Recovery and Adherence

Illness Cognition from Anosognosia to Adjustment

APNA 9th Clinical Psychopharmacology Institute
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What Does This Title Mean?

I am going to explore this question....

Why would or should a patient take a medication for an illness s/he....

– Is in the throes of either the first episode or recurrent psychosis and has lost a sense of self.
– Is totally afraid/ashamed/embarrassed/angry about.
– Doesn’t believe s/he really has.
– Is completely terrified of side effects and what the medication may do to his/her brain.
– Doesn’t have accurate understanding of diagnosis.
– Doesn’t have any idea about treatment trajectory?
Disclosures

Mary D. Moller has received research funding from Astra Zeneca Pharmaceuticals for a non-pharmaceutical study involving case manager education.
Objectives

1. Identify constructs of treatment adherence.
   a) Client/provider goals of recovery
   b) Medication ‘rookie’ vs ‘pro’
   c) Treatment ‘rookie’ vs ‘pro’

2. Discuss the concept of illness cognition.
   a) Cognitive Insight vs Anosognosia
   b) Neurobiological implications for cognition

3. Describe the relationship between cognitive functioning and ability to adhere to a therapeutic treatment plan.
   a) Role of post-psychotic psychological adjustment in the **readiness** for recovery and adherence
DEFINITIONS
CONCEPTS
CONSTRUCTS
RECOVERY
Original Definition

• Recovery is
  – a deeply personal, unique process of changing one’s attitudes, values, feelings, goals, skills and/or roles.
  – a way of living a satisfying, hopeful, and contributing life even with limitations caused by the illness.
  – involves the development of new meaning and purpose in one’s life as one grows beyond the catastrophic effects of mental illness.

Jacobson and Greeley (2001)

- Internal and external conditions in understanding recovery.
  - Internal: hope, healing, empowerment, connection
  - External: human rights, positive culture of healing, recovery-oriented services

SAMHSA, 2004

“Mental health recovery is a journey of healing and transformation enabling a person with a mental health problem to live a meaningful life in a community of his or her choice while striving to achieve his or her full potential”

SAMHSA and Recovery: 10 Components

1. Self-direction
2. Individualized and person-centered
3. Empowerment
4. Holistic
5. Nonlinear
6. Strengths-based
7. Peer support
8. Respect
9. Responsibility
10. Hope

Davidson & Roe, 2007

- Two complimentary meanings:
  - Clinical improvement over time
    - Grounded in the medical model-recovery FROM mental illness
  - Person’s right to self-determination and inclusion in community life
    - Grounded in the consumer-survivor movement-recovery IN mental illness

Recovery: A Dimensional Approach, 2010

- **Clinical**: symptoms, medical care, psychotropic medications, talking and behavioral therapies
- **Existential**: religion and spirituality, agency and self-efficacy, personal empowerment
- **Functional**: employment, education, housing
- **Physical**: diet, exercise, smoking, substance abuse
- **Social**: family, friends, peers, community social activity

Following a recommended course of treatment

ADHERENCE
Key Themes of Adherence

• Poor adherence is the norm across all chronic disease states

• Ongoing or breakthrough symptoms are common in bipolar disorder and schizophrenia

• Consequences of poor adherence for patients with bipolar disorder or schizophrenia
  – Increased frequency and severity of illness
  – Preventable episodes of illness relapse and hospitalization
  – Risk of hospitalization increased with number of consecutive days of antipsychotic medication missed
  – Death due to suicide

Poor Adherence Is the Norm

Disease State (Drug Class)

- Multiple sclerosis (biologic)
- High cholesterol (statin)
- Hypertension (CCB)
- Osteoporosis (SERM)
- Asthma (inhaled steroid)

% of Patients Continuing Therapy

CCB=calcium channel blocker. SERM=selective estrogen receptor modulator.
In Bipolar Disorder and Schizophrenia, Ongoing and Breakthrough Symptoms Are the Rule, Not the Exception

<table>
<thead>
<tr>
<th>Bipolar disorder(^1) (STEP-BD)</th>
<th>Schizophrenia(^2) (CATIE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 58% of symptomatic patients with bipolar at study entry achieved recovery over a 2-year period</td>
<td>• 74% of patients discontinued study medication by 18 months</td>
</tr>
<tr>
<td>• 48% of these patients subsequently experienced recurrences</td>
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</tbody>
</table>

Testing a Hypothesis

• High levels of adherence are possible
• Study of >25,000 patients on antipsychotics revealed several important insights
  – High levels of adherence can be obtained, as 71% of patients on clozapine remained on therapy after 9 months
  – High levels of adherence for conventional patients begs the question: Is patient experience in managing an illness a predictor of high compliance and adherence?

