraindicated for the treatment of impulsivity/aggression?**
- A. SSRI's**
 - B. Lithium carbonate**
 - C. Carbamazepine**
 - D. Amphetamine**

Question 4

- 4. All of these Axis I disorders are often comorbid with personality disorders except:**
- A. Panic disorder**
 - B. Major depressive disorder**
 - C. Chronic schizophrenic**
 - D. Generalized anxiety disorder**

Question 5

- 5. Which are important aspects of the psychiatric history in personality disorder patients?**
- A. Axis I symptoms**
 - B. Substance abuse history**
 - C. Family history**
 - D. All of the above**

Question 6

- 6. All of the following are useful strategies in initiating pharmacologic treatment in personality disorder patients except:**
- A. Rapid titration to maximal doses to reduce symptomatology**
 - B. Discussion of meanings of medications to patient**
 - C. Address potential for abuse**
 - D. Acknowledge possibility of sensitivity to side effects and need to start with low doses**

Question 7

- 7. Manifestations of anxious personality disorders include:**
- A. Hypomania
 - B. Shyness
 - C. Thought disorder
 - D. Impulsivity

Question 8

- 8. Which medications are often used for anxious personality disorders?**
- A. SSRI's**
 - B. Neuroleptic medications**
 - C. Stimulants**
 - D. Barbituates**

Question 9

- 9. Which neuromodulator system has been most consistently implicated in impulsivity/aggression?**
- A. GABA
 - B. Serotonin
 - C. Substance P
 - D. HPA Axis

Question 10

- 10. Benzodiazepines may induce all of the following in people with personality disorders except:**
- A. Disinhibition
 - B. Depression
 - C. Mania
 - D. Somnolence

INTRODUCTION

- **Pharmacotherapy: therapeutic mainstay of the major Axis I syndromes**
- **More recent treatment options for the severe personality disorders**
- **Biologic factors in the pathogenesis of the personality disorders**
- **Specific etiology of the disorder may not necessarily determine its treatment**

IMPETUS FOR PHARMACOTHERAPY OF PERSONALITY DISORDERS

- **New studies of biologic correlates of personality disorder**
- **Dimensional approach to targeting symptoms**
- **Double-blind studies of pharmacotherapy of personality disorders**

PHARMACOLOGIC INTERVENTION MAY BE BENEFICIAL IN PERSONALITY DISORDER PATIENTS WITH TARGET SYMPTOMS OF:

- **Affective instability or transient depression**
- **Psychotic-like symptoms of cognitive/ perceptual distortions**
- **Impulsivity/aggression**
- **Anxiety**

Growing evidence from controlled treatment trials demonstrates the efficacy of psychopharmacologic interventions in the treatment of personality disorders signs and symptoms

ISSUES OF PHARMACOTHERAPY FOR PERSONALITY DISORDER PATIENTS

- **Appropriate selection and assessment**
- **Initiating and maintaining psychopharmacologic treatment**
- **Specific syndromes/behavioral dimensions**

A WIDE ARRAY OF PSYCHOTHERAPIES EXIST AND ARE IN USE TO TREAT PERSONALITY DISORDERS

Issues

- **Efficacy**
- **Duration of treatment**
- **Verbal and introspective abilities of individual**
- **Cost**

ASSESSMENT FOR TREATMENT

- Detailed psychiatric history
- Substance abuse history
- Family history
- Medical history
- Physical and laboratory examination
- Differential diagnosis
- Differential therapeutics

PSYCHIATRIC HISTORY

Many Present with a Bewildering Array of Problems & Complaints

Systematic Approach to Information Gathering Essential

- Psychiatric symptomatology
- Clinical contracts
- Medication history
- Specific response to each psychotherapeutic and psychopharmacologic intervention

- **In general, Axis disorders such as schizophrenia, major depression, and bipolar disorder take precedence in the differential diagnosis and treatment priority**
- **Example:**
 - **Treat Bipolar Disorder Type I**
 - **When optimally treated, then target residual personality disorder disturbances**

