



# *HDSA Annual Convention June 2013*

## **Behavior Issues: Irritability and Depression**

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## Huntington's Disease Society of America

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**Peg Nopoulos**

**The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:**

**No relationships to disclose  
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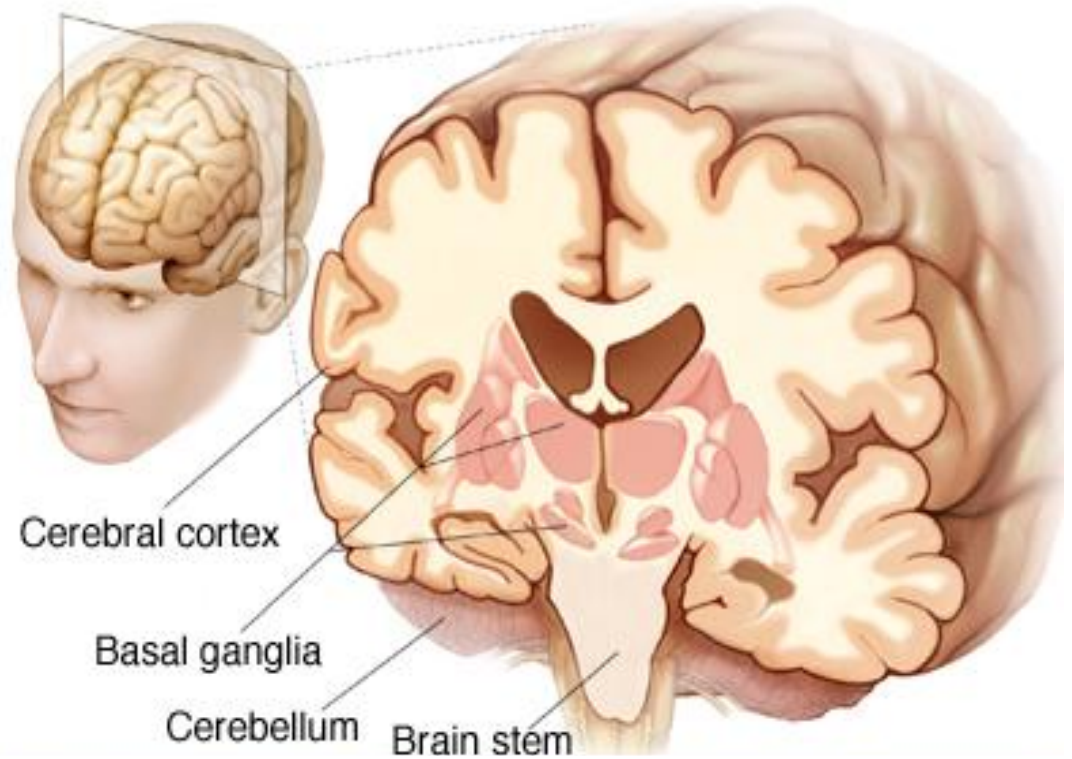
## Outline

- Basic Brain Structure and Function
- Psychiatric / Behavioral Symptoms of HD
  - Depression
  - Irritability
- Treatment

