M555 Medical Neuroscience

Basal Ganglia

Background for Basal Ganglia and Basal Ganglia Disorders
basal ganglia modulate activity of other brain regions

Two Notes on Terminology
“basal ganglia” and “basal nuclei”

pyramidal -vs- extrapyramidal - a traditional distinction
pyramidal (system or disorder):
extrapyramidal (system or disorder):
   BG to spinal cord
   BG does influence activity in spinal cord

Basal Ganglia Disorders: Traditionally Associated with Movement Disturbances
“negative signs” -
   slow movements =
   lack of movement =

   “poverty of movement”

“positive signs” -
   uncontrollable jerking movements =
   uncontrollable writhing movements =
   uncontrollable flailing movements =
   uncontrollable shaking movements =

dystonia

some of the disorders associated with the BG
   Parkinson’s Disease
   progressive supranuclear palsy
   Huntington’s Disease
   (Athetoid) Cerebral Palsy
   Hemiballismus
   Sydenham chorea
   Wilson’s disease (hepatolenticular degeneration)
   tardive dyskinesia

   possibly, Tourette’s syndrome and obsessive-compulsive disorders

Basal Ganglia Disorders - Not Only Movement Disturbances
Basal Ganglia
Structure
basic parts of basal ganglia
caudate nucleus
putamen
globus pallidus

Structures Often Included with Basal Ganglia
substantia nigra
reticular part (pars reticulata)

compact part (pars compacta)

subthalamic nucleus
below thalamus, near substantia nigra

Nomenclature
striatum =
palladium =
lenticular (or lentiform) nucleus =

Blood Supply to Basal Ganglia Proper
via branch of anterior cerebral artery
medial striate artery
via branches of middle cerebral artery
lenticulostriate arteries
via branches anterior choroidal artery
via posterior cerebral and posterior communicating arteries
Dorsal and Ventral Parts of Basal Ganglia

two structural and functional divisions
dorsal division is better known

**Dorsal Striatum**
- caudate
- putamen

**Dorsal Palladium**
- globus pallidus

components of ventral division
are comparable to components of dorsal division

**Ventral Striatum**
- nucleus accumbens

**Ventral Palladium**
- substantia innominata

---

Basal Ganglia - Components, Connections and Functions

**Striatum**

“entry point” into BG
caudate and putamen

similar
1) embryonic origin
2) structure
3) neurotransmitters
4) head of caudate and putamen join
   across internal capsule

primary efferents: medium spiny neurons
1) neurotransmitter -
2) peptide neuromodulators -
3) project to globus pallidus

cholinergic neurons
cholinergic neurons in striatum
1) local circuit neurons
   modulate activity within striatum
2) matrix - acetylcholinesterase-rich regions
3) small striosomes - acetylcholinesterase-poor regions

Palladium
“exit” point from BG
medial (internal) GP and lateral (external) GP (dorsal part)
neurotransmitters -
high rate of spontaneous activity

Basic Connections
BG - part a loop with cerebral cortex
cortex -> striatum
striatum -> pallidum
pallidum -> thalamus
thalamus -> cortex
several, parallel loops
somatomotor
oculomotor loop
cognitive loop
limbic loop

fig. 19-8
fig. 19-11
Disturbances of Basal Ganglia Functions - Parkinson's Disease

Characteristics

common disease

second most common degenerative disease of nervous system
more than 1,000,000 cases in US
at least 40,000 new cases diagnosed each year
described in 1817 by Dr. James Parkinson
ancient accounts likely describe PD

neurodegenerative disease

decision of nerve cells in brain, particularly in SN pars compacta
gradual loss of dopamine in nigrostriatal pathway

SN pars compacta >> caudate and putamen
results in an abnormal pattern of brain activity involving BG
leads, in turn, to a disruption in brain functions

progressive disease

onset usually at 55 years or later though 15% younger than 40 years
symptoms worsen with time

formidable disease

likely a family of diseases
several possible causes
similar pathology and similar effects
no cure
effective treatments, but many side effects
not fully understood
new insights available

Central Problem

normally, about 4% of nerve cells in substantia nigra lost per decade
PD symptoms begin when about 70% of nerve cells in SN are lost
disease progresses as loss continues
appears to be earlier and greater loss of SN nerve cells in those with PD
not enough dopamine in striatum; relatively too much acetylcholine

darkly pigmented cells of substantia nigra (sn) die as PD progresses
Youdim and Reader, Scientific American, Jan 1997
Signs and Symptoms

movement disorders
  rigidity
    lead pipe or cogwheel

bradykinesia/akinesia
  limited facial expression
  micrographia

  tremor at rest
  flexed posture
  impaired balancing reflexes
  shuffling gait

visceral (autonomic) disorders
  low blood pressure (while standing up)
  constipation and incontinence
  excessive sweating

sensory disorders
  anosmia
  sense of body position
  pain
  sense of inner restlessness (akathisia)

cognitive disorders
  depression
  anxiety
  diminished executive function
  memory problems
  dementia

Youdim and Reiderr, Scientific American, 276, p.55
PD and Loss of Cells in Substantia Nigra
recognized causes - 25% of PD cases
head injury
genetic related, may include “early onset”
strokes involving the substantia nigra
infections
drugs that damage nerve cells in the substantia nigra

idiopathic - 75% of PD cases
one idea - focus on environmental factors
metal exposure (iron, manganese)
pesticide/herbicide/fungicide exposure
suspected compounds include paraquat, maneb, rotenone
chronic, low-level exposure may suffice
exposure early in life, re-exposure later in life
environmental factors may combine with innate susceptibility of neurons in substantia nigra

another idea - special susceptibility of substantia nigra neurons
generation of highly reactive free radicals in SN take a toll on cells
“targets” of free radicals: cell membranes, nuclear components, enzymes and mitochondria
neurons in SNr may be at particular risk for damage due to free radicals
combined interaction of several factors foster production of free radicals
presence of dopamine and melanin in the cells
active microglial cells
high level of iron

iron promotes production of free radicals during dopamine oxidation
iron also binds to melanin which becomes an oxidant and generates free radicals

normal catabolism of dopamine and melanin

free iron from storage generates more free radicals
glial cells help in oxidation of dopamine that produces free radicals

high iron levels in neurons of Substantia Nigra

 generation of free radicals

active microglial cells