AXIS CO-MORBID CONDITIONS

- **Major Depressive Disorder**
- **Panic Disorder**
- **Generalized Anxiety Disorder**
- **Brief Reactive Psychosis**
- **Posttraumatic Stress Disorder**

- **Attend not only to the signs and symptoms of psychiatric illness per se, but also to the pattern and timing of their presentation.**
- **Example:**
 - **Impulsive/aggressive behavior, sexual promiscuity, and labile affect**
 - **If stable over time and present since adolescence, consider Dramatic Cluster. If episodic and associated with increased energy and decreased sleep, consider Bipolar Disorder (mania) or substance intoxication or withdrawal**

MEDICATION HISTORY

- **For each psychotropic medication:**
 - **Target symptoms**
 - **Dose**
 - **Duration**
 - **Efficacy**
- **Given the frequent ambiguity of the behavioral, affective, and cognitive complaints, operationally define each of the target symptoms**

SUBSTANCE ABUSE/ DEPENDENCE HISTORY

- **First find and treat any substance abuse/ dependence**
- **Affective lability, impulsivity, and aggression that might be ascribed to personality disorder may remit with the treatment of substance abuse/dependence**

INTERVIEWING OF FAMILY MEMBERS

- Interview family members, with the knowledge and permission of the patient
- Information to elicit:
 - Nature, duration, extent, and severity of the intra- and inter-personal disturbances experienced by the patient

FAMILY HISTORY

- **Family history may suggest the existence of biologic vulnerabilities to:**
 - **Mood disorders**
 - **Drug/alcohol abuse**
 - **Personality Disorders**
- **Speak with family members directly (with the permission of the patient) to evaluate the potential presence of psychiatric illness**

- **When the clinician is convinced that:**
 - **No other treatable physical illness is present and**
 - **Substance abuse/dependence is controlled (if present)**

then personality disorder diagnoses may be made and interventions initiated

TREATMENT INITIATION

Discuss the Recommended Treatment in Detail with the Patient, and Where Possible, the Patient's Family

Specific Issues to be Addressed Include:

- **Clinician-patient agreement about the existence of a problem and the desirability of treating that problem**
- **Discussion of the logic of the medication selection, its target symptoms and potential toxic effects**
- **An objective procedure for the assessment of treatment progress, or lack thereof**

ISSUES IN PHARMACOTHERAPY OF PERSONALITY DISORDERS

- Doctor-patient therapeutic alliance
- Education
- Sensitivity to side effects
- Compliance
- “Transferential” issues
- Meaning of medications to patient
- Potential for overdose
- Potential for abuse

MANAGEMENT OF TOXIC EFFECTS

- **To enhance the probability of a successful medication trial, attempt to minimize or avoid toxic effects**
- **Begin with a minimal dose of medication**
- **Incrementally and gradually increase to a therapeutic level**
- **Operationally, start with half the dose and half the rate of dosage increase that might be used in an Axis I condition**

MEDICATIONS MAY HAVE SUBTLE OR PROFOUND COGNITIVE, BEHAVIORAL, OR AFFECTIVE CONSEQUENCES

- **Example: Steroids in the treatment of severe asthma, chronic obstructive pulmonary disease, or systemic lupus erythematosus**
- **Potential complications include agitation, aggressive behavior, and affective lability**

ASSESSMENT OF RESPONSE

GLOBAL ASSESSMENT OF FUNCTIONING

- **Target symptoms may be operationalized and followed at each visit to determine treatment efficacy**
- **Relevant sections of brief standardized instruments (e.g., the Brief Psychiatric Rating Scale [BPRS])**
- **Patient-specific visual analog scales**

