Mood Disorders and Suicide II
Causes of Mood Disorders: Biological

- Familial and Genetic Influences
  - Family Studies
    - Rate of family members having a mood disorder is 2-3x higher if they have a depressed relative than if they do not.
      » But is this because of environment?

  - Twin Studies in part control for environmental confound.
    - Because the disorder is present in identical twins to a much greater extent than in fraternal twins (sharing less genetic material or concordance), this suggest a strong heritability.
    - Bipolar (higher genetic influence)
    - Unipolar (40% women, 20% men): still leaves room for environment (up to 80%)

- Higher concordance with higher severity

- Higher heritability for females
Causes of Mood Disorders: Biological

- Neurotransmitter Systems
  - Serotonin – depression
  - We are more impulsive and have mood swings when serotonin is low, as this regulates DA and norepinephrine.
  - The “permissive” hypothesis (when serotonin levels are low other neurotransmitters are permitted to range more widely, becoming deregulated, and this contributes to mood irregularities including depression).
  - Dopamine - mania
Endocrine System

- “Stress hypothesis”
  - Overactive HPA axis
  - Neurohormones
  - Elevated cortisol
  - Suppressed hippocampal neurogenesis

- Dexamethasone suppression test (DST)
  - Suppresses cortisol secretion in healthy subjects
  - But, not in 50% of patients with DP
    - Adrenal cortex secreted enough cortisol to overwhelm suppressive effects of dexamethasone.
    - But, this is not specific to DP – it also is in anxiety disorder.
Causes of Mood Disorders: Biological

- Sleep and Circadian Rhythms
  - REM sleep (only when depressed—not during period of remission; endophenotype?)
    - Reduced latency
    - Increased intensity
  - Decreased slow wave sleep

- Sleep deprivation effects
  - Improves condition!
Causes of Mood Disorders: Psychological

• Stressful life events
  – Context
  – Meaning
  – Timing

• Recall bias

• Effects of stress
  – Poorer treatment response
  – Delayed remission
  – Trigger for episode or relapse
Causes of Mood Disorders: Psychological

- **Learned Helplessness** (Seligman/Maier)
  - Lack of perceived control

- **Depressive Attributional Style**
  - Internal
  - Stable
  - Global

- Also characterizes anxiety
Causes of Mood Disorders: Biological

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Causes of Mood Disorders: Psychological

- **Sense of hopelessness**
  - Lack of perceived control
  - Will not regain control

- Pessimism
  - Causality?
  - Before or after?
Causes of Mood Disorders: Psychological

- **Negative Cognitive Styles**
  - Cognitive Theory of Depression (Beck)
  - Depressive triad
  - Negative schema
    - Self blame
    - Self evaluation

- Cognitive errors in depression
  - Negative interpretations

- Types of Cognitive Errors
  - **Arbitrary inference**
    - DP individual emphasizes negative rather than positive aspects
  - **Overgeneralization**
    - Teacher makes one comment critical and you assume you are a failure.

People with a negative cognitive style are 12x more likely to later develop depression.
Mood Disorders: Social and Cultural Dimensions

- **Marriage and Interpersonal Relationships**
  - Relationship disruption precedes depression
    - Females (21%)
    - Strongest effects for males 17% is 9x higher than those who stayed married.
    However...
    When ruling out history of DP, it stayed at 14% for men, and dropped to only 5% for women.

- **Martial conflict vs. marital support**
  - Can coexist
    - High conflict + low support is among the worst conditions.

- **Gender differences in causal direction**
  - Men get depressed and this causes withdraw and problems whereas women react to the declining relationship and feel depressed.
Mood Disorders: Social and Cultural Dimensions

• Mood Disorders in Women
  – Prevalence: Females > Males
  – True for all mood disorders (similar to anxiety rates)
    • Except bipolar- evenly divided
Mood Disorders in Women

Gender roles: 70% of depressed individuals are Females

- Perceptions of uncontrollability
- Socialization

Access to resources

Emphasis on relationships
Mood Disorders: Social and Cultural Dimensions

• Social Support
  – Related to depression
  – Following a life event:
    • 10% women with a close friend became depression whereas 37% without a friend did.
  – Lack of support
    • predicts late onset depression
  – Substantial support
    • predicts recovery for depression (not mania)
Treatment: Antidepressant Medications

- **Tricyclics (Tofranil, Elavil)**
  - Frequently used for severe depression
  - “work” for 50-70% of cases
  - Block reuptake/down-regulate
    - Norepinephrine
    - Serotonin
  - 2 to 8 weeks to work
  - Many negative side effects
    - So many that people stop taking it
  - Lethality
Treatment: Antidepressant Medications

- Monoamine Oxidase (MAO) Inhibitors
  - Block MAO - the enzyme that breaks down norepinephrine and serotonin (5HTP)
  - Higher efficacy than TCAs
  - Specifically in atypical DP
  - Fewer side effects
  - Interactions
    - Foods
    - Medicines
Alcoholic beverages - avoid Chianti wine and vermouth. Consumption of red, white, and port wine in quantities less than 120 mL present little risk (Anon, 1989; Da Prada et al, 1988; McCabe, 1986). Beer and ale should also be avoided (McCabe, 1986), however other investigators feel major domestic (US) brands of beer is safe in small quantities (½ cup or less than 120 mL) (Anon, 1989; Da Prada, 1988), but imported beer should not be consumed unless a specific brand is known to be safe. Whiskey and liqueurs such as Drambuie and Chartreuse have caused reactions. Nonalcoholic beverages (alcohol-free beer and wines) may contain tyramine and should be avoided (Anon, 1989; Stockley, 1993).