## Outline

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# THE HUMAN BRAIN



# Magnetic Resonance Image (MRI)

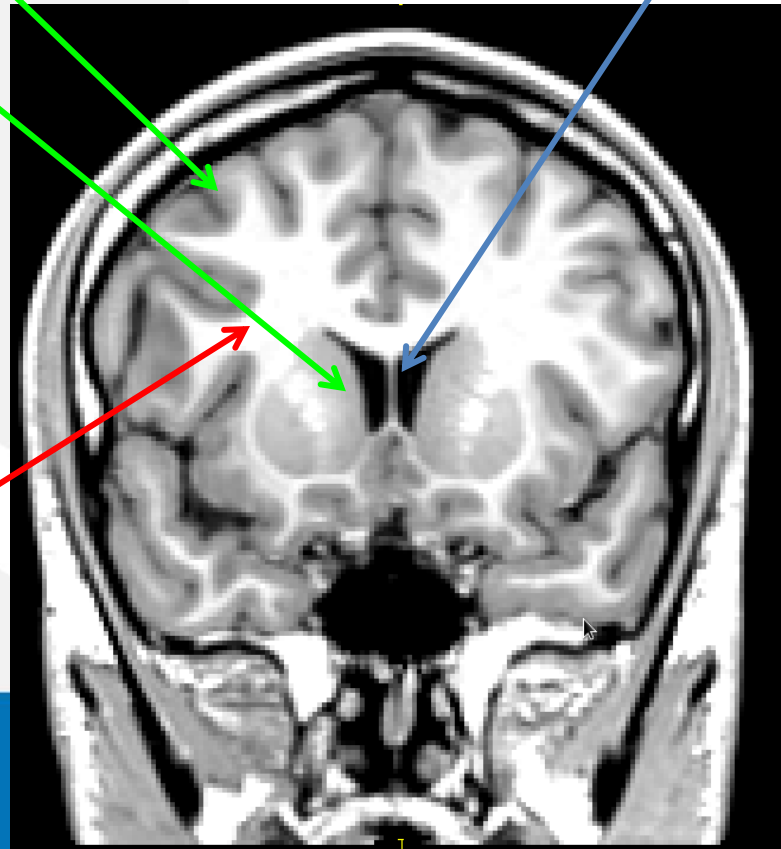
## Gray Matter

Dendrites  
Cell Bodies  
Synapses

**Cerebral spinal fluid (CSF) :**  
surrounds the brain and fills  
internal cavities

## White Matter

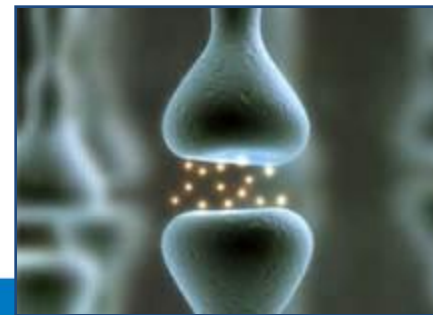
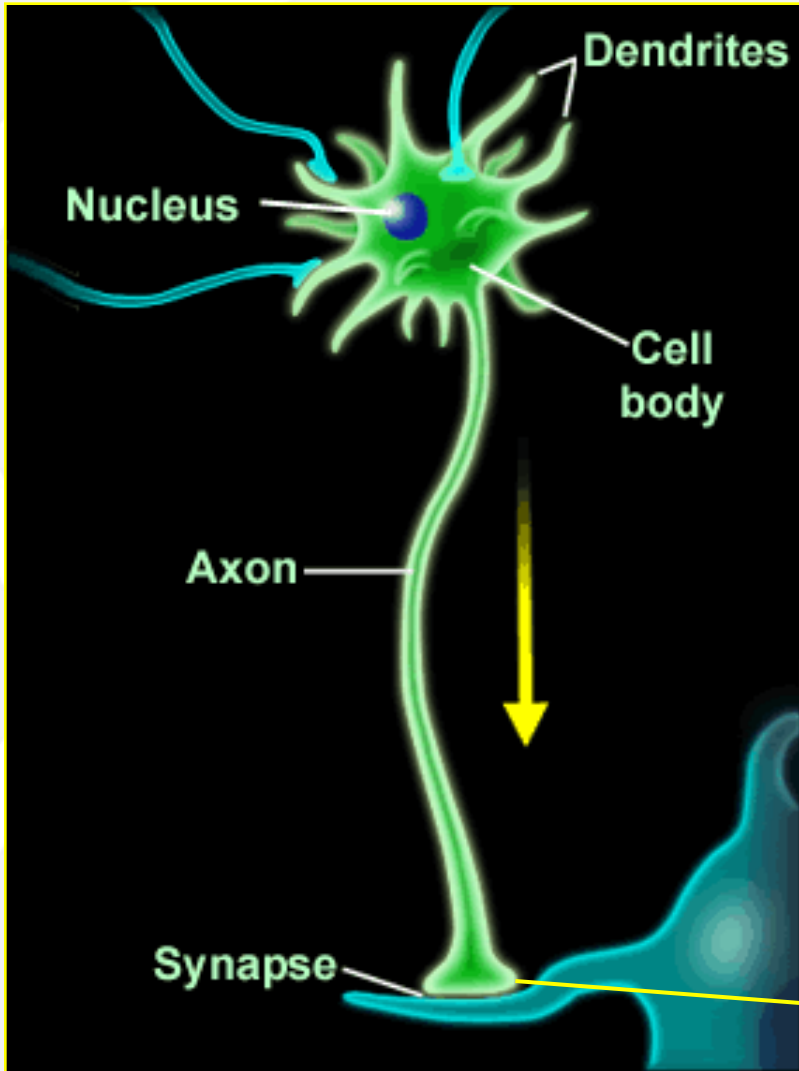
Axons