ASSESSMENT OF RESPONSE

Define Desired Target Symptoms and
Operationalize the Outcome Measures

- Operationalized treatment of behavioral, cognitive, anxiety, and/or affective symptoms in personality disorder patients:
 - Reduces the risk of inappropriate expectations
 - Reduces ambiguous results
 - Minimizes the potential for power struggles between patient and clinician

EXAMPLE

The Target Symptom is Reduction of Affective Instability. A Simple 10 cm Visual Analog Scale Might Be Employed

“Most erratic, unstable emotions I have ever experienced”

“Most stable I have ever experienced my emotions to be”

Record for the preceding week at baseline and at each subsequent office visit

SCALES PROVIDE

- **An easy way to objectively chart target symptom change**
- **Objective criteria to justify continuation of medication with improvement**
- **Objective criteria to justify altering the medication dose or selection with inadequate progress**

MAINTENANCE AND MONITORING

Many Symptoms Are Themselves Inconstant

- **Frequent need to modify the dosing of medications appropriately**
 - **Increasing selected medications at times of stress**
 - **Reducing others at times that toxic side effects outweigh benefits**
- **Monitoring blood levels of medication, where available**
 - **Assure appropriate adherence to the medication regimen**
 - **Confirm that therapeutic levels are being maintained**

MAINTENANCE AND MONITORING

- **Where indicated by normal standards of care, periodic monitoring of blood chemistry, electrocardiography, and hematologic indices should be performed**

TREATMENT RESISTANCE

- **By definition, interpersonal relationships are disturbed in personality disorder patients**
- **These disturbances may intrude upon the therapeutic relationships**
- **Potential problems with medications:**
 - **Adherence to a prescribed medication regimen**
 - **Consistently and accurately reporting missed doses or side effects**
 - **Willingness to discuss treatment-related issues**

TREATMENT RESISTANCE INTERVENTION

- **Discussions at the onset of treatment and at appropriate intervals to assure one another of concern on the clinician's part and cooperation/collaboration on the patient's part**

INDICATIONS FOR REFERRAL TO A PSYCHOPHARMACOLOGIST

- **Affective symptoms**
 - Major depressive disorder
 - Marked affectivity, instability
- **Impulsive symptoms**
 - Repeated self-destructive or aggressive behaviors
- **Cognitive symptoms**
 - Psychotic-like symptoms
- **Anxiety symptoms**
 - Severe social phobia, generalized inhibition

AXIS II TARGET SYMPTOMS

- **Affective instability**
- **Impulsivity/aggression (self- or other-directed)**
- **Cognitive disorganization (psychotic-like symptoms)**
- **Anxiety**

SPECIFIC SYNDROMAL TREATMENT

- **Eccentric Personality Disorders**
 - **Schizotypal Personality Disorder**
- **Impulsive and Affective Unstable Personality Disorders**
 - **Borderline Personality Disorder**
- **Anxious Personality Disorders**
 - **Avoidant Personality Disorder**

ECCENTRIC PERSONALITY DISORDER SCHIZOTYPICAL PERSONALITY DISORDER

- **Dysfunction in perceptual and/or cognitive organization which may be reflected in the impairment of attentional and selective attentional processes**
 - **Odd speech**
 - **Magical thinking**
 - **Ideas of reference**
 - **Fleeting perceptual distortions (illusions, transient auditory hallucinations)**

ECCENTRIC PERSONALITY DISORDER SCHIZOTYPICAL PERSONALITY DISORDER

- **Compromised interpersonal relationships (normal motivations of others may be misconstrued)**
- **Suspiciousness that may episodically become paranoia**
- **Social anxiety**
- **“Loners” only minimally interacting with those outside of the immediate family**

SCHIZOTYPAL PERSONALITY DISORDER as a Schizophrenia-Related Disorder, or a Schizophrenia Spectrum

- **Genetic association between schizophrenia and SPD**

Silverman et al. 1996; 1993; Thaker et al. 1993

- **Neuropsychological abnormalities, impairment in attention and information processing, in auditory event related potentials, and in smooth pursuit eye movement in common between schizophrenia and SPD**

