“It is not so much our friends’ help that helps us as the confident knowledge that they will help us.”

Epicurus, philosopher (c. 341-270 BC)
The Psychology of Psychopharmacology

Learning Objectives
1. To appreciate that psychological factors have an important influence on pharmacotherapy outcomes
2. To describe pill, patient, prescriber, and partnership variables that play a role in pharmacotherapy
3. To explain how psychological factors can influence pharmacotherapy, with reference to the meaning of medication, defence mechanisms, transference, countertransference, and resistance

Outline
- Review of the evidence on psychological factors in psychopharmacology
- Split vs. combined treatment
- Meanings of medication for children/adolescents, parents, families, and clinicians
- Medication as defence: patients & physicians
- Transference & countertransference
- Treatment resistance
- Value of a psychodynamic formulation

Should ACP be Revamped?
“Given that the evidence suggests that nonpharmacologic aspects of medications play a major (and perhaps even primary) role, it seems clear that this evidence should be well represented in the psychopharmacology curriculum. One might even argue that if more than half the benefit that patients derive from medications comes from meaning and interpersonal factors, then more than half of the psychopharmacology didactics should focus on those factors.”
Mallo & Mintz, 2013

Evidence on Psychological Factors in Psychopharmacology
- Mallo & Mintz, 2013:
  - A strong evidence base supports the influence of psychological and interpersonal factors in psychopharmacology
  - Most studies emerge from primary care medicine and psychology, and evidence specific to child psychopharmacology is still limited
  - Non-pharmacological factors that influence pharmacotherapy outcome can be divided into 4 types of variables: pills, patients, prescribers, partnerships

Pill Variables
- The following pill characteristics have been found to affect pharmacotherapy outcome:
  - Colour (de Craen et al., 1996)
  - Expense (Waber et al., 2008)
  - Route (de Craen et al., 2000)
  - Brand vs. generic (Weissenfeld et al., 2010)
  - Setting (Fisher & Greenberg, 1997)
- Other variables to consider (Mallo & Mintz, 2013):
  - Drug name
  - Packaging

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Patient Variables

- The following patient characteristics have been found to affect pharmacotherapy outcome:
  - Treatment preference (Kocsis et al., 2009)
  - Expectations of treatment (Leuchter et al., 2014; Rutherford et al., 2017)
  - Locus of control (Reynaert et al., 1995)
  - Tendency to acquiesce (McNair et al., 1968)
  - Readiness to change (Lewis et al., 2009)
  - Social disadvantage (Hahn, 1997)
  - Personality traits (Davis et al., 1995)
  - Attachment style (Ciechanowski et al., 2006)
  - Ambivalence about medication or illness (Warden et al., 2009; Van Egmond & Kummeling, 2002)

Treatment Preference: Kocsis et al., 2009

- RCT of 429 chronically depressed adults treated with an antidepressant, psychotherapy, or the combination
- Remission rates:
  - ~50% in patients receiving their preferred treatment
  - 22% in patients who preferred medication but received psychotherapy
  - 8% in patients who preferred psychotherapy but received medication
- In child psychiatry, both child and parent preference are likely important
- Implications for the value of RCTs?

Expectations of Treatment: Rutherford et al., 2017

- 54 adults with MDD were randomly assigned to open or PBO-controlled citalopram (CIT) treatment for 8 weeks:
  - 28 were randomized to open CIT, 21 to PBO-controlled CIT, and 5 to PBO
- Pre-randomization expectancy scores did not differ significantly between groups
- Post-randomization (but pre-treatment) expectancy scores were significantly higher in the open group compared to the PBO-controlled group
- HAM-D scores for CIT-treated patients ↓ at a faster rate in the open group compared to the PBO-controlled group

Rutherford et al., 2017 (cont.)

