50 Shades of Depression

Hilly Rubinsky, Ph.D.
Tina Paul, Psy.D., ABPP
6th Annual Current Concepts in Brain Injury Rehabilitation
November 7, 2015

Objectives:

• To define depression following brain injury and to distinguish between depression and other neuropsychiatric conditions
• Discuss factors which increase the risk for depression post brain injury
• Screening and assessment of depression
• Treatment approaches/the role of the multidisciplinary team
Reality Testing (Perceptual Accuracy)

Depression or not?
Why is assessing for depression following brain injury so important?

• Major depressive disorder (MDD) is the most prevalent psychiatric disorder following TBI and acquired brain injury (Fann et. Al, 2009; Robinson & Spalletta, 2010)
• Shown to have an impact on ADLs, quality of life, mortality, health outcomes, increased use of healthcare services, regardless of injury severity or time since injury (Bombardier, 2010; Gordon et al., 2006, Hart et al., 2011)
• Should be addressed early in rehabilitation
Challenges in assessing and diagnosing depression post-injury

Paraphrased from the British Geriatrics Society (2012)

• The etiology of depression in brain impairment is often multi-factorial.
• Important to understand the reasons why it occurs in order to determine the circumstances in which antidepressants may or may not help.
• Antidepressants may be helpful for depression but are unlikely to be helpful where clinical features of the brain impairment mimic depression.
• “Other emotional disorders associated with brain injury, such as apathy or emotional lability, may give the appearance of depression, even in the absence of a depressive disorder.
• Somatic symptoms which characterize depression in the normal population may occur as a result of hospitalization or from the brain injury itself. This may lead to over-estimation of the degree of depression on standard tests.”

These symptoms may include:

• Loss of energy, appetite and libido
• Altered sleeping habits
• Poor concentration; inability to make decisions, etc.
Understanding the different shades of depression

• **The temporary “blues”** - sadness, shock, grief regarding the loss of one’s abilities

• **Reactive depression** - Bad things happen, resulting in a period of “extreme” sadness and despair. It’s a common response, part of the grieving process, primarily psychological rather than biological. (hint, hint- these reactions do not usually interfere with one’s ability to engage in the recovery/rehab process)
Different shades of depression

Adjustment Disorder with Depressed Mood- (APA, 2013)

Emotional or behavioral symptoms develop in response to the identifiable stressor within 3 months of onset of the stressor, with either or both of the following:

1. Marked distress that is out of proportion to the severity or intensity of the stressor, even when external or cultural factors that might influence symptom severity and presentation are taken into account, and/or
2. Significant impairment in social, occupational, or other areas of functioning.

Adjustment Disorder with Depressed Mood (Continue)

– Doesn’t meet the criteria for another mental disorder and is not merely an exacerbation of a pre-existing mental disorder
– Symptoms do not represent a normal bereavement
– After termination of the stressor (or its consequences), the symptoms persist no longer than an additional 6 months
Depressive Disorder Due to a Medical Condition

- For the purpose of this presentation, depression following a traumatic or acquired brain injury which cannot be ascribed to another mental illness
- Can arise from structural alterations of the brain, patient’s emotional response to the sudden and disabling illness, or a combination of both (Caplan, 2010)
- Symptoms can occur suddenly following injury, weeks, months, or a year

Specify: with depressive features, with major depressive like features, with mixed features (APA, 2013)

Signs and symptoms of depression following brain injury

- Persistent depressed mood
- Persistent feelings of guilt or feeling a burden to one’s family
- Hopelessness, helplessness, worthlessness
- Loss of interest in previous pleasurable activities/anhedonia
- Passive death wishes or active suicidal ideation
- Low frustration tolerance, restlessness, irritability
- Sleep disturbance (insomnia or hypersomnia)
- Appetite disturbance
- Interferes with your social, occupational, or other areas of functioning.
More shades of depression

- Cyclothymic Disorder
- Atypical Depression
- Seasonal Affective Disorder (SAD)
- Post-partum Depression
- Premenstrual Dysphoric Disorder
- Substance/ Medication-Induced Depressive Disorder
- Disruptive Mood Dysregulation Disorder (DMDD)
- Bereavement
- Bipolar Disorder

One might think it’s depression, but in fact, it is...

