Discussion Session 10

Lectures XXVI-XXVII  Dec 9, 2005

Important stuff

- Final Exam - Tues Dec 20 from 10:30-12:30 in Rebstock 215
- REVIEW Sessions - Sun Dec 18 and Mon Dec 19 from 7-9pm...location TBA
- Problem Set 10
  - DUE Monday Dec 12, 2005 (that’s three days from now)
Today

- Parkinson’s Disease
  - Pathways of the basal ganglia
  - Treatments (from logical to just plain crazy)
- Schizophrenia
  - Key points, role of DA signaling in
- Depression
  - Monoamine vs alternative hypothesis
- Alzheimer’s Disease

Parkinson’s Disease

Figure AB-18: Basal Ganglia

- Structures Involved
Connections between structures

Normal vs Parkinson’s

Loss of DA neurons in substantia nigra (SNc) leads to a net increase in the inhibitory projection from the globus palidus (GPi) to the thalamus.

inhibition of thalamus = decrease in movement
Treatments

- L-Dopa (precursor to DA)
  - Why not give dopamine?
    - Doesn’t cross the blood brain barrier
  - What cells make the dopamine?
    - Cells in substantia nigra (that send projections to Putamen)
  - Does this treat the symptoms or cause?
    - Symptoms only…stops working when all DA cells are dead
  - Side effects?

- Lesion of the subthalamic nuclei or GPi reduces inhibitory output to thalamus
- Stimulation of STN reduces inhibitory input to thalamus
  - Contradictory?

Treatments

- Virus is used to deliver growth factor to substantia nigra
  - Saves DA neurons
  - Problem…miss the SNc and get schizophrenia
- DA Stem cells into striatum (Kirk Freed)
  - Helps BUT you get dyskinesia
- Virus delivered DDC (converts L-Dopa to DA) into striatum
  - What does this do?
    - It creates cells in the putamen that can now produce DA from L-Dopa (even after DA cells in SNc are dead)
Schizophrenia

- Complicated disorder
- Lots of brain abnormalities (structural and functional)
  - Identified with PET and fMRI
- Increased DA signaling can account for some of positive (new behaviors) and negative (absence or normal behaviors) symptoms
- Treatment usually involves blocking DA receptors

Depression

- Symptoms: anhedonia, sleep problems, eating problems, feelings of despair
- Brain Changes
  - Structural - Change in hippocampal and amygdala volume
    - In Rats - Block hippocampal neurogenesis to Block antidepressant effects
  - Functional - Changes in amygdalar activation
Causes of Depression

- Monoaminergic hypothesis - Reduction in 5-HT, DA, acetylcholine, adrenergic signaling is involved
  - Most antidepressents increase monoamines
  - BUT...They take 3-4 weeks to work...why?
- Alternate Hypothesis - Dysregulation of the stress pathway causes/perpetuates depression
  - 50-70% of patients have elevated levels of the stress hormone Cortisol and fail to turn off stress response

HPA Axis - Dysregulated in MDD
Alzheimer’s Disease

- Symptoms - Progressive loss of memory
- Usually occurs in aged population
- Pathology - Senile plaques and Cell death

![Senile plaque]

Alzheimer's Disease

- Senile Plaques
  - Made up of A-Beta amyloid protein
    - Mutations in the precursor of A-Beta cause early onset Alzheimer’s
- Treatment
  - Antibodies to A-Beta (in clinical trials)
    - Too little too late?
  - Acetylcholinesterase inhibitors
    - Cells in locus coeruleus die in AD
    - Slows progression…but not a cure
    - $$$$$