- Compared to patients treated with PBO-controlled CIT, patients treated with open CIT had significantly ↓ HAM-D scores from weeks 4 to 8
- Post-randomization expectancy partially mediated group effects on the HAM-D at week 8
- The difference in improvement between patients treated with open CIT vs. PBO-controlled CIT was greater than the typically observed differences between drug and PBO in antidepressant trials

Prescriber Variables

- The influence of prescriber variables on outcome is supported by evidence from the Treatment of Depression Collaborative Research Program (TDCRP)
- The TDCRP involved an RCT in which 250 adults with MDD were randomized to the following (Elkin et al., 1989):
  1. IPT
  2. CBT
  3. Imipramine (plus clinical management)
  4. PBO (plus clinical management)
- Overall pattern of results:
  - Imipramine > IPT = CBT > PBO
A subsequent analysis considered the effect of the psychiatrists on patient outcomes, and compared this to the effect of medication (McKay et al., 2006):

- 1/3 of psychiatrists were highly effective, 1/3 were average, and 1/3 were relatively ineffective
- For both BDI and HAM-D scores, the proportion of variance due to psychiatrists was greater than that due to medication
- The highly effective psychiatrists achieved better outcomes with PBO than the least effective psychiatrists achieved with active medication

Beyond warmth (Rickels et al., 1971) and empathy (Downing et al., 1973), little is known about which prescriber factors are important.

Considerable evidence indicates that the therapeutic alliance has an important influence on pharmacotherapy outcome (Mallo & Mintz, 2013):

- For example, in a TDCRP analysis comparing PBO patients with good alliance to antidepressant patients with poor alliance, the quality of the alliance predicted response much more strongly than drug condition, accounting for 17 times more variance (Krupnick et al., 1996)

Dealing with the child or adolescent in the context of their family in psychiatry requires the negotiation of multiple alliances:

- Alliance with the child/adolescent
- Alliance with the parents
- Alliance with their teachers
- Alliance with the therapist
- Alliance with the treatment team

Pressure from parents, teachers, or a therapist to initiate or change medication may threaten the alliance between the child/adolescent and the physician.

Study objective was to examine the effects of pill administration, expectation, and therapeutic alliance on the PBO response in MDD:

- 88 adults with at least moderate MDD (no comorbidities) were randomized to 8 weeks of:
  1. Supportive care alone
  2. Supportive care + antidepressant (VLX, DLX, or eCIT)*
  3. Supportive care + PBO*

  Analyzed the effect of the following on treatment outcome:
  - Patients’ expectations of treatment/medication efficacy
  - Therapeutic alliance

Note: By chance, patients randomly assigned to supportive care only had lower expectations of treatment in general (prior to randomization) than those assigned to the pill-taking conditions.

Reference: Leuchter et al., 2014

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Effect of Therapeutic Alliance

- Therapeutic alliance was assessed with the California Pharmacotherapy Alliance Scale (CALPAS), which measures:
  a) Patients’ commitment to treatment
  b) Patients’ working capacity
  c) Treatment providers’ understanding and involvement
  d) Goal and working strategy consensus between patient and treatment provider

- Of the 4 CALPAS subscales, only (d) predicted symptom change in the PBO and medication groups

Reference: Leuchter et al., 2014

Split vs. Combined Treatment

- Definitions:
  a) Split treatment: one clinician provides pharmacotherapy, while another provides psychotherapy to the same patient
  b) Combined treatment: a single clinician provides both pharmacotherapy and psychotherapy to the same patient

Split Treatment

Advantages
- Enables sufficient focus on both psychotherapeutic and medication issues
- Greater support for both families and clinicians

Challenges
- Communication
- Competition
- Differences in opinion
- Splitting

Reference: Mintz, 2005

Combined Treatment

Advantages
- Greater opportunity to explore psychological factors related to medication
- Increased interaction with parents to discuss medication can facilitate psychotherapy with the child/adolescent

Challenges
- Can be difficult to focus sufficiently on both psychotherapeutic and medication issues
- Increased interaction with parents to discuss medication can disrupt the therapeutic alliance with the child/adolescent

Reference: Chubinsky & Rappaport, 2006

Meanings of Medication for Youth

(Rappaport & Chubinsky, 2000; Chubinsky & Rappaport, 2006)

- Worries about being defective, crazy, bad, or stupid
- Interference with self-image as autonomous, perfect, or invulnerable
- Fears regarding the effects of the medication
- Criticized, blamed, punished, or controlled, especially with respect to aggressive or sexual impulses
- Uncomfortable feelings of dependence on the physician
- Relieved and empowered, as symptoms are now viewed as part of a treatable medical problem, not a personal failing

Reference: Floersch et al., 2009

(Enlarged slide appended)
Psychodynamic Models to Consider in Relation to the Meaning of Medication

- **Freud:**
  - Oral fantasies
  - Anal struggles for control
- **Erikson:**
  - Basic trust vs. mistrust
  - Autonomy vs. shame and doubt
  - Identity vs. role confusion
- **Winnicott:**
  - Medication as a transitional object
- **Kohut:**
  - Development of the self
  - Narcissism
  - Idealization