## Microscopic

Brain Cell = Neuron

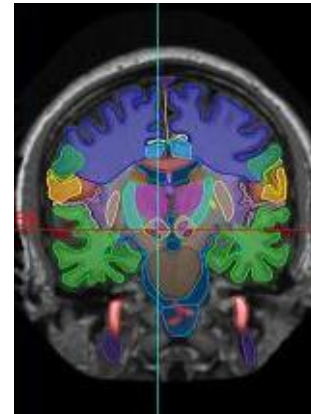
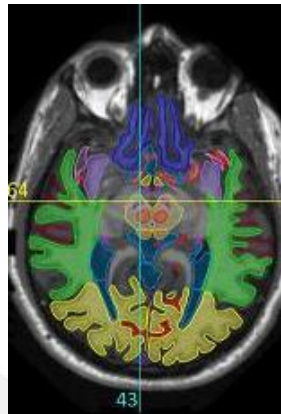
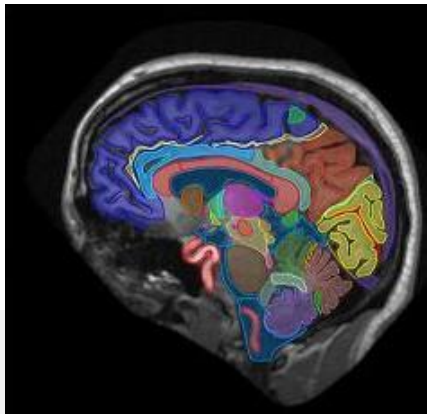
- **Dendrites** – communication with other neurons
- **Cell Body** – where all of the functions happen – metabolism
- **Axon** – sends electrical impulses across long distances (electrical cable)
- **Synapse** – communications between cells through exchange of neurotransmitters (brain chemicals)





## Brain Structure and Function

- The brain has about 86 BILLION neurons
- They work by communicating together in circuits – neurons talking to each other constantly
  - By electrical impulses and neurotransmitters (brain chemicals)
- The brain is divided into specific regions and *each region has a different brain function*
  - Each color represents a different region



# Regions of the Brain – Outside Surface

## Frontal Lobe

- Organization
- Planning
- Reasoning
- Impulse Control
- Attention
- Insight
- Social Skills
- Movement

## Temporal Lobe

- Hearing
- Language Speech
- Memory

## Parietal Lobe

- Visuo-spatial skills
- Sensory (skin senses)