Role of Patient Treatment Experience in Adherence With Atypical Antipsychotics

Testing the hypothesis: Patients who are more experienced with treatment are more adherent.

- De-identified computerized pharmacy records were used to select patients who obtained a prescription for certain atypical antipsychotics (index drugs)
- Selected patients were divided into “rookies” and “veterans”
  - Rookies have no prior use of any antipsychotic in the 180-day period prior to the index fill
  - Veterans were those patients with a history of antipsychotic use in the preceding 180 days
- Patients were defined as having discontinued medication once they were 30 days late for a prescription refill

Large Differences in Adherence for Rookies vs Veterans

Risk of discontinuation of 6 index antipsychotics greatest among rookies during the first month of treatment

*Median time to antipsychotic discontinuation.
Median Days to Discontinuation of 6 Index Antipsychotics: Rookies vs Veterans

Antidepressants–Large Difference in Adherence for Rookies vs Veterans

* Median time in days to antidepressant discontinuation

Conclusions

• Patients new to antidepressant and antipsychotic therapy are likely to be at greater risk of discontinuing treatment than patients who have previously been on therapy\textsuperscript{1,2}
  • This risk may be greatest in the first 30 to 45 days after the start of treatment
  • Close follow-up during this period of time is needed

• A “learning curve” related to prior medication use can help predict adherence to antipsychotics and antidepressants\textsuperscript{1,2}

Prevalence of Risk Factors for Medication Non-Adherence in Schizophrenia

• Demonstrated BOTH association and little or no association:
  – Poor insight
  – Negative attitude toward medications
  – Substance abuse
  – More severe psychotic symptoms
  – Presence of mood symptoms

Risk Factors that Both Affected and Didn’t Affect Adherence (cont’)

- Shorter duration of illness or treatment
- Current inpatient status
- Higher educational level
- Nonwhite ethnicity
- Younger age
- Male gender
- Higher antipsychotic dose
- Medication regimen complexity

Risk Factors that Both Affected and Didn’t Affect Adherence (cont’)

- Use of typical vs atypical antipsychotic
- Oral vs depot
- More severe side effects
- Unstable living arrangement

Little or no association:

- Neurocognitive impairment
- Marital status
- Poor family involvement

What Risk Factors Consistently Affected Future Non-Adherence?

- Poor therapeutic alliance
- Less outpatient contact
- Inadequate discharge planning
- Poor aftercare environment
- Negative *subjective* response to medication
- Previous nonadherence

Domains and Executive Function
Circuits, Neurotransmitters, and Psychopharm
Illness Cognition
Insight-Anosognosia
Cognitive Insight

THE ROLE OF COGNITION
Research Now Shows…

“Cognitive function in schizophrenia is one of the most critical determinants of social and occupational function, potentially more so than the severity of other aspects/symptoms such as hallucinations, delusions, or even negative symptoms”

Domains of Cognitive Function

- **Executive function**
  - Coined by Hans Lukss-Teuber, MIT, 1969

- **Memory**: working, declarative, long-term-hippocampus

- **Language**: speech production-Broca’s area=Naming and fluency

- **Attention**: involves prefrontal cortex, parietal, temporal, occipital, cingulate, hippocampus, cerebellum

- **Visuospatial function**: Of or relating to visual perception of spatial relationships among objects
Executive Function
(5 agreed upon components)

- Cognitive tracking: “I choose this path”
- Set maintenance: “I’ll stay on this path”
- Set shifting: “Switch strategies-see a detour and figure way back to path”
- Abstraction: Extract common element from amount of data
- Response suppression: self-inhibition