Banana peels - a single case report implicates a banana as the causative agent, which involved the consumption of whole stewed green banana, including the peel. Ripe banana pulp contains 7 µg/gram of tyramine compared to a peel which contains 65 µg/gram and 700 µg of tyramine and dopamine, respectively (McCabe, 1986).

Bean curd - fermented bean curd, fermented soya bean, soya bean pastes contain a significant amount of tyramine (Anon, 1989).

Broad (fava) bean pods - these beans contain dopa, not tyramine, which is metabolized to dopamine and may cause a pressor reaction and therefore should not be eaten particularly if overripe (McCabe, 1986; Anon, 1989; Brown & Bryant, 1988).

Cheese - tyramine content cannot be predicted based on appearance, flavor, or variety and therefore should be avoided. Cream cheese and cottage cheese have no detectable level of tyramine (McCabe, 1986; Anon, 1989, Brown & Bryant, 1988).

Fish - fresh fish (Anon, 1989; McCabe, 1986) and vacuum-packed pickled fish or caviar contain only small amounts of tyramine and are safe if consumed promptly or refrigerated for short periods; longer storage may be dangerous (Anon, 1989). Smoked, fermented, pickled (Herring) and otherwise aged fish, meat, or any spoiled food may contain high levels of tyramine and should be avoided (Anon, 1989; Brown & Bryant, 1988).

Ginseng - some preparations have resulted in a headache, tremulousness, and manic-like symptoms (Anon, 1989).

Protein extracts - three brands of meat extract contained 95, 206, and 304 µg/gram of tyramine and therefore meat extracts should be avoided (McCabe, 1986). Avoid liquid and powdered protein dietary supplements (Anon, 1989).

Meat, nonfresh or liver - no detectable levels identified in fresh chicken livers; high tyramine content found in spoiled or unfresh livers (McCabe, 1986). Fresh meat is safe, caution suggested in restaurants (Anon, 1989; Da Prada et al, 1988).

Sausage, bologna, pepperoni and salami contain large amounts of tyramine (Anon, 1989; Da Prada et al, 1988; McCabe, 1986). No detectable tyramine levels were identified in country cured ham (McCabe, 1986).

Sauerkraut - tyramine content has varied from 20 to 95 µg/gram and should be avoided (McCabe, 1986).

Shrimp paste - contain a large amount of tyramine (Anon, 1989).

Soups - should be avoided as protein extracts may be present; miso soup is prepared from fermented bean curd and contain tyramine in large amounts and should not be consumed (Anon, 1989).

Yeast, Brewer’s or extracts - yeast extracts (Marmite) which are spread on bread or mixed with water, Brewer’s yeast, or yeast vitamin supplements should not be consumed. Yeast used in baking is safe (Anon, 1989; Da Prada et al, 1988; McCabe, 1986).
Selective Serotonin Reuptake Inhibitors
- Fluoxetine (Prozac)
- First treatment choice
- Block presynaptic reuptake
- No unique risks
  - Suicide or violence
- Delay
- Many negative side effects
  - Sexual dysfunction in 50-75%
- Suicidality debate

New BD law suites!
Multiple antidepressant prescription:
- Some drugs may work for some and not others
- SSRIs help alleviate symptoms in 50% (favorable response) but only “cure” 25% (complete remission)

Other issues
- Efficacy in special populations
  - Children
  - Elderly
  - Expecting mothers
- Preventing relapse
- Maintaining benefits

Antidepressants can also trigger mania
Treatment of Mood Disorders: Lithium

• Most Common Problem: They don’t want to take it because they miss or enjoy the mania.

• Common salt

• Primary treatment for bipolar disorders
  – 50% respond (a significant reduction 50% in mania)
  – May help in prevention of future episodes in over 60% of patients

• Unsure of mechanism of action

• Narrow therapeutic window
  – Too little – ineffective
  – Too much – toxic, lethal
    • Thyroid functioning is lowered (energy down)
Treatment of Mood Disorders: ECT

- **Electroconvulsive Therapy**
  - Brief electrical current – less than 1 second.
  - Temporary seizures
  - 6 to 10 treatments

- **High efficacy**
  - Severe depression in patients who medications don’t work well for

- **Few side effects**

- Relapse is common (60%) so treatment with psychotherapy and SSRIs is also necessary
Psychological Treatment

• Cognitive Therapy 10-20 weekly sessions
  – Logs (incorporate collaboration of patient and therapist)
    • Bring unconscious pervasive patterns to attention
  – Hypothesis testing
  – Identify errors in thinking
  – Correct cognitive errors
  – Substitute more adaptive thoughts
  – Correct negative cognitive schemas