## Occipital Lobe

Vision

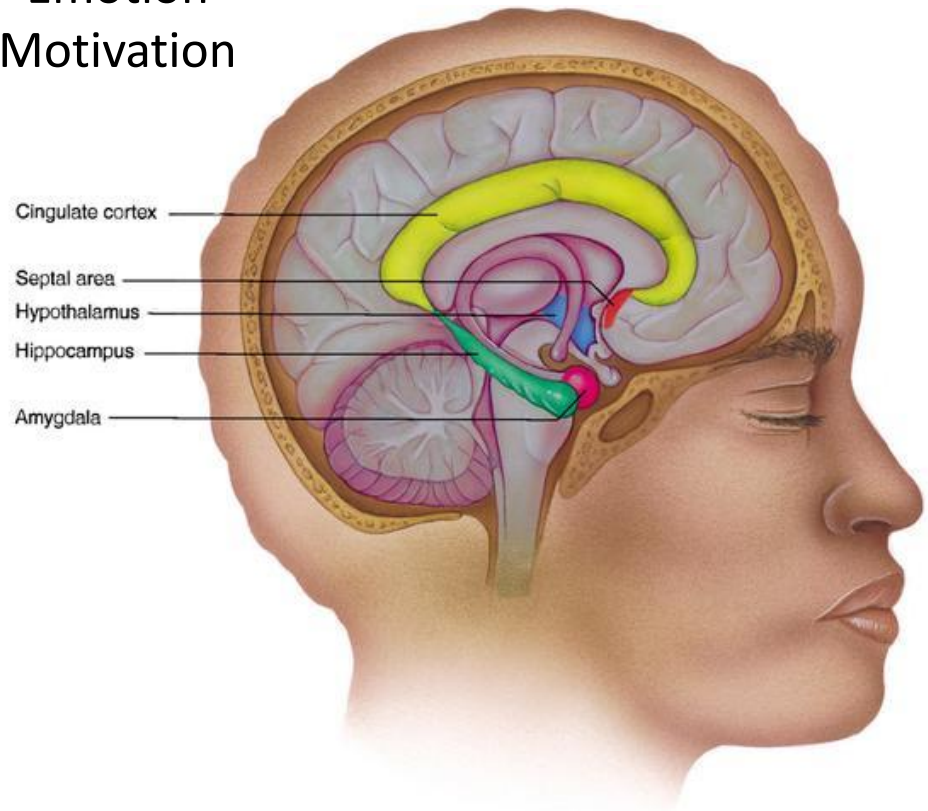
## Cerebellum

Motor coordination

# Regions of the Brain – Inside Surface

## Limbic System

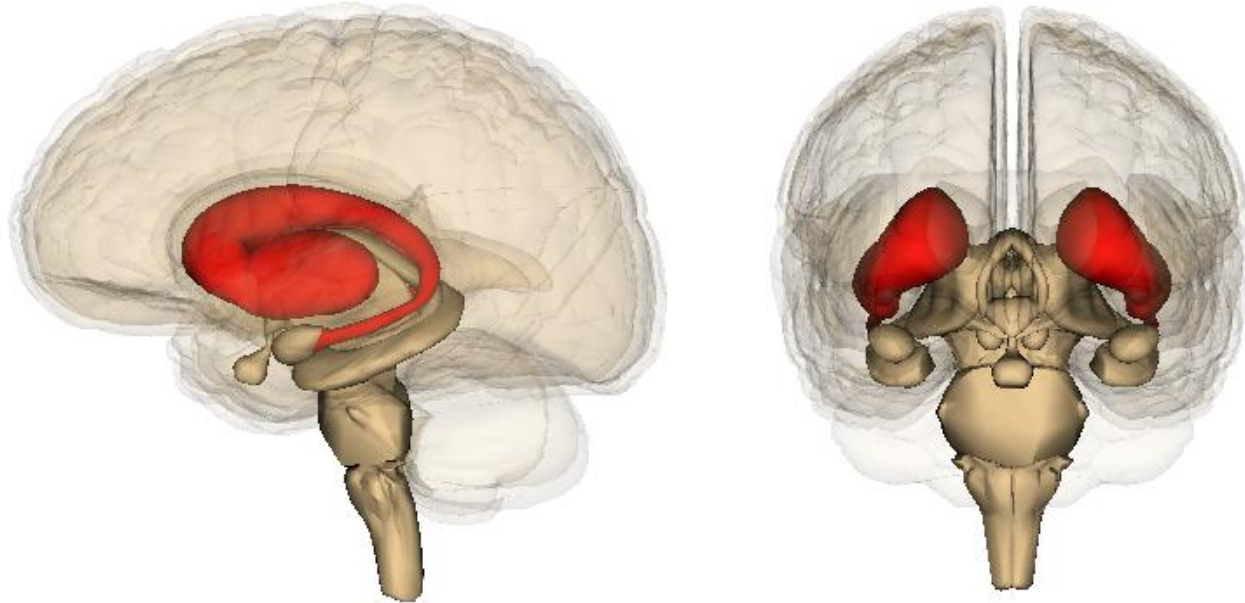
Emotion  
Motivation



# Region of the Brain Affected Most by HD

**Caudate + Putamen = STRIATUM**

**Striatum is part of the BASAL GANGLIA**



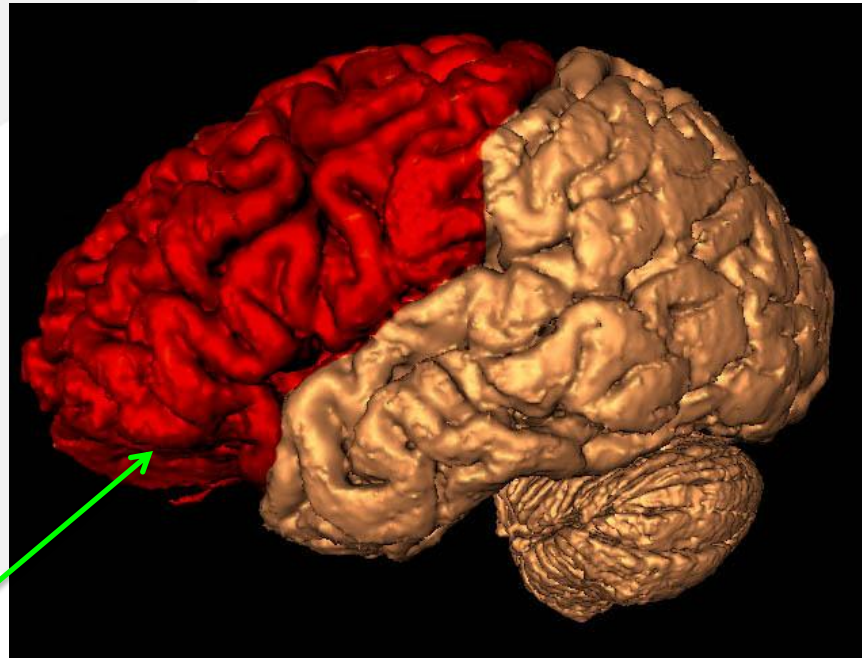
**The Striatum is heavily connected to the FRONTAL LOBE**



# The Striatum is Heavily Connected to the Frontal Lobe

## Frontal Lobe

Organization  
Planning  
Reasoning  
Impulse Control  
Attention  
Insight  
Social Skills  
Movement



**The ventral portion of the Frontal lobe is Highly Connected to the Limbic System (emotions)**

# Symptoms of Huntington's Disease

- In HD, the neurons of the striatum become dysfunctional, then die. This causes disruption of the circuits connected to the striatum and creates symptoms
  - Motor Symptoms
    - Chorea
    - Balance problems
  - Cognitive Symptoms
    - Thinking skills like concentration, memory, planning
  - Psychiatric Symptoms
    - Emotions and behavior

## Outline

- Basic Brain Structure and Function
- **Psychiatric / Behavioral Symptoms of HD**
  - Depression
  - Irritability
- Treatment

# Psychiatric Symptoms

- Why Psychiatric symptoms are important to learn about
  - They often appear years before the onset of motor symptoms
  - They can have a large impact on functioning
  - Many of them are treatable (!)