Moss, M. B. (Workshop attended March, 2011). Understanding the frontal lobes: Emotional regulation, social intelligence, and motivation. Institute for Brain Potential, Mountain View, CA
Frontal-Subcortical Circuits: Key Brain Regions

# Frontal-Subcortical Circuits

<table>
<thead>
<tr>
<th>Circuit</th>
<th>Function</th>
<th>Dysfunction</th>
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<tbody>
<tr>
<td>DLPFC</td>
<td>Problem Solving</td>
<td>↓ Working Memory</td>
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<tr>
<td></td>
<td>Cognitive Flexibility</td>
<td>↑ Thought disorganization</td>
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<tr>
<td></td>
<td>Self Monitoring</td>
<td>↓ Organization Skills</td>
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<tr>
<td></td>
<td>Planning</td>
<td>↓ Concentration</td>
</tr>
<tr>
<td>OFC</td>
<td>Sensory Integration</td>
<td>↑ Impulsivity</td>
</tr>
<tr>
<td></td>
<td>Response Inhibition</td>
<td>↑ Distractibility</td>
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<tr>
<td></td>
<td>Emotional Regulation</td>
<td>↑ Disordered Behavior</td>
</tr>
<tr>
<td>ACC</td>
<td>Goal Directed Behavior</td>
<td>↓ Error Monitoring</td>
</tr>
<tr>
<td></td>
<td>Error Processing</td>
<td>↑ Perseverative worry</td>
</tr>
<tr>
<td></td>
<td>Emotional Output</td>
<td>↑ Sensitive to criticism</td>
</tr>
<tr>
<td></td>
<td>Attention</td>
<td>↑ Focused on emotion</td>
</tr>
</tbody>
</table>


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Neurotransmitter Receptors and Negative Cognitive Implications

• Histamine antagonism \(^1\)
  – Perceptual processing—impaired
  – Motor responses—impaired
  – Memory and attention—mild impairment

• Glutamatergic excitation \(^2\)
  – Loss of executive function
  – Psychosis


Neurotransmitters Associated with Enhancing Cognition

• Goal: Improvements in general cognition, executive function, and verbal memory occur by:
  – Increasing dopamine, norepinephrine, and acetylcholine in key prefrontal cortex regions
  – Antagonizing serotonin 5-HT2C receptors will increase cortex dopamine and norepinephrine
  – Agonizing serotonin 5-HT2A, 5-HT2C, 5-HT4 receptors-inhibits NE/DA at mesolimbic
  – Antagonizing 5-HT1A, 5-HT3, 5 HT7 receptors decreases anxiety
  – Antagonizing 5HT1D receptor decreases pain

Receptor Binding Properties Potentially Related to Mood and Cognition

- 5-HT$_{2a}$ and 5-HT$_{2c}$ antagonist properties
  - 5-HT *inhibits* DA and NE release via 5-HT$_{2A}$ and 5-HT$_{2C}$ receptors,
  - 5-HT$_{2A}$ antagonists and 5-HT$_{2C}$ antagonists *disinhibit* both DA and NE release in the cortex, leading to increased NE and DA activity

- 5-HT1A agonist properties (dopamine accelerator)
  - Presynaptic actions may enhance 5-HT neuronal disinhibition and add to antianxiety effects
  - Postsynaptic actions may enhance cognitive effects
  - Prefrontal increases in DA and NE are blocked by 5-HT1A antagonists

We Now Have 9 2nd Generation Atypical Antipsychotics!

- Clozapine (Clozaril)
- Risperidone (Risperdal)
- Paliperidone (Invega/Consta)
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Ziprasidone (Geodon)
- Lloperidone (Fanapt)
- Asenapine (Saphris)
- Lurasidone (Latuda)
- Aripiprazole (Abilify)—3rd generation

