Mood Disorders I and II
2/12/19

Materials

- The PP follows the handout but is designed to provide a broad understanding
- The handout is sufficient to do well in this course and on national exams
- For further in depth information consult Up-To-Date or DSM5: both available online through the library
- Any questions regarding this material – contact me at RALPH.ORLAND@va.gov

Objectives – of this PP

- Summarize the main symptoms of mood disorders characterized as mental illnesses
- Distinguish between Major Depression and Bipolar Disorders
- Appreciate the vastly different clinical presentations of these illnesses
- Become aware of the different underlying pathophysiology of mood disorders
- Recognize the prevalence and warning signs of suicide
Why Study Major Depression?

- Common – 8–10% of men; 15–20% of women – lifetime; 1 year prevalence 6% – 18 million Americans
- Incidence and prevalence are both rising
- 2nd leading cause of worldwide disability by 2020

Cost in US is 100 billion dollars per year (2012)

Why study Depression?

- Treatable if someone seeks help (only 50%)
- Adverse effects on others around you – consumes much emotional and economic resources
- Suicide/suicide attempts are a major health issue both because of the medical care and psychological scars

DSM-5 Criteria for Major Depression

Five or more of the following nine must be present for two weeks and represent a change from previous functioning. The five symptoms must include depressed mood and/or anhedonia.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report or observation by others (in children and adolescents, can be irritable mood).
(2) Markedly diminished interest or pleasure in all, or almost all activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).

(3) Significant weight loss when not dieting or weight gain or increased or decreased appetite nearly every day.

(4) Insomnia or hypersomnia nearly every day.

(5) Psychomotor agitation or retardation (Observable by others).

(6) Fatigue or loss of energy nearly every day.

(7) Feelings of worthlessness or excessive/inappropriate guilt.

(8) Diminished ability to think or concentrate—or indecisiveness.

(9) Thoughts of death or suicide.

Causes significant impairment or distress in social, occupational, or other functioning

Note—These cannot be due to a general medical condition or the direct physiological effects of a substance or medication
Many students use pneumonic Sig. E. Caps to remember the above 9 criteria.

- S(leep)
- I(nterest)
- G(uilt)
- E(nergy)
- C(oncentration)
- A(ppetite)
- P(sychomotor agitation or retardation)
- S(uicidal thoughts)

Video

- 31 y/o divorced professional woman – abusive ex-husband, raising daughter as a single mom
- What depressive signs and symptoms is she showing?
- Does she meet criteria for Major Depression?
- Begin to think, what would you do to treat her? – Medicines? Therapy? Exercise?
Depression Risk Factors
- Women 2:1 men – ratio 1:1 after menopause
- Peak age onset 20–40 – decreasing with time
  - second peak smaller peak >65
- Alcoholism often found in families

Risk Factors continued
- Single, divorced, widowed > married
- Income, profession, religion, geography – minimal impact
- Culture – lower in AA men; Asians; higher in Hispanic females; American Indians
- Major childhood traumas – loss, neglect, abuse

Risks continued
- Onset of illness usually after a series of negative life events
  - or Catastrophic events – deaths, losses, medical illness, etc.
- 50% 1 episode; if 2 episodes 70% relapse; if 3 episodes 90% relapse – chronic reoccurring illness in most
- Triggers to relapse are less over time
How does Major Depression Develop?
- Genetic predisposition
- Poor coping strategies secondary to past (lack of resiliency)
- Triggering events
- Change in brain process and conceptualization
- Inability to return to normal – difficulty in social connections, exercise, new learning

A Neurodegenerative Brain Disorder
- Closest biological marker is chronically elevated cortisol (chronic stress) – greater neurodegeneration and less neurogenesis
- Many other potential deficits and excesses may be occurring particularly inflammation
- The longer the depression is untreated the greater the chronicity of illness and evidence of physiological brain changes
Theories of Major Depression

- Monoamine theory
- Inflammatory theory
- Structural theory
- Network hypothesis

All of these are further explored in your handouts. All are hypotheses.