# Stages of HD

- Prodromal stage
  - Prior to onset of motor symptoms (diagnosis)
  - Psychiatric symptoms may be present
- Early Stage
  - May still be able to drive and hold down job, but might require extra help
- Mid Stage
  - Lose ability to work, drive, need help with activities of daily living (ADLs).
  - Often the time of applying for disability
- Late Stage
  - Help is needed in all ADLs
  - 24/7 care needed, often in a care facility

# Psychiatric Symptoms

- **Depression**
- Apathy
- Frontal lobe symptoms
  - Agitation/Irritability
  - Impulsivity / disinhibition
  - Lack of insight
- Anxiety
- Obsessions and Compulsions
- Psychosis

# Psychiatric Symptoms

- Symptoms of depression
  - Depressed Mood
  - Loss of interest
  - Insomnia
  - Weight loss or gain
  - Decreased energy
  - Psychomotor agitation or retardation
  - Worthlessness/guilt
  - Poor concentration
  - Thoughts of death or suicide

# Symptoms versus Syndrome (collection of Symptoms)

- A Major Depressive Syndrome is determined by number of symptoms and severity of symptoms
  - At least 5 of the list of 9 symptoms on previous page present for at least 2 weeks, interfering with function
- Most patients with HD do not meet full criteria for Major Depressive Syndrome, but have depressive symptoms
  - Presence of symptoms can lead to dysfunction and suffering
- Analogy:
  - bad cough = symptom
  - Bad cough + fever + sputum = pneumonia (syndrome)

# Prevalence of Depression in the Stages of HD

- Prodrome
  - In particular, higher in the year prior to onset
- Early
  - In particular in the years right after diagnosis
- Mid
  - Lower rates of depression compared to prodrome and early stage
- Advanced
  - May be hard to assess due to poor communication
- So depression does not increase with disease progression

# Prevalence of Depression in the Stages of HD

- How common?
  - Symptoms alone are common
    - 33-69% will report a depressed mood
  - Those with major depression
    - Near 20%
  - Lifetime prevalence of depression in the general population is 15%
- Risk factors for developing depression
  - More common in females
  - Family History (on non-HD side)
    - Depression has a major genetic component

# Stress / Environment and Depression in HD

- Many aspects of HD can cause stress
  - Dealing with a positive (or negative) gene result, onset of symptoms, loss of function, other family members who may be ill, guilt of passing on the disease
- Is depression caused by the disease affecting the region of the brain governing mood (the limbic system?)
- Is depression in HD caused by the stress of living with HD?
- This distinction is artificial
- Most likely it is a combination of both and a complex interplay of HD and family history for mood disorders
- Important thing is to monitor and treat it when it happens

# Suicide

- Rate of suicide in HD is estimated to be 4-5%
  - Lower than seen in general population who suffer from depression (15%)
- In a study that looked at the % of persons *having thoughts* of suicide
  - At risk, no neurologic signs: 9%
  - At risk, subtle neurologic signs: 18%
  - Motor signs, not yet diagnosed: 23.5%
  - Early stage after diagnosis: 21%
- Like depressive symptoms, the time just prior to diagnosis and after diagnosis are highest
- Monitoring for suicide at the time of genetic testing is also important



# Suicide

- Risk factors for suicide
  - Depression
  - Aggression / irritability
  - Substance use

# Psychiatric Symptoms

- Depression
- **Apathy**
- Frontal lobe symptoms
  - Agitation/Irritability
  - Impulsivity / disinhibition
  - Lack of insight
- Anxiety
- Obsessions and Compulsions
- Psychosis

# Psychiatric Symptoms

- Apathy
  - Lack of interest, drive, motivation
  - Can sometime be a part of depression
  - However, can be a distinct syndrome
  - More common than depression in HD
  - Can often be mistaken for depression
    - Difficult for family members to distinguish
  - Unlike depression, increases with disease progression
    - Directly related to cognitive dysfunction