• Behavioral Activation
  – Increased positive events
  – Focus on preventing avoidance of social and environmental cues that produce negative affect or depression and result in avoidance and inactivity. The individual is helped to face the cues/triggers and work through them and the depression they produce by working with the therapist and developing improved coping.
  – As effective or more effective than cognitive approaches (Jacobson et al., 2001. Sona!)
  – Exercise- can help DP symptoms in itself!!!
  – Exercise is better at preventing relapse than Zoloft or combined Zoloft/exercising (Babyak, et al., 2000)
Psychological Treatment

- **Interpersonal Psychotherapy** 15-20 weekly sessions
  - Address interpersonal issues in relationships
    - Role disputes
    - Loss
    - New relationships
    - Social skill deficits
Combined Treatment

- **TADS study (March)!**
- Possible benefits above individual treatments
  - 48% benefit from meds or CBT
  - 73% benefit from combined

- More research is needed
- Benefits of Maintenance treatments
  - e.g. CBT teaches skills to avoid future relapse
Psychological Treatment of Bipolar Disorders

- Management of interpersonal problems
- **Increase medication compliance**
- Interpersonal and Social Rhythm Therapy
  - Helping patients regulate circadian rhythms by teaching to regulate sleep cycles and everyday routines.
- **Family-focused treatment**
  - Family tension and relapse in Bipolar
Treatment of Mood Disorders

Across Cultures

– Similar prevalence among US subcultures
  • Exceptions

– Physical or somatic symptoms

– Treatment
Prevention of Mood Disorders

• Selected interventions
  – Children of divorce
  – Alcoholism in family

• Indicated interventions
  – Pt is already showing mild DP

• Risk for postpartum depression (Zlotnick et al., 2006)

• Preventing relapse
  – (families with one depressed parent) (Beardslee et al, 1996)
Suicide: Statistics

Population specific

Increasing rates
- Adolescents
  - 3rd leading cause of death
  - Rose from 3.6-11.3%
    - 1960-1988
- Elderly

Indices
- Attempts
- Ideations

- Epidemiologist estimate that it is actually 2-3x more common than reported (car accidents/overdose etc)
  - Phillips Traffic study (single car accidents)
Statistics

- Over 30,000 per year
  - 1 in 10,000 people

- More suicides than murders

- Third leading cause of death among teens and Fourth leading cause of death among 9-12 year olds

- 50 attempts for every completed suicide

- 5:1 Male to female completed suicide
  - Believed to be due to the type of attempts
    - In reality, females attempt it 3x more often
Highest suicide rates: Nevada, Montana, Arizona, New Mexico, and Colorado
Lowest suicide rates: New York, New Jersey, Massachusetts

**GUNS**
Most frequent method of completed suicide

More than half the gun deaths in the US

Nearly always lethal

< 10% purchase gun to kill themselves
Risk Factors through 
Psychological Autopsy

• Low serotonin levels
  – SSRI example (somato-dendritic autoreceptor feedback)
• Preexisting disorder
• Alcohol: up to $\frac{1}{2}$ of all suicides are associated!
• Past suicidal behavior
• Shameful/humiliating stressor
• Suicide publicity and media coverage- 9 day window
  – This is serious- 5% of all teenage suicides are due to this
    • Specificity of event/demographic of initial person
    • Permission?
General Risk factors

• Family history (6x increase; Brent et al., 2002)

• Demographic
  - Caucasian (90% of completed suicides)
  - American Indian / Native American

• Psychopathologies (90% of all suicide cases have mental illness)
  - Previous attempts
  - Depression: 10-15% completion
  - Bipolar: up to 50% attempt, 20% completion
  - 60-70% of completed suicides had a mood disorder
  - Substance Use
  - Conduct Disorder / Impulsivity
Biological and Cognitive Risk Factors

- Extremely low serotonin
  - aggression / explosive
  - depression
  - impulsivity

Psychological Pain / Distress
- Illness – especially terminal
- Loss
- Financial difficulty – especially if coupled with loss of hope
- Sexual orientation – esp. if rejection by family

Bullying

Assisted Suicide

Cultural normalization / glorification
- Women in rural China if family difficulties
- WWII Kamikaze pilots
- Islamic terrorists
Individual Intervention / Treatment for Suicide

- Treat underlying mood or substance use disorder
- Ask questions
  - Ideation
    - “I do not think about killing myself”
    - “I think about killing myself, but would not do it”
    - “I want to kill myself”
  - Plan
  - Access to methods
- Safety Contract
  - Available resources
  - Emergency contact
- Hospitalization
Suicide: Treatment

• Importance of assessment
  – Previous attempts
  – Recent events
  – Ideation
  – Plan
  – Means
  – Access

• **Contract**

• Hospitalization
  – Complete or partial

• Problem solving therapy
Future Directions

• Interaction between biology and psychology
  – Biological challenge studies
  – Broader Prevention efforts
  – Induced depression
    • Serotonin and pessimism