Monoamine hypotheses of depression

- Abnormalities within the monoamine systems causative of depression.

The monoamine systems:
  - Serotonin
  - Norepinephrine
  - Dopamine

Traditionally what has been taught for 50 years – based on antidepressants actions and response but much too simple to explain this complex, heterogeneous disorder.

Serotonin tracts
Different select brain areas especially the amygdala, dorsal prefrontal cortex, and the hippocampus are either structurally aberrant or the tracts between these areas are abnormal. Depression will only improve if neurogenesis can occur in those tracts to return the interaction and perceptions to normal. Abnormalities can be seen on various types of Neuroimaging.

Network hypothesis
- Different select brain areas especially the amygdala, dorsal prefrontal cortex, and the hippocampus are either structurally aberrant or the tracts between these areas are abnormal.
- Depression will only improve if neurogenesis can occur in those tracts to return the interaction and perceptions to normal.
- Abnormalities can be seen on various types of Neuroimaging.

PET scans and other neuroimaging show major changes.
Untreated/Undertreated Depression leads to:
- More Major Depressive episodes
- Other Psychiatric co-morbidity – 60% of the time something is found
- Cardiac events – CAD (cytokines – inflammation)
- Neurological events – strokes, seizures, Parkinsonism, Alzheimers

Other etiologies
- Psychological – wealth of knowledge and theories (see handout for details)
  - Aggression turned inward (Abraham)
  - Object loss (Freud and Bowlby)
  - Cognitive distortions (Beck)
  - Self-esteem (Bibring)
- Environmental – poverty, deaths, wars, oppression, learned helplessness, infectious diseases, medical conditions, etc
- These can explain why a person feels depressed but does it lead to MDD episode?
Major Depression is far from a homogenous entity that responds to one approach. For the best outcome, one needs to understand the patient and all of the variables effecting their presentation— their personal narrative. Where do you put the emphasis for treatment? — based on a combination of your understanding and their conception of their illness. Biological, psychological, and/or environmental or social.

Brittany is a 25 y/o white single female with a history of depression going back to age 16. She has clear episodes of depression lasting 6–8 months, but even in between has never felt normal except for brief periods. She has struggled through college enough to get into law school. Unfortunately her symptoms returned with the rigors of law school and she dropped out. She now works as a teacher’s aide, but is hoping to enter graduate school for English. She is fatigued, irritable, has a tough time concentration and has initial insomnia.

She lives with her parents and younger sister who has anorexia. Her father has been diagnosed as Bipolar and her mother has been treated for depression with antidepressants. The father is often in and out of work creating continued financial hardship. She views the world as critically and feels like she has been a failure. Until recently she has been reluctant to stick with therapy because it does no good. She has been tried on over 20 combinations of medicines from all psychiatric classes. Recently she has shown interest in a boyfriend and this has brightened her mood.

Where should the treatment emphasis be? Choose your camp?

1. Biological – medicines as the primary intervention
2. Psychological – therapy to address concerns and develop new cognitive coping strategies
3. Social/environmental – work to change her behaviors or her environment so that the depression symptoms will lift
### Conditions which may cause or mimic major depression (cont.):

**Medications—**
- Corticosteroids
- Oral contraceptives
- Antipsychotics
- Immunosuppressives
- Interferons
- Reserpine
- Isotretinoin
- Propranolol/B-Blockers

### Conditions which may cause or mimic major depression:

**Infectious:**
- Mononucleosis
- Tertiary syphilis
- Toxoplasmosis
- Influenza
- Viral hepatitis
- HIV

### Conditions which may cause or mimic major depression (Cont.):

**Endocrine—**
- Hyper or hypoparathyroidism
- Hyper or hypoadrenocortical function (Cushing’s and Addison’s)
- Hyper or hypothyroidism
- Diabetes

**Metabolic/nutritional—**
- Uremia, pellagra, anemia
### Conditions which may cause or mimic major depression (Cont.):

- **Neurologic**
  - Frontotemporal dementia
  - Parkinson's
  - Huntington's
  - Subdural hematoma
  - Temporal lobe epilepsy
  - Strokes
  - MS
  - Head trauma