Meanings of Medication for Parents
(Rappaport & Chubinsky, 2000; Chubinsky & Rappaport, 2006)

- Loss and grief (e.g., about the fantasy of a perfect child)
- Shame and guilt (e.g., about the child being “damaged,” being bad parents, or transmitting an inherited condition)
- Fear of chronic illness or addiction
- Expression of unconscious anger towards the child
- Devaluing of psychosocial factors
- Relieved, hopeful, and validated as parents, as the child’s symptoms are now viewed as part of a treatable medical problem, not the result of poor parenting

Meanings of Medication for Families

- It has been suggested that medicating a child/adolescent is “symbolically medicating a family because the effects of medication generate meanings that implicate an entire family system” (Floersch et al., 2009)
- Prescribing medication for a child/adolescent may create or reinforce narratives and perceived roles within the family (e.g., the “bad” or “sick” sibling vs. the “good” or “healthy” sibling)
- Pharmacotherapy may also influence family dynamics related to themes of attention and specialness, in part because medication can mean “treat” as well as “treatment” (Pruett et al., 2011)

Meanings of Medication for Clinicians
(Mintz, 2005; Mallo & Mintz, 2013)

- Prescribing medication may cause a physician to perceive a child as a “biological object” as opposed to a subject with internal resources that can be recruited in the service of recovery
- Prescribing medication may cause a physician to view symptoms only as problems in themselves, as opposed to “partial solutions” to deeper or more complex problems (e.g., overwhelming affect, unconscious conflict)
- Decisions to prescribe or not prescribe medication can have meanings related to a physician’s professional identity (e.g., “a real doctor” vs. “not just a pill pusher”)

Psychodynamic Definitions

- **Defence:**
  - Unconscious mechanism that serves to protect against intolerable drives, wishes, or affects
- **Transference:**
  - A largely unconscious process where patterns of feelings, thoughts, and behaviour that were originally experienced in relation to significant figures during childhood are displaced onto a person in a current relationship

Definitions (cont.)

- **Countertransference:**
  - A clinician’s transference towards a patient/family
- **Resistance:**
  - Largely unconscious forces that interfere with treatment and improvement
Medication as Defence: Patients

- Taking medication may serve unconscious defensive functions for the patient
- Examples include (Mintz & Flynn, 2012):
  - To support a split between the “good” self and the “bad” illness
  - To disavow ownership of feelings or responsibility for actions
  - To avoid interpersonal interactions (“replace people with pills”)

Transference & Countertransference

- “A psychodynamic psychopharmacologist recognizes that the psychiatric relationship is an encounter between a big mess and an even bigger mess.” (Mintz, 2011)
- As in psychotherapy, the psychopharmacological encounter has the potential for both patient and physician to get caught up in irrational processes that relate to previous relationships and other unconscious factors

Medication as Defence: Physicians

- Prescribing medication may serve unconscious defensive functions for the physician
- Examples include (Mintz, 2005):
  - To avoid feeling powerless or helpless and instead feel good and giving
  - To de-intensify an intense engagement with a patient
  - To avoid feelings of loss by promoting a patient’s dependency
  - To act out feelings of anger that cannot be tolerated or expressed verbally

Transference

(Mintz & Flynn, 2012)

- Negative transferences can lead to poor pharmacotherapy outcomes, including poor response, non-adherence, and emergence of side effects (“nocebo” effect)
- Negative transferences to a prescriber may result from previous experiences with medications, physicians, parents, or other caregivers
- Patients can also have transferences towards medications themselves, which become imbued with meaning based on past experiences

Countertransference

(Mintz & Flynn, 2012)

- “A hallmark of countertransference prescribing is its focus on managing the experience of the prescriber rather than the experience of the patient”
- Children/adolescents and their parents may trigger unconscious processes in a prescriber related to the prescriber’s own experiences as a child/adolescent or parent, and these unconscious processes can influence prescribing behaviour
- Consultation with colleagues is critical when working with patients or families who elicit strong countertransference reactions

Treatment Resistance

(Mintz & Flynn, 2012)