- Apathy
- Catastrophic reaction
- Pseudobulbar affect
- Abulia (particularly with frontal lobe injury)
- Aprosodic speech (i.e., lacking rhythm and “melody,” non-inflected) may be mistakenly viewed as depressed because they “sound sad,” even if words/behaviors do not conform to that diagnosis
- Behavioral disturbances due to the brain injury
- General physical slowness
- Disorders of facial expression
Depressed or Happy?

The million small victories Institute.
UPMC Rehabilitation Institute

Depressed or Happy?

The million small victories Institute.
UPMC Rehabilitation Institute
Risk factors for depression following brain injury

• Psychosocial factors (e.g., h/o substance use)
• Age
• Gender
• Prior h/o mental/behavioral health disorder
• Cultural factors?

Insight/Awareness: Be careful what you ask for!

• Strong relationship between degree of insight/awareness and potential for depressed mood
Screening and diagnosing depression following brain injury

• Clinical evaluation of the patient
• When appropriate, use of screening measures
• Behavioral observation
• Input from the various team members, family
• Most diagnostic instruments were not constructed for the assessment of traumatic or acquired brain injury patients

Screening tools

• The Patient Health Questionnaire-9 (PHQ-9)
• Hospital Anxiety and Depression Questionnaire (HADS)
• Geriatric Depression Scale (GDS)
• Stroke Aphasic Depression Questionnaire
• Center for Epidemiologic Studies Depression (CES-D)
• The Yale Question
Screening methods for depression: The “Yale Question”*

“Do you often feel sad or depressed?”

1) Requires intact comprehension and reliable “Yes/No” responses.

2) Two different components: A) Can be sad about the loss but not depressed; and B) Need to compare to the pt’s normal mood state.

3) Does not provide a sensitive measure for assessing benefits of treatment (i.e., partial improvement).

*From the British Geriatric Society

Center for the Epidemiologic Studies Depression (CES-D)

During the past week: (Rarely, Some, Occasionally, Most)

1. “I was bothered by things that usually don’t bother me.”
5. “I had trouble keeping my mind on what I was doing.”
6. “I felt depressed”
8. “I felt hopeful about the future”
11. “My sleep was restless”
14. “I felt lonely”
17. “I had crying spells”
20. “I could not get going”
The Patient Health Questionnaire-9 (PHQ-9)

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep, or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself— that you are a failure or you let your family down
7. Trouble concentrating
8. Moving or speaking slowly, or being restless
9. Thoughts you would be better off dead

What screening tools tell us and what they do not

- Screening instruments are beneficial for assessing gradations of symptoms over time
- Do not distinguish between depression and other neuropsychiatric conditions associated with brain injury that may give the appearance of depression
- Do not include input from caregivers
Treatments

Most treatment studies have demonstrated significant improvements in depressive symptoms, but not always in complete remission.

Non-Pharmacological Treatments
Who is it most appropriate for?

Appropriate and most researched on patients with mild to no cognitive impairment

Why? Cognitive reserve and capacity needed in order to engage in the “talk therapy”

Motivational Interviewing (MI) (Watkins et al., 2011)

• A talk-based therapy applied to many health problems requiring behavior change, but could also support adjustment
• Therapist sets the agenda
• Talk about adjustment to stroke, adopt an empathic approach, listen to what the patient is saying, summarize what has been said, reflect this back to check understanding and let the patient know they have been heard
• Clarify patients’ personal, realistic goals for recovery, perceived barriers to attaining them
MI (continue)

• By working through their dilemmas and ambivalence, and through supporting and reinforcing optimism and self-efficacy, therapist enable patients to identify their own solutions
• Shown to be effective during the early recovery process (first four weeks following acquired brain injury diagnosis) to improve mood and reduce mortality rate

Cognitive Behavioral Therapies (CBT)

• Remains an area for more research, but has potential and are the most promising and widely accepted in rehabilitation psychology (Elliott & Jackson, 2005)
• Must be tailored to the individual, to meet the needs and problems perceived by the individual
Other therapies

- Family or couples therapy
- Group therapy or support group
- Exercise therapy
- Mindfulness therapies
- Problem Solving Therapy

Tips on how to respond to emotional distress (Barton, 2012)

1. Listen to the patient, using verbal and nonverbal methods
2. Let the patient know that you have heard what he/she is saying and that you understand (reflective listening). If you don’t understand, let them know.
3. Try to concentrate on what the patient is trying to communicate to you. Focus on how the patient is behaving, as well as what he/she is saying
Tips (continued)

4. Remember, if a patient is distressed or crying, acknowledge the distress, do not avoid it. Sometimes, the last thing people want to hear is, “Everything will be alright.” Of course, people want reassurance, but they also want their distress acknowledged and validated.