### Conditions which may cause or mimic major depression (cont.):

- **Neoplasms**
  - Abdominal malignancies (particularly pancreatic CA)
  - Brain tumors
  - Lymphomas

**Substances** – especially alcohol, heroin, marijuana or many prescribed psychotropics: benzodiazepines, opiates, antipsychotics may mimic depression. These are Substance/Medication Induced Depressive Disorder

### A good medical work-up

- History, physical, labs
- Pure medical disorders have many other physical signs and symptoms
- Depression and the medical illness may coexist – can’t just treat one alone
- Hoof beats usually indicate Horses not Zebras
Other disorders and variants on Major Depression
- Important to identify other disorders as the treatment and prognosis may be different
- In some cases removing the offending agent or condition (substance – Etoh, disease state – hypothyroidism) may make big difference in outcomes
- Diagnosis ultimately is never as important as treating the patient for their unique circumstances

Persistent Depressive Disorder
- Depressed mood for most of the day on most days for 2 years. (One year and mood can be irritable if an adolescent).
  - And at least two of the following:
    - 1. Poor appetite or overeating
    - 2. Insomnia/Hypersomnia
    - 3. Low energy/fatigue
    - 4. Low self-esteem
    - 5. Poor concentration or difficulty with decisions
    - 6. Feelings of hopelessness
  - Has never been free of depressive symptoms for more than 2 months
  - Can have both Major Depression along with this condition

PMDD
Premenstrual Dysphoric Disorder is now a diagnosable in DSM 5 – see the handout for details
MDD specifiers – Melancholia
- Major Depression but also
  - lack of reactivity of any pleasure situation
  - early AM mood worse
  - early morning awakening
  - marked agitation or retardation
  - excessive guilt
- Use of antidepressants essential
- DST usually positive – clear HPA axis dysfunction

MDD specifier – Atypical
- oversleeping
- overeating
- leaden paralysis
- interpersonal sensitivity
- mood reactivity – leading to roller-coaster type of mood

MDD specifier – Psychotic
- MDD features but also presence of psychotic element
- Nihilism( there is no future – the world will end)
- delusions – “I am bad”, “I have caused others to be poisoned” “I have cancer in my bowel– I am rotting from the inside”
- hallucinations – Usually negative and auditory
Psychotic cont.

- Use of antipsychotic or ECT essential
- newer agents (SSRI’S) may not work as well
- Don’t confuse with schizophrenia
- Be careful to rule out Bipolar
- 10% of all Major Depressions

MDD - specifier - Seasonal

- 20% of people at this latitude have a seasonal mood fluctuation
- Sxs similar to Atypical depression but patients tend to become hyper in the summer
- worst part of year is October – February
- Light therapy of some help–50%
- antidepressants just as effective

MDD versus Bereavement

- Often MDD is precipitated by bereavement
- If there is enough criteria for MDD then the person should be given that diagnosis regardless if there has been a recent loss
- Feeling empty, grieving, sadness, insomnia, irritability coming in waves are all normal
- Stronger signals: guilt about life areas outside of the death, worthlessness psychomotor retardation, sustained suicidal ideation, prolonged functional impairment indicate a more severe condition
Stages of Bereavement

- Paula Clayton’s work on loss and grief
  - Numbness – hours to days – seldom weeks
  - Depression – few weeks to < 1 year – exacerbations on holidays, b-days, or other memorable events (insomnia, restlessness, irritability)
  - Some days good; some bad
  - Recovery – usually < 6 months – accept the loss and return to a pre-morbid level of functioning which might include previous or new roles
  Most people start to feel better 6 – 10 weeks after the death

Do you treat uncomplicated bereavement?