- *Siever et al. 1990; 1993b*

SCHIZOTYPAL PERSONALITY DISORDER as a Schizophrenia-Related Disorder, or a Schizophrenia Spectrum

- **Plasma homovanillic acid (HVA), a peripheral index of dopaminergic activity:**
 - **Higher CSF and plasma HVA in SPD compared to normal controls**

Siever et al. 1991; 1993a

- **A correlation between the number of psychotic-like symptoms and CSF HVA**

Siever et al. 1991; 1993a

NEUROCHEMICAL ABNORMALITIES IN PSYCHOTIC PERSONALITY DISORDERS

- Dopamine system (CSF, plasma HVA)
 - Deficit-like symptoms - decreased
 - Psychotic-like symptoms - increased
- Serotonin system
- Other neurochemical systems
 - Noradrenergic, glutamatergic, GABA-minergic

TREATMENT SELECTION ANTIPSYCHOTICS

- There are no studies of long-term use of antipsychotics in SPD or related personality disorder patients. Clinical caution, coupled with concerns for the development of tardive dyskinesia/ dystonia, argue that if antipsychotic medications are used in this population, they should be:
 - Administered for short-term use (months)
 - Subsequence medication withdrawal (if clinically tolerated)
 - Subject to reassessment
 - Probably be atypical antipsychotic drugs

TREATMENT SELECTION ANTIPSYCHOTICS

- **Low doses of antipsychotic medication (1-2 mg/day of haloperidol equivalent) are effective in at least temporarily reducing or relieving the symptoms of cognitive/ perceptual dysfunction in personality disorder patients**

SCHIZOTYPICAL PERSONALITY DISORDER

Outcome of Neuroleptics

- **Ideas of reference, odd communication, social isolation and transient psychosis respond to neuroleptics**
- **Haloperidol 0.5-6 mg (or its equivalent) often effective range**
- **High drop out rate (as much as 50%)**

TREATMENT SELECTION ANTIPSYCHOTICS

- **New antipsychotic medications that are mixed serotonin and dopamine D₂ antagonists with putatively minimal hematologic risk (e.g., risperidone), may provide improved treatment of the deficit- like symptoms and a reduced risk of tardive dyskinesia/dystonia**

TREATMENT INITIATION

- **Start antipsychotics at 1 mg/d or less of haloperidol equivalent**
- **After 1-2 weeks, increase to a treatment dose of 2 mg/d haloperidol equivalent, if tolerated.**
- **Document dyskinesias or dystonias at baseline to determine if any subsequent changes occur**

PHARMACOLOGIC MANAGEMENT

- **Neuroleptics**
 - Typical
 - Atypical
- **Dopamine agonists?**
- **Alpha₂ agonists**
- **The next frontier - glutamatergic,
(GABA-aminergic drugs**

MANAGEMENT OF SIDE EFFECTS

At Low Antipsychotic Doses, Minimal Side Effects Are Expected

- However, akathisia or dystonia/ dyskinesia are possible
- Treat by:
 - Reducing dose
 - Discontinuing or switching medication
 - Adjuvant medication
- Periodic assessment should be made for occurrence of, or change in, dyskinesia or dystonia

TREATMENT RESISTANCE

- **Some SPD patients are uncomfortable even on low doses of antipsychotic medication, due primarily to behavioral toxicity; dysphoria or a worsening of some of the deficit-like symptoms**
- **Consider reducing the dose of anti- psychotic to the lowest effective level and initiating supportive psychotherapy**
- **If the symptoms persist and the benefit of the antipsychotic argues against dis-continuation, a trial with an anti- depressant may be considered**

IMPULSIVITY/AGGRESSION

- **May be a dimension of behavior not restricted to a single psychiatric diagnosis**
- **May occur in both the Cluster B personality disorders in certain Axis I disorders as well:**
 - **Intermittent Explosive Disorder**
 - **Bipolar Disorder - Manic Type**
 - **Conduct Disorder**