5. Be mindful of nonverbal communication you display, eye contact, open body posture, so the patient knows that you are interested in what he/she is communicating to you.

Improving one’s quality of life

• Offer ways to increase sense of autonomy
• Social/family support (church community, day program, club)
Common antidepressants used on our units

• Fluxoxetine (Prozac)
• Remeron
• Celexa
• Zoloft
• Effexor
• Lexapro
• Amitriptyline (Elavil)

Common side effects of antidepressants

• Headaches
• Nausea
• Dry Mouth
• Decreased Libido
• Sedation
• Appetite Loss
• Appetite Increase with Weight Gain
• Disruptive Sleep
Selective Serotonin Reuptake Inhibitors (SSRIs)

• Citalopram (Celexa)
• Escitalopram (Lexapro, Cipralex)
• Paroxetine (Paxil, Seroxat)
• Fluoxetine (Prozac)
• Fluvoxamine (Luvox)
• Sertraline (Zoloft, Lustral)

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

• Desvenlafaxine (Pristiq)
• Duloxetine (Cymbalta)
• Levomilnacipran (Fetzima)
• Milnacipran (Ixel, Savella)
• Tofenacin (Elamol, Tofacine)
• Venlafaxine (Effexor)
Serotonin Modulators and Stimulators (SMSs)

- **Vilazodone** (Viibryd)
- **Vortioxetine** (Brintellix)
- These drugs act as serotonin reuptake inhibitors and agonize/antagonize various serotonin receptors.

Serotonin Antagonists and Reuptake Inhibitors (SARIs)

- **Etoperidone** (Axiomin, Etonin)
- **Nefazodone** (Nefadar, Serzone) – withdrawn/discontinued in many countries
- **Trazodone** (Desyrel)
- These drugs act as antagonists of various serotonin receptors and as weak monoamine reuptake inhibitors.
Norepinephrine Reuptake Inhibitors (NRIs)

- **Reboxetine** (Edronax)
- **Viloxazine** (Vivalan)
- **Atomoxetine** (Strattera) is also sometimes used as an antidepressant, but is not specifically approved for this purpose

Tricyclic Antidepressants (TCAs)

- **Amitriptyline** (Elavil, Endep)
- **Amitriptyline Oxide** (Amioxid, Ambivalon, Equilibrin)
- **Clomipramine** (Anafranil)
- **Desipramine** (Norpramin, Pertofrane)
- **Dibenzepin** (Noveril, Victoril)
- **Dosulepin** (Prothiaden)
- **Doxepin** (Adapin, Sinequan)
- **Imipramine** (Tofranil)
- **Lofepramine** (Lomont, Gamanil)
- **Melitracen** (Dixeran, Melixeran, Trausabun)
- **Nitroxazepine** (Sintamil)
- **Nortriptyline** (Pamelor, Aventyl)
- **Noxiptiline** (Agedal, Eltronon, Nogedal)
- **Pipofezine** (Azafen/Azaphen)
- **Protriptyline** (Vivactil)
- **Trimipramine** (Surmontil)
- **Opipramol** (Insidon) – **sigma receptor agonist**
- **Tianeptine** (Stablon) – unknown/unclear mechanism of action
Tetracyclic Antidepressants (TeCAs)

- **Amoxapine** (Asendin)
- **Maprotiline** (Ludiomil)
- **Mianserin** (Bolvidon, Norval, Tolvon)
- **Mirtazapine** (Remeron)
- **Setiptiline** (Tecipul)

Mianserin, mirtazapine, and setiptiline are also sometimes described as **noradrenergic and specific serotonergic antidepressants** (NaSSAs)

Monoamine Oxidase Inhibitors (MAOIs)

- **Isocarboxazid** (Marplan)
- **Phenelzine** (Nardil)
- **Tranylcypromine** (Parnate)
- **Selective for MAO-B**
- **Selegiline** (Eldepryl, Zelapar, Emsam)
- **Selective for MAO-A**
- **Metralindole** (Inkazan)
- **Moclobemide** (Aurorix, Manerix)
- **Pirlindole** (Pirazidol)
- **Toloxatone** (Humoryl)
Atypical Antipsychotics