<table>
<thead>
<tr>
<th>Olanzapine</th>
<th>Clozapine</th>
<th>Risperidone</th>
<th>Ziprasidone</th>
<th>Quetiapine</th>
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<tr>
<td>5HT1A (PA)</td>
<td>5HT 2A/2C</td>
<td>5HT 2A/2C</td>
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<td>5HT1A-PA</td>
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<td>5HT7</td>
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<td>5HT6</td>
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<td>D - 1,2,3,4</td>
<td>H1, α 1, α 2</td>
<td>D2</td>
<td>NRI</td>
<td>D2(PA)</td>
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<td>M1</td>
<td>SRI</td>
<td>D2, H1</td>
<td>D3</td>
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<tr>
<td>D - 1,2,3,4</td>
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<td>α1</td>
<td>5HT 1A/1C</td>
<td>D2/D3</td>
<td>α1</td>
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<tr>
<td>α1</td>
<td>M2</td>
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<td>2D6; 1A2</td>
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<td>2D6</td>
<td>3A4, aldehyde oxidase</td>
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<td>QTc 6-10 msec</td>
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<td>&lt;Clearance: Ris, Fluox</td>
<td>&gt;Clearance: Smoking</td>
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</table>
The Newest Kids on the Block: Asenapine (Saphris)

- Approved in 2009 for acute RX of both SCZ, manic, mixed episodes BPD
- Sublingual-5mg BID
- Somnolence most frequent side effect
- Little weight gain
- Mild EPS
- Very mild akathisia
- Lipid neutral
- Favorable prolactin profile
- May be helpful in negative symptoms

2009 Product Information on file, Merck Pharmaceuticals
The Newest Kids on the Block: Iloperidone (Fanapt)

- Approved in 2009 for RX of SCZ
- 12mg BID—titration required
- Common SE: dizziness, headache, pulse increases related to orthostatic changes (alpha 1) retrograde ejaculation
- Some nausea and dry mouth, despite weak affinity for M1 receptors
- No EPS or akathisia
- Mild weight gain—modest glucose increase
- Lipid neutral
- QTC prolongation of 9ms

NE (α_{2C}), D_{2A} and D_{3}, 5-HT_{1A} and 5-HT_{6}

2009 Product Information on file, Novartis Pharmaceuticals
The Newest Kids on the Block: Lurasidone (Latuda)

- Approved in October 2010, release February 2011
- 40-80mg—must be taken with at least 350 kcal
- Highly protein bound
- CYP 3A4
- Side effects: akathisia, nausea, somnolence, sedation
- Low rates of parkinsonism
- Minimal effects on weight and lipids
- May improve cognition, mood, and negative symptoms through Dopamine-2, serotonin-2A, serotonin-7, serotonin-1A and noradrenaline-2c receptor antagonist

High affinities for D(2), 5-HT(7), 5-HT(2A), 5-HT(1A), NE alpha(2C)
Minimal-to-no affinity for H(1) M(1)

2010 Product Information on file, Sunovion Pharmaceuticals
Illness Cognition

• A concept described in Levanthal’s self-regulatory mode
• Based on the premise that individuals are active problem solvers who make sense of a threat to their health, such as symptoms or an illness, by developing their own cognitive representation of the threat, which then determines how they will respond.

Illness Perception Questionnaire
http://www.uib.no/ipq/index.html

• Encompasses five major domains that serve to define the nature of a health threat:
  1) identity (the label the individual uses to describe the condition and associated symptoms)
  2) beliefs about the cause(s) of the condition
  3) expectations about illness duration
  4) consequences of the condition (emotionally, socially, physically)
  5) extent to which the illness is amenable to cure and/or control.

Illness Cognition Outcomes

• Helplessness as a way of emphasizing the aversive meaning of the disease/disorder
• Acceptance as a way to diminish the aversive meaning
• Perceived benefits as a way of adding a positive meaning to the disease/disorder

Anosognosia

- Anosognosia, an organic neurological deficit, was first described in 1899 in relation to persons who experienced a cerebrovascular accident with paralysis and had no awareness of the affected side.
- Individuals with schizophrenia often experience anosognosia, a neurological term referring to lack of awareness of illness.
- Unfortunately, many people living with psychiatric disabilities have been erroneously psychologically labeled as lacking in insight, rather than the more accurate neurological term of anosognosia.

Insight

• Ability to see and understand clearly the inner nature of things, esp. by intuition

• A clear understanding of the inner nature of some specific thing
  – Psychology: awareness of one's own mental attitudes and behavior
  – Psychiatry: recognition of one's own mental disorder

• Ability to have a clear, deep and sometimes sudden understanding of a complicated problem or situation

http://www.yourdictionary.com/insight
http://dictionary.cambridge.org/dictionary/british/insight
A patient’s current capacity to evaluate his/her anomalous experiences and atypical interpretations of events.