IMPULSIVITY/AGGRESSION

- **Antidepressants**
 - SSRIs

- **Mood stabilizers**
 - Lithium carbonate
 - Carbamazepine (Tegretol)
 - Gabapentin

AFFECTIVE INSTABILITY

- **Rapid, exaggerated shifts in emotion in response to environmental stimuli such as criticism, separation from a significant person, or frustration may impair a stable sense of self and thus disrupt inter- personal relationships**

AFFECTIVE INSTABILITY

- **Antidepressants**
 - **SSRIs**

- **Mood stabilizers**
 - **Lithium carbonate**
 - **Valproate (Depakote)**
 - **Carbamazepine (Tegretol)**
 - **Gabapentin**

TREATMENT SELECTION

SEROTONIN REUPTAKE INHIBITORS

- **Tentative evidence that SSRIs are effective for the treatment of BPD patients:**
 - **Reducing severity of global symptomatology**
 - **Reducing severity of impulsive aggression and affective instability**
- **Overall, fluoxetine seems a reasonable first choice for the treatment of impulsive aggressive behavior, since it is relatively safe in an overdose and may also treat depression and affective lability**

SSRIs

- **Effective in treating co-morbid depressive disorder**
- **Effective in treating anger/impulse dyscontrol**
- **Relatively well tolerated**
- **Low lethality for overdose**

MONOAMINE OXIDASE INHIBITORS

- **Limited evidence of MAOI efficacy for affective instability**
- **Practical concern: risk of a hypertensive crisis, particularly in patients who may also have difficulties with impulse regulation and therefore be liable to overdose**
- **Reversible inhibitors of MAO-A, which are less likely to induce a hypertensive crisis, provide an excellent alternative if proven to be as effective as the present non-selective MAOIs for the treatment of affective instability**

TRICYCLIC ANTIDEPRESSANTS

- **Generally poor response to treatment**
- **Lethal potential of overdose**
- **Anticholinergic toxicity**
- **Tricyclic antidepressants are not generally recommended for the treatment of BPD patients.**

5-HT1a AGONISTS

Ipsapirone, Buspirone, Gepirone, Eltoprazine

- **Reduces serotonergic activity by acting on 5-HT1a receptors and acts on post-synaptic 5-HT1a receptors**
- **Antidepressants and anti-anxiety efficacy**
- **Preliminary trials suggest therapeutic efficacy for impulsivity/aggression**

SSRI/5-HT_{1a} AGONISTS

Trazodone, Nefazadone

- **Effective antidepressants**
- **Minimal sexual side-effects
(Trazodone- priapism)**
- **Useful for sleep induction**

NOREPINEPHRINE-SEROTONIN REUPTAKE INHIBITORS

Dual Action or Broad Spectrum Antidepressants

Venlafaxine, Duloxetine

- **Increase output of both norepinephrine and serotonin**
- **Side effect profile closer to that of SSRIs than TCAs without muscarinic, histaminergic, alpha-adrenergic related side effects**
- **Indicated in major depressive disorder, both mild and severe**

LITHIUM CARBONATE

- Lithium may treat affective lability regardless of the syndrome per se
- Lithium may be effective in decreasing:
 - Impulsivity in general (Shader et al, 1974)
 - Impulsivity associated with affective lability (Rifkin et al. 1972a)
 - Impulsivity associated with episodic violence, esp. in antisocial personality disorder patients (Schiff et al. 1982)

CARBAMAZEPINE

- **May dampen limbic irritability implicated in BPD**
- **Effective in reducing impulsive behavior, angry outbursts in BPD patients (Cowdry et al. 1988)**
- **May be effective in dampening affective instability**