- **Amisulpride** (Solian) – specifically approved as a monotherapy for dysthymia
- **Lurasidone** (Latuda) – specifically approved as a monotherapy for depressive episodes in bipolar disorder
- **Quetiapine** (Seroquel) – specifically approved as a monotherapy for depressive episodes in bipolar disorder

Marketed

- **Agomelatine** (Valdoxan) – 5-HT<sub>2C</sub> receptor antagonist and MT<sub>1</sub> and MT<sub>2</sub> receptor agonist – sometimes described as a norepinephrine-dopamine disinhibitor (NDDI)
- **Bupropion** (Wellbutrin) – NRI and non-competitive antagonist of various neuronal nACh receptors
- **Ketamine** (Ketalar) – primarily a non-competitive NMDA receptor antagonist – not specifically approved for depression (used off-label)
- **Tandospirone** (Sediel) – 5-HT<sub>1A</sub> receptor partial agonist
- **Teniloxazine** (Lucelan, Metatone) – NRI and 5-HT<sub>2A</sub> receptor antagonist
Over-the-counter

- The following antidepressants are available both with a prescription and over-the-counter:
- Ademetionine [S-Adenosyl-L-methionine (SAMe)] (Heptral, Transmetil, Samyl) – cofactor in monoamine neurotransmitter biosynthesis
- Hypericum perforatum [St. John's Wort (SJW)] (Jarsin, Kira, Movina) – TRPC6 activator, and various other actions
- Oxitriptan [5-Hydroxytryptophan (5-HTP)] (Cincofarm, Levothym, Triptum) – precursor in serotonin biosynthesis
- Tryptophan (Tryptan, Optimax, Aminomine) – precursor in serotonin biosynthesis

Adjunctive Treatments
Atypical Antipsychotics

- Aripiprazole (Abilify) – specifically approved as an adjunct for major depressive disorder
- Brexpiprazole (Rexulti) – specifically approved as an adjunct for major depressive disorder
- Lurasidone (Latuda) – specifically approved as an adjunct for depressive episodes in bipolar disorder
- Olanzapine (Zyprexa) – specifically approved as an adjunct for major depressive disorder
- Quetiapine (Seroquel) – approved as an adjunct for both major depressive disorder and depressive episodes in bipolar disorder
Adjunctive Treatments

Others

- **Buspirone** (BuSpar) – 5-HT$_{1A}$ receptor partial agonist – not specifically approved for depression (used off-label)
- **Lithium** (Eskalith, Lithobid) – mood stabilizer (exact mechanism of action unknown) – not specifically approved for depression (used off-label)
- **Thyroxine** ($T_4$) – thyroid hormone (THR agonist) – not specifically approved for depression (used off-label)
- **Triiodothyronine** ($T_3$) – thyroid hormone (THR agonist) – not specifically approved for depression (used off-label)

Combination Products

- **Amitriptyline/perphenazine** (Etafron) – TCA and typical antipsychotic combination
- **Flupentixol/melitracen** (Deanxit) – TCA and typical antipsychotic combination
- **Olanzapine/fluoxetine** (Symbyax) – SSRI and atypical antipsychotic combination – specifically approved as a monotherapy for depressive episodes in bipolar disorder
Currently in clinical trials (Investigational)

- ALKS-5461 (buprenorphine/samidorphan) – κ-opioid receptor antagonist
- AV-101 – NMDA receptor glycine site antagonist
- Basimglurant (RG7090) – mGlu₆ receptor negative allosteric modulator
- CERC-301 (MK-0657) – NMDA receptor subunit 2B (NR2B) antagonist
- CERC-501 (LY-2456302) – κ-opioid receptor antagonist
- Esketamine – non-competitive NMDA receptor antagonist
- LY-2940094 – nociceptin receptor antagonist
- NRX-1074 – NMDA receptor glycine site partial agonist
- NSI-189 – hippocampal neurotrophin (exact mechanism of action unknown)
- Rapastinel (GLYX-13) – NMDA receptor glycine site partial agonist
- RO4491533 – mGlu₅ and mGlu₃ receptor negative allosteric modulator
- Tramadol (ETS6103/Viotra) – μ-opioid receptor agonist, δ- and κ-opioid receptor ligand, serotonin releasing agent (SRA), NRI, 5-HT₂C receptor antagonist, NMDAR antagonist, αᵥ nAChR antagonist, M₁ and M₃ receptor antagonist, and TRPV1 agonist

Questions?