- Most people are resilient and do fine
- If concerned about MDD consider: past history, intensity, duration, pervasiveness of symptoms
- Don’t wait and normalize – longer the delay to treat the depression the worse the prognosis

DSM 5: Adjustment Disorder

- Development of clinically significant emotional or behavioral disturbances in response to an identifiable stressor
- Within 3 months of stressor
- Does not meet criteria for a more significant mental disorder
- Once the stressor is removed the symptoms disappear within 6 months
- Can be depressed, anxious, or behavioral
Other uncommon presentations of MDD; Agitated/Anxious
- Diagnosis often missed because of absence of sadness
- High risk of acting out and suicidal or homicidal potential
- Seen often in Elderly and Adolescence
- Watch for substance induced

Elderly Depression
- New incident rate increases past age 65
- Suicide rate highest in elderly males
- Highest growing population
- Misconception that part of aging or not treatable
- Less likely to seek out help
- Response rate to intervention is just as good as adults

Elderly Depression cont.
- Masked depression
- Agitation and irritability more common than sadness
- Somatic preoccupation to point of delusional common
- Cognitive changes often confused with dementia (pseudodementia – see handout for differentiation)
Teenage Depression
- high risk for impulsive actions
- often missed because of teenage angst misconception
- teenagers unaware of what depression is – they don’t trust adults
- high risk suicide group
- treatment intervention available – more controversial and variable
  - most severe mental illnesses start now

Teenage Depression
- irritability often prominent
- sadness present but hidden by irritability
- Acting out behavior
- Impulsivity/recklessness
- Substance experimentation
- Change in friends, grades, behaviors
- withdrawn

Take a break for a minute
Bipolar Disorders
- One of the most dramatic illnesses in psychiatry (famous and creative)
- Diagnosis is often ignored or missed because of lack of good history taking
- Missing diagnosis leads to morbidity and delay of treatment (average is 5 years)
- Treatments are very helpful if applied

Manic Episode
- Distinct abnormal mood that is elevated, expansive, or irritable for at least 1 week
- Three or more of the following seven (four if the mood is irritable)
  - Inflated self esteem or grandiosity
  - Decreased sleep
  - More talkative than usual or pressured to talk
  - Thoughts are racing
  - Distractible
  - Increase in goal directed activities
  - Reckless behaviors in pleasurable areas - consequences

What does it look like?
- 35 y/o being interviewed by a first year resident
- Pay attention to the signs and symptoms that suggest a Bipolar illness
- Think about the difficulty in conducting such an interview and getting patients to comply with treatment
What was the most prominent symptom that you witnessed?

1. Irritability
2. Grandiose thoughts
3. Reckless behaviors
4. Excessive activities
5. Pressured speech
6. Distractibility

Types of Bipolar

- Bipolar I – 0.6%–0.8% lifetime prevalence
- Bipolar II – 0.5% – 0.8% lifetime prevalence
- Bipolar Spectrum – 4–6% lifetime prevalence (controversial)
- Bipolar secondary to medical conditions or substances
- Men=women; higher socioeconomic, onset late adolescence, early adulthood, strong genetics – monozygotic twin concordance = 65–80%; dizygotic = 10–15%

Distinguishing Bipolar Disorders

- Bipolar I – a manic episode (depressive episode is not needed although usually occurs)
- Bipolar II – hypomanic symptoms – at least 4 days in row; at least 3 symptoms of mania but not severe enough to cause impairment in functioning or hospitalization; no psychosis
- Must have history of Major Depression
- Cyclothymic Disorder – 2 years duration – hypomanic symptoms at times but depression never to point of Major Depression criteria
- A graph may be a good way to visualize it
Bipolar pathophysiology

- Neurodegenerative process even when the mood is stable – evidence of cognitive changes in verbal memory, attention, and executive functioning
- In depression the neuroimaging looks similar to Major Depression but mania involves activation of many areas
- With age there is a cerebral atrophy and the brains look more similar to schizophrenia

Bipolar cellular pathophysiology

- The fact that lithium was such a successful treatment led to many theories but none substantiated
- Use of anticonvulsants leads to theories on calcium or sodium gate abnormalities and stabilization of neuronal pathways
- Some evidence of a specific gene defect associated with chromosome 18q or 22q in linkage studies
- This remains a huge unknown
Course of Bipolar illness
- Only 1/3 recover at 1 year out
- Most Bipolar will gravitate to the depressive end of the spectrum
- Only 50% were working at 3 years after the diagnosis
- Impulsivity, addictions, distractibility leads to high co morbidity and potential suicide
- Medications are essential along with support