# Psychiatric Symptoms

- Depression
- Apathy
- Frontal lobe symptoms
  - Agitation / Irritability
  - Impulsivity / disinhibition
  - Lack of insight
- Anxiety
- Obsessions and Compulsions
- Psychosis

## Agitation / Irritability

- A mood state characterized by a reduction in control over temper
  - Feelings of being edgy or irritated
  - Quick shifts in mood – ‘hair trigger’ for anger
  - Getting angry at small things that used to not cause a response
  - Poor adjustment to change in plans
  - Insisting on always having things their way
  - Disagreements lead to arguments
  - Having a much more intense response to something that in the past would get a mild response
  - Unable to control temper with persons outside the family
  - Can be a verbal outburst; when it becomes a physical outburst, then more serious

## Agitation / Irritability

- One of the most common problems in HD
  - Not nearly as well studied as depression
  - In general, consequences not as dire as in depression (suicide)
  - Prevalence rates of 33-75% of patients with some irritability
    - Like depression, those with more severe levels are less common – 12-20%

# Psychiatric Symptoms

- Agitation / Irritability
  - Seen throughout all stages of disease
    - Early in the course can be irritability with quick mood shifts into anger or rage
    - Later in the course can be a major problem in the context of placement into care facilities
      - Aggression is typically the main factor in getting 'let go' from a facility, or not being admitted to one

# Psychiatric Symptoms

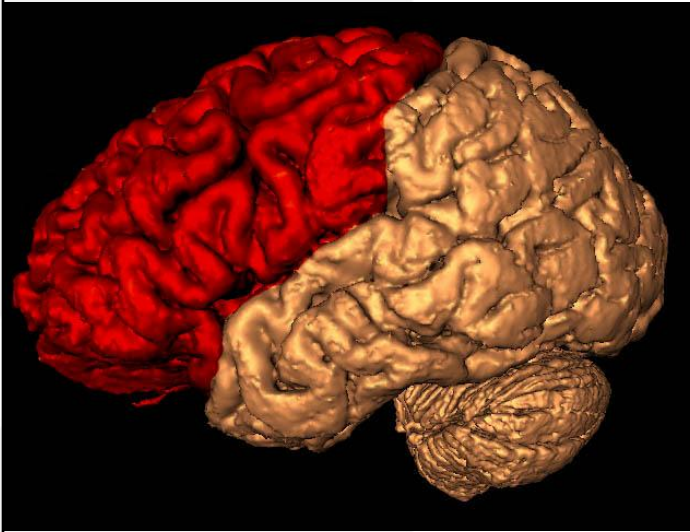
- Frontal Lobe Symptoms
  - Impulsivity and disinhibition
    - May lead to poor decision making with negative consequences
  - These symptoms are often combined with irritability and agitation
  - Lack of insight – unawareness
    - Persons may be unaware that they have chorea, or unaware that their behavior has changed or is problematic



# Brain circuits and the Frontal Lobe

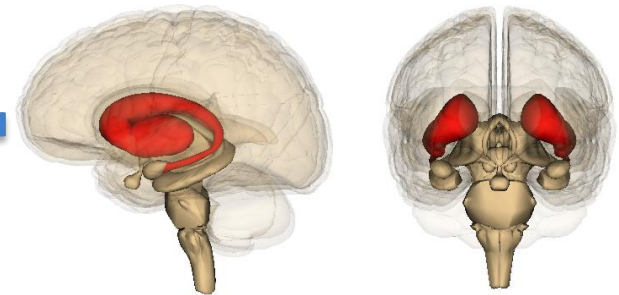
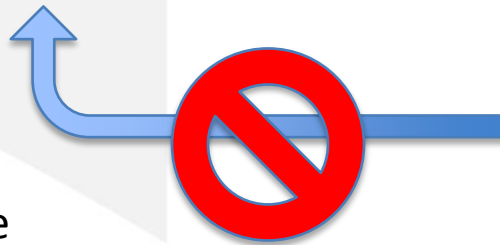
## FRONTAL LOBE