1. Impairment of ability to be objective about delusional experiences and cognitive distortions
2. Reduced capacity to put these experiences into perspective
3. Unresponsiveness to corrective information from others
4. Overconfidence in delusional judgments

Beck Cognitive Insight Scale

• Measures patients’ capacity for distancing themselves from and re-evaluating anomalous beliefs and misinterpretations
  – 18 items (examples)
    • Other people can understand the cause of my unusual experiences better than I can
    • Even though I feel strongly that I am right, I could be wrong
    • I cannot trust other people’s opinion about my experiences

Putting it All Together....

*How Do We Know Someone is Ready to Engage Cognitively, Emotionally, Interpersonally, and Physically?*

READINESS FOR RECOVERY
Milestones of Adjustment Post-Psychosis (MAPP) Recovery Model

Identifies phases and trajectory of psychological adjustment post-psychosis

1. Cognitive dissonance (6-12 months)
2. Insight (6-12 months)
3. Cognitive constancy (12-24 months)
4. Ordinariness (2+ years)

Or...

From the couch, to the bus depot, to the mall, to school and work!

Cognitive Dissonance: Definition (Festinger, 1957)

• A state of being in which a person experiences conflict and personal distress because of a perceived inconsistency between two beliefs

• Typically one of the beliefs is known and the other is not known or has not been experienced

• The discord between the beliefs results in behaviors that are incongruent with previously held attitudes, values, emotions, or beliefs.
Cognitive Dissonance: Metaphor

On the COUCH

– Spending time recognizing the effect of psychotic symptoms on daily functioning.
– This means the person has to first understand that symptoms were psychosis and not reality.
Cognitive Dissonance: Milestones of Achievement

- Measurable outcomes
  - Consistent reduction in psychotic symptoms resulting in diminution of emotional, interpersonal, cognitive and physiological states

- Dependent on
  - pharmacological efficacy
  - family support

- Duration: **6-12 months**
Insight: Definition

• Recognition that illness symptoms are indeed pathological and have created serious consequences in all aspects of life.

• Ability to understand the origin and progression of symptoms.

• Ability to internalize and verbalize the consequences of the symptoms.

• Overlays cognitive dissonance
Insight:
Metaphor

At the Bus Depot

– Gaining an understanding of the relation of symptoms to actual reality.
– Experimenting with having symptoms and watching how others respond when subjective symptoms occur.
Insight:
Milestones of Achievement

Measurable outcomes

– Ability to master the process of conducting reliable reality checks-- “SORT IT OUT”.
– Demonstrating the ability to ‘get used to it’,
– Cope with life now,
– Re-establish ability to communicate with others.

• Dependent on medication efficacy, family support, and understanding treatment team.
• Duration: 6-18 months.
Cognitive Constancy: Definition

- Change in attitude and beliefs about illness that result in stabilizing the emotional, behavioral, and cognitive incongruencies of psychosis.
- There is stability in all aspects of behavior based on reality-based attitudes and beliefs.
Cognitive Constancy: Metaphor

Able to go to the mall

– Achieving stability in thinking and responding to others
– Forcing oneself to interact with others
Cognitive Constancy: Milestones

• Measurable outcome:
  – Ability to muster the internal grit to begin re-engaging in age-appropriate activities related to work and school.

• Dependent on:
  – A positive initial treatment (FEP) experience
  – Dependable support system
  – Constructive use of time
  – Medication efficacy

• Duration: 1-3 years
Ordinariness: Definition

The ability to consistently and reliably engage in and complete normal activities of daily living that are reflective of pre-psychosis functioning (but not identical).
Ordinariness: Metaphor

Finally back To School or To WORK!