Signs that Depression could be Bipolar
- Early age of onset or post-partum onset
- Rapid changes in and out of depression
- Many episodes of depression - non responsive to usual intervention
- Bipolar family history
- Loss of antidepressant efficacy repeatedly
- Depression with many anxious or mixed hyper features - racing, irritable, hostile
- Psychotic features as part of the depression

Let's see what you have learned so far? Typical exam question: What is the diagnosis?
- A 45y/o man is brought to you by his spouse. He has started drinking a bottle of vodka daily since he was passed over for a job promotion 3 weeks ago. He stayed in bed over the weekend. He has no history of psychiatric disorders and no history of alcohol misuse in himself or family. His energy is low, he is sleeping poorly, says he has no interest, has lost 10 lbs and cries when stating “I can’t believe it”. When asked what he will do, he states “I don’t know, but if I don’t go back to work tomorrow, I’ll lose my job and life won’t be worth living”
What is his diagnosis?

1. Bipolar Disorder Type II
2. Adjustment disorder with depressed mood
3. Persistent Depressive Disorder
4. Major Depressive Disorder
5. Substance Induced Depressive Disorder
6. No Psychiatric Disorder—normal life reaction

Suicide

10th leading cause of death in the US
>43,000 people in 2013 in the US
Over 460,000 suicide attempts documented
Devastating action that effects both families of the victim (guilt, anger, loss, shame) but also for the health care providers
Major emphasis in clinical practice to prevent suicide extensive screening for this and mood disorders

Statistics

12.9/100,000 people per year in US
Males – 19.9
Females–5.5
Adolescents – 10.5 (but often impulsive without warning)
Elderly– 17.6 (often after a diagnosis of a terminal disease)
Middle age (45–64)– 18.6 (highest)
Post military– 34.9 –problems with transitions
Statistics

- Presence of a mental disorder >90% of the time
- Bipolar (15x normal) > Schizophrenia > Major Depression
- Anxiety Disorders, Eating Disorders, and Substance Use disorders also high on the list
- Greatest risk of suicide is within the 1st year of diagnosis

Terminology

- Suicide ideation
- Suicide plan or intent
- Suicide attempt
- Completed suicide
- Self harm
- 34% of those with suicide ideation think of plan
- 72% of those with a plan try an attempt
- Ratio of attempts to success 12:1; women try suicide 3:1 over men; men are successful 3:1 over women– firearms– 51%, hanging–25%, poisoning– 17%

Who will attempt suicide?

70% who die decide in last 10 minutes of life

High risk factors
- Past history of suicide attempts
- Psychosis (esp. command hallucinations)
- Has a feasible plan in mind
- High “psychic” anxiety
- Active substance use
- Impulsivity
- Hopelessness
- Lack of support
- Presence of a gun at home
- Significant life event in last 3 months
Prevention

- Explore each person individually for risk analysis - combination of risks and protective measures (support, faith or religion, on medication, having children)
- Always ask about suicidal thoughts and plans
- Use behavioral incidents and appropriate gates to get to this highly sensitive area
- Remove means from the patient and triage the patient to make sure they are safe

After watching this video what is the best course of action

1. Call in a family member and ask them to be responsible for the patient’s safety until the antidepressants begin to work
2. Further explore the nature of the suicide attempt to be absolutely sure that the patient will not attempt suicide
3. Suggest to the patient that she needs to be in the hospital to protect herself from suicide. If she refuses commit her against her will.
4. Send her to the emergency room for further assessment of the Benadryl overdose to be sure that she is medically stable and safe to go home
5. Finish the interview, make sure the gun is out of the house, start an antidepressant, refer her to a therapist, and see her 3 weeks to review her status
6. None of the above

That’s about it – time for?

- Questions
- Good luck

"It is not which disease the patient has which is foremost; It is which patient has the disease"

Sir William Osler