- If a patient doesn’t respond to medication, think about “treatment resistance” in the psychological sense, not just the pharmacological sense
- Pharmacotherapy can reinforce resistance in various ways, such as:
  - Externalizing responsibility for improvement
  - Interfering with the opportunity to learn from difficult feelings or experiences by turning them into symptoms that become targets for medication
  - Promoting secondary gain in the form of increased attention from the physician
Value of a Psychodynamic Formulation
(Mintz & Flynn, 2012)
• Exerts a containing and conservative influence in the face of strong disorganizing affect (on the part of both patient and prescriber)
• Helps the prescriber to:
  – Anticipate and avoid prescribing enactments
  – Maintain empathy
  – Recognize psychological resistance
• Can be brief and focused on the relationship of the patient/family to medication and treatment providers

Psychodynamic Formulation Guidelines
(Perry et al., 1987)
• Four parts (totalling 500-750 words):
  i. Case summary, including current problems, life situation, and developmental history
  ii. Description of nondynamic factors contributing to the psychiatric difficulties
  iii. Psychodynamic explanation of central conflicts, including their role in the current situation and their origins in the developmental history
  iv. A prediction of how these conflicts are likely to affect treatment (including pharmacotherapy) and the therapeutic relationship

Take-Home Points
1. Substantial evidence indicates that psychological factors—especially patients’ treatment preference, their expectations, and the therapeutic alliance—have a strong influence on pharmacotherapy outcomes
2. It is important to explore the meaning of medications for patients, parents, families, and clinicians
3. The role of psychodynamic mechanisms (e.g., defences, transference, countertransference, resistance) should be considered in pharmacotherapy as well as in psychotherapy
4. A brief psychodynamic formulation is helpful to contain disorganizing affect, avoid prescribing enactments, maintain empathy, and recognize resistance
Note: By chance, patients randomly assigned to supportive care only had lower expectations of treatment in general (prior to randomization) than those assigned to the pill-taking conditions.

Reference: Leuchter et al., 2014
Effect of Expectations of Medication

% change in the 17-item Hamilton Rating Scale for Depression

Reference: Leuchter et al., 2014
<table>
<thead>
<tr>
<th>Theme</th>
<th>Need for Medication Treatment</th>
<th>How Medications Work</th>
<th>Adherence to Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis/Disorder/Symptom</td>
<td>‘it was for anxiety attacks and depression’</td>
<td>‘They balance off my mood swings to where I won’t have as many.’</td>
<td>[negative]² ‘I don’t want to get hooked on it or anything like that.’</td>
</tr>
<tr>
<td>Emotion</td>
<td>‘I think it’s mostly because I had a really, really bad attitude.’</td>
<td>[positive]</td>
<td>‘At first my parents told me to, but once I see that that actually help, I take it.’</td>
</tr>
<tr>
<td>Expectation/Hope</td>
<td>[positive]</td>
<td>‘...when I get angry, make me not like want to hurt my little sister cause she just gets on my nerves.’</td>
<td>[negative]² ‘Oh D, you can’t behave? Oh D, you’re bad. You’re on medicine, cause kids in my school, they’ll make fun of you.’</td>
</tr>
<tr>
<td>Self</td>
<td>‘I’m a mental case.’</td>
<td>[positive]</td>
<td>‘It’s making me act better.’</td>
</tr>
<tr>
<td>Behavior/Action</td>
<td>‘...because I was having problems, real problems in school.’</td>
<td>[positive]</td>
<td>‘It’s my sleeping pill.’</td>
</tr>
<tr>
<td>Intersubjective</td>
<td>‘...they thought that I was disrespecting them if I told them no.’</td>
<td>[negative]² ‘Oh D, you can’t behave? Oh D, you’re bad. You’re on medicine, cause kids in my school, they’ll make fun of you.’</td>
<td></td>
</tr>
<tr>
<td>Cognition/Thought</td>
<td>‘...when I wasn’t paying attention in school.’</td>
<td>[positive]</td>
<td>‘I think it actually helps me to focus and I think that anger is more like in my own hands.’</td>
</tr>
<tr>
<td>Body</td>
<td>‘...like headaches and stomachache.’</td>
<td>[negative]² ‘I don’t want to take it trying to help something else and then it messes up another thing.’</td>
<td></td>
</tr>
<tr>
<td>Management</td>
<td></td>
<td>[negative]² ‘That I’m going to get like five medicines at a time to take four times a day.’</td>
<td></td>
</tr>
</tbody>
</table>

Reference: Floersch et al., 2009

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