Organization  
Planning  
Reasoning  
Impulse Control  
Attention  
Insight  
Social Skills  
Movement



The basal ganglia have an inhibitory effect on the frontal lobe. Signals from here will allow for control of impulses whether they are movement, decisions, or anger

When this circuit is disrupted, the frontal lobe functions go 'uncontrolled' or unchecked: involuntary movements, poor attention, poor planning, impulsive behavior, quick temper



## Outline

- Basic Brain Structure and Function
- Psychiatric / Behavioral Symptoms of HD
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  - Irritability
- **Treatment**

# Treatment

- No cure; symptom management
- Three domains of HD symptoms
  - Motor symptoms
    - Chorea – very responsive
    - Balance, speech, swallowing – less responsive
  - Cognitive symptoms – not very responsive
  - Psychiatric symptoms
    - Irritability – very responsive
    - Depression – very responsive
    - Apathy – less responsive

# Treatment

- All 'brain' medications work by changing the amount of neurotransmitters in certain areas of the brain
  - Irritability: too much dopamine
  - Depression: not enough serotonin, norepinephrine
- This is the same way that the medications used to treat motor symptoms work
  - Chorea: too much dopamine
  - Slowed movements (Parkinsons): not enough dopamine



Neurotransmitters in the Synapse

# Psychiatric Symptoms

- Treatment of Depression
  - Often good response to treatment with medications
  - **Red text = neurotransmitter**
  - Lost of different kind of antidepressants:
    - SSRI = Selective **Serotonin** Reuptake Inhibitors
      - Prozac, Celexa, Paxil, Lexapro, Zoloft
    - SNRI = **Serotonin-norepinephrine** reuptake inhibitors
      - Cymbalta, Effexor
    - **Norepinephrine-dopamine** reuptake inhibitors
      - Wellbutrin
  - **No specific medication has been shown to be more effective in HD**

# Psychiatric Symptoms

- Agitation / Irritability
  - IS responsive to medication treatment
    - In particular, early in the course
  - Class of medications used to ‘block’ dopamine in the synapse
    - Called Antipsychotics (psychosis = hallucinations and delusions)
      - Used a lot for patients with psychosis (schizophrenia, dementia)
    - VERY useful in HD
      - Helps BOTH agitation/irritability and chorea

# Psychiatric Symptoms

- Agitation / Irritability
  - Other medications that can be used
    - Antidepressants
    - Can also try ‘mood stabilizers’
      - Used to treat bipolar affective disorder or manic depression
      - Lithium, Depakote
    - Benzodiazepines: Valium and similar medications
      - Like antipsychotics, have multiple effects
        - » Antianxiety
        - » *May* help with mood shifts
        - » Decreases involuntary movements

# Psychiatric Symptoms

- Treatment other than medications
  - Important!
    - Education
    - Family support
    - Counseling



# Psychotherapy in early stage of HD

- Psychotherapy
  - General: Education and support
  - A great adjunct to medications
  - If symptoms are mild then can use only psychotherapy
  - Rarely any ‘specific’ psychotherapy used
    - Cognitive - depression
    - Interpersonal - depression/ borderline
    - Behavioral – Obsessive/compulsive disorder
  - Less useful as disease progresses as cognitive function impairs usefulness

# Psychiatric Symptoms

- Who to get treatment from
  - A psychiatrist is good but not necessary
    - Few psychiatrists will know HD
    - More important to understand the medications than the disease
  - Many Neurologists are excellent at treating psychiatric symptoms
  - Family Practice physicians are also well-versed in psychiatric medications
  - **CONSULTATION**
    - HDSA Physicians Guide (available free at <http://www.hdsa.org/new-physicians-guide.html>)
    - Download and give to your doctor

# Questions & Discussion