– Performing age appropriate activities of daily living as others do
Ordinariness
Milestones

• Measurable outcome:
  – Successfully enrolled in and completing a desired course of study and/or
  – Successfully sustaining employment for one year

• Dependent on:
  – An absence of cognitive dissonance.
  – Ability to complete age-appropriate activities related to work and school

• Duration: 2+ years
<table>
<thead>
<tr>
<th>Emotional Component</th>
<th>Cognitive Dissonance</th>
<th>Insight</th>
<th>Cognitive Constancy</th>
<th>Ordinariness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Embarrassment</td>
<td>Learning how to cope with life now</td>
<td>Importance of having a positive initial hospital experience</td>
<td>Be able to think about the future</td>
</tr>
<tr>
<td></td>
<td>Fear</td>
<td></td>
<td>Dependable support system</td>
<td>Accomplish life goals</td>
</tr>
<tr>
<td></td>
<td>Frustration</td>
<td></td>
<td>Something to do with my time</td>
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<td></td>
<td>Inability to handle stress</td>
<td></td>
<td>Reassurance/ encouragement</td>
<td>Have my own place to live</td>
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<td></td>
<td>Lost self-confidence</td>
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<td>Treatment environment that feels safe</td>
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<td></td>
<td>Not having too much quiet time</td>
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<td></td>
<td></td>
<td></td>
<td>Being around people</td>
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<td></td>
<td>Having hope</td>
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# Cognitive Component

<table>
<thead>
<tr>
<th>Cognitive Dissonance</th>
<th>Insight</th>
<th>Cognitive Constancy</th>
<th>Ordinariness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion</td>
<td>Trying to figure out own thoughts</td>
<td>Something to distract from the symptoms</td>
<td>Manage symptoms</td>
</tr>
<tr>
<td>Fear of saying something wrong</td>
<td>Conducting own reality checks</td>
<td>Accepting the need for treatment</td>
<td>Finish education</td>
</tr>
<tr>
<td></td>
<td>Getting control of symptoms</td>
<td>Learning I’m not the only one with schizophrenia</td>
<td>Become employed</td>
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<tr>
<td></td>
<td>Recognize limitations</td>
<td>Getting back to what I used to do</td>
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<td></td>
<td>Getting used to it</td>
<td>Think positive</td>
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<td>Being given choices</td>
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## Interpersonal Component

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<th>Insight</th>
<th>Cognitive Constancy</th>
<th>Ordinariness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hard to go out in public</td>
<td>Communicate with others</td>
<td>Have someone listen to me/understand me</td>
<td>Do what other people do</td>
</tr>
<tr>
<td>Hard to be around people</td>
<td></td>
<td>Someone to talk to about me</td>
<td>Confidence in the counselor/therapist</td>
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<tr>
<td></td>
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<td>People need to be honest with reality</td>
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<td><strong>HAVING PEOPLE EXPLAIN THINGS</strong></td>
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<td>Someone to talk to about general things</td>
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<td>Having help available when first get sick</td>
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## Physiological Component

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<th>Insight</th>
<th>Cognitive Constancy</th>
<th>Ordinariness</th>
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</thead>
<tbody>
<tr>
<td>Used drugs and alcohol</td>
<td>Length of time to stabilize from the first episode</td>
<td>Right medication</td>
<td></td>
</tr>
<tr>
<td>Required too much energy</td>
<td></td>
<td>Taking care of the body</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Having a routine</td>
</tr>
</tbody>
</table>
What Does This All Mean for the RN and APRN?

• In order to fully engage in all of the recovery components, the person must at least……..
  – Have adequate cognitive functioning to fully engage with the demands of recovery
  – Experience symptom relief and management at a level that promotes self-confidence and courage to approach the world
  – Have safe housing and economic resources
  – BE IN SAFE, RELIABLE, SUSTAINABLE RELATIONSHIPS WITH PROVIDERS AND SUPPORT PERSONS
What Have We Covered Today?

1. Identify constructs of treatment adherence.
   a) Client/provider goals of recovery
   b) Medication ‘rookie’ vs ‘pro’
   c) Treatment ‘rookie’ vs ‘pro’

2. Discuss the concept of illness cognition.
   a) Cognitive Insight vs Anosognosia
   b) Neurobiological implications for cognition

3. Describe the relationship between cognitive functioning and ability to adhere to a therapeutic treatment plan.
   a) Role of post-psychotic psychological adjustment in the readiness for recovery and adherence
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