BORDERLINE PERSONALITY DISORDER MAOI VS CARBAMAZEPINE

- **Patients preferred MAOI because it improved their mood**
- **Physicians preferred carbamazepine because it decreased patients destructive, impulsive acts, e.g., self cutting**
 - **Patients agreed that they behaved better but they didn't "feel" better on carbamazepine**

VALPROATE

- **Effective in bipolar conditions, particularly “mixed” states, rapid cycling patients**
 - ? Affective instability
- **Results of pilot study suggest improvement in mood of BPD patients with valproate (4/8) (Hollander et al., unpublished data)**

BORDERLINE PERSONALITY DISORDER BENZODIAZEPINES

- **No evidence of efficacy**
- **Risks disinhibition**
- **In high doses, worse depression**
- **Dangerous withdrawal symptoms from impulsively stopping medication**

NOVEL AGENTS

- **New anticonvulsants**
 - Lamotrigine (Lamictal)
 - Gabapentin (Neurontin)
- **Opioid agents**
 - Antagonists (Naloxone)
 - Mixed agents/antagonists
 - Buprenorphine
 - Tramadol

ANXIOUS PERSONALITY DISORDERS AVOIDANT PERSONALITY DISORDERS

- **Hyerarousal as a concomitant of a low stimulation threshold may contribute to the pathology of the anxious cluster diagnosis**

ANXIOUS PERSONALITY DISORDERS AVOIDANT PERSONALITY DISORDERS

Behavioral Manifestations

- **Shyness**
- **Rejection sensitivity**
- **Diminished ability to perceive and take advantage of position opportunities**

ANXIOUS PERSONALITY DISORDERS AVOIDANT PERSONALITY DISORDERS

Physiological Manifestations

- **Restlessness**
- **Wringing of hands**
- **Pacing**
- **Diaphoresis**
- **Palpitations**
- **Gastrointestinal disturbance**

BIOLOGICAL CORRELATES AND PSYCHOPHARMACOLOGY OF ANXIETY/INHIBITION

- **Increased tonic levels of sympathetic activity**
- **Increased tonic levels of cortical arousal**
- **Slower habituation to new stimuli**
- **Lower sedation thresholds**

ANXIOUS PERSONALITY DISORDERS AVOIDANT PERSONALITY DISORDERS

Cognitive Manifestations

- **Impaired concentration**
- **Confusion and perceptual distortion**

DIFFERENTIAL DIAGNOSIS

- **Generalized Anxiety Disorder**
- **Panic Disorder**
- **Obsessive-Compulsive Disorder (OCD)**
 - **With anxious/dependent features**
 - **With avoidant or dependent personality disorder**
- **Phobic Disorders**
- **Major Depression**
 - **With anxious/dependent features**
 - **With avoidant or dependent personality disorder**

TREATMENT SELECTION

- **Adjunctive therapy to the overall treatment of patients with personality disorders characterized by anxiety or excessive inhibition:**
- **Monoamine oxidase inhibitors**
 - **Selective serotonin reuptake inhibitors**
 - **Beta-adrenergic receptor antagonists**
 - **Benzodiazepines**

ANXIETY

- **Non-benzodiazepines**
 - Buspirone
- **Benzodiazepines**
 - Klonopin
 - Xanax

AVOIDANT PERSONALITY DISORDER MAOI

- **In 1 study of patients who stayed on MAOI 1 year**
 - **70% no longer met criteria for avoidant personality disorder**
- **Challenge the diagnosis**
 - **May better be seen as a chronic pervasive social phobia**

OBSESSIVE COMPULSIVE PERSONALITY DISORDER - SSRI_s

- **Some data suggesting a decrease in symptoms**
- **No well controlled studies yet**

- **Potential pathophysiology may relate more closely to neurobiologic dimensions than to categorical diagnosis**

- **The observed personality disorders may therefore arise from the patterns of the underlying disturbances acting in concert**

Post Lecture Exam

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Answers to Pre & Post Competency Exams

1. C

2. B

3. D

4. C

5. D

6. A

7. B

8. A

9. B

10. C