Last Discussion Section!

Diseases of the Nervous System +
Other interesting tidbits about the
reward system
Jessica Andrews

Final exam: Tues. Dec 20 10:30-12:30 Rebstock 215
Review sessions?
Small group reviews?
Please fill out course evaluations!

ALZHEIMER’S DISEASE

1) Leading cause of dementia
2) Most common neurodegenerative
disease – 5 million Americans

3) Genetic predisposition

1) Alois Alzheimer (1864-1915)
2) Auguste D.

“She sits on the bed with a helpless expression. What is your name?
Auguste.
Last name?
Auguste.
What is your husband’s name?
Auguste, I think.
Your husband?
Ah, my husband.
She looks as if she didn’t understand the question. Are you married?
To Auguste.
Mrs D?
Yes, yes, Auguste D.
What is this? I show her a pencil.
A pen.
At lunch she eats cauliflower and pork.
Asked what she is eating she answers spinach. When she was chewing meat and
asked what she was doing, she answered potatoes and then horseradish. When
objects are shown to her, she does not remember after a short time which objects
have been shown.”

“What is your name?”
“Auguste.”
“Last name?”
“Auguste.”
“What is your husband’s name?”
“Auguste, I think.”

Cognitive
Molecular/Cellular
Structural
Metabolic

Structural

Metabolic

Hebert et al. (2003)
MOLECULAR CHANGES

Neurofibrillary tangles

Amyloid plaques

STRUCTURAL CHANGES

Image courtesy of Clifford Jack, Mayo Clinic

(Sanders-Brown Center on Aging, University of Kentucky)

Atrophy of hippocampus and several cortical areas that probably accounts for early memory loss and later loss of executive functions

METABOLIC CHANGES

Reduced metabolism in AD and individuals at genetic risk for AD throughout the cortex

COGNITIVE CHANGES

“...death of autonomy, death of memory, death of self-consciousness, death of personality, death of body...its particular sadness and horror stem from the sufferer’s loss of his or her “self” long before the body dies.” (Franzen, My Father’s Brain, 2001)

Clinical Dementia Rating (CDR):

<table>
<thead>
<tr>
<th></th>
<th>none</th>
<th>quest.</th>
<th>mild</th>
<th>mod</th>
<th>sev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) memory</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2) orientation</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3) judgment &amp; problem solving</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4) community affairs</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5) home and hobbies</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6) personal care</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
**BASAL GANGLIA AND MODULATION OF MOVEMENT**

*Disclaimer*: The BG is actually more complicated than this in that it involves direct and indirect pathways, so I tried to simplify (see your book for completeness). For these reasons, please don’t memorize these schematics! Instead, get the take-home messages:

1) the BG’s output is inhibitory; thus, to initiate movement, you have to disinhibit the BG (e.g. dopaminergic pathway via substantia nigra).
2) Lesion SN (Parkinson’s), then more inhibition and less movement. Lesion C/P (Huntington’s), then less inhibition and more movement.

Also, these figures came from *Neuroscience*, ch. 17

**Anatomy**

Includes several structures:

1) Striatum (caudate + putamen)
2) Globus pallidus (internal + external)
3) Substantia nigra
4) Subthalamic nucleus

**Functions**

- regulates activity of upper motor neurons via thalamic connections and thus modulates movement
- Important for control of voluntary movement, especially initiating movements and terminating movements
- Important for preventing unwanted movements (e.g. sitting still)
- When lesioned, lead to movement disorders, including Parkinson’s disease or Huntington Disease, depending on where the lesion

**Circuits**

Project from cortex to BG and back to cortex
In the absence of movement, the thalamus is tonically inhibited.

In the anticipation of movement, the thalamus is disinhibited by dopaminergic inputs.

Dopaminergic projections result in movement.

Inhibitory DA projections result in movement.
In anticipation of movement, the thalamus is disinhibited.

Thus, more tonic inhibition

In anticipation of movement, the substantia nigra isn't effective (loss of DA neurons) and thus cannot initiate movement as well.
1976: Barry Kidston, a 23-yr old chemistry grad student, made a mistake while synthesizing MPPP (Demerol), an addictive heroin-like opioid analgesic street drug, and also synthesized a byproduct, MPTP, a compound that when metabolized, rapidly destroys substantia nigra DA neurons. Within 3 days after injection, he exhibited symptoms of Parkinson’s.

1982: Seven people in CA showed up at various hospitals immobile, mute, and unblinking hours after taking MPTP contaminated with MPPP. A neurologist isolated the MPTP and used it to discover a lot more about the role of the substantia nigra in Parkinson’s Disease.

The thalamus receives less tonic inhibition and thus more movement.

Huntington’s Disease

PET imaging of dopamine receptors

Less DA receptors in Parkinson’s Disease in Basal Ganglia

The Reward System
Medial forebrain bundle sends dopaminergic projections to the ventral tegmental area and onto the rest of the reward system (nucleus accumbens, medial prefrontal cortex).

1965: Rats will refrain from sleeping or eating in order to press a lever that resulted in stimulation of MFB (Routtenberg & Lindy, 1965)

Using the reward system to direct behavior - example of the “remote control rat”

Even money activates reward system!

**Nucleus Accumbens**: anticipation of $$$

**mPFC**: receipt of $$$

Even extends to pleasant tastes, sexual images, attractive faces, sports cars, and socially rewarding behaviors

Knutson et al., 2000