The basal ganglia: a functional approach

“But, what is it for?”
Finding out with computational neuroscience
Phenomenology

Damage to BG is main cause of:
- Parkinson’s disease
  - Bradykinesia, akiensia, tremor
- Huntington’s disease
  - Involuntary movements (when slow and extended = chorea)

Damage to BG implicated in:
- ADHD
  - Attention deficit hyperactivity disorder
- Schizophrenia
  - Complex condition with positive symptoms (e.g. delusions) and negative symptoms (e.g. lack of affect)
Rationale for tackling the problem

● If brain area/system X is damaged, what are the consequences?

● Strategy: find out the main function of X.

● Then, understanding of the phenomena will be unified: each deficit is an aspect of loss of the main function of X.

● So, what do the basal ganglia do....?
Action selection

Predisposing conditions (sensory input, cognitive state, homeostasis, etc)

Energy balance (A1: feeding)

Fluid balance (A2: drinking)

Threat (A3: escape)

Motor resources

Behavioural output (feeding)
Cognitive example

● Students in this lecture
  ■ ‘shall I pay attention or think about plans for this evening’? ['action' of defining cognitive state]
  ■ ‘pay attention or act on my being hungry’
  ■ but then fire alarm goes off….

● Salience issues (again)

● ‘lower’ and ‘higher’ level processing
  ■ social protocols and long term planning versus biological drives and homeostasis
  ■ Probably mediated by cortical and sub-cortical centres respectively
Mediating competition between actions

Central switch has a ‘wiring’ advantage over the ‘distributed’ alternative

Distributed (all-to-all) connectivity.
Number of connections $\sim N^2$

Central switch
Number of connections $\sim N$
Hypothesis for basal ganglia function

- basal ganglia is the central ‘switch’ in the vertebrate brain that enables ‘action’ selection
  - Here ‘action’ may mean ‘internalised behaviour’ defined by cognitive state

- Therefore disorders of the basal ganglia are disorders of action selection
  - E.g. PD, HD = inability to select motor actions appropriately
  - E.g. ADHD, Schiz. = inability to suppress unwanted actions or cognitive states

Redgrave, et al. 1999
Evidence for this hypothesis: 1

If the action selection hypothesis is true then we require that …

1. The BG must take input from a wide variety of brain areas
   • i.e. putative ‘command centres’ for ‘action requests’
   • These should be cortical and subcortical

2. There must be some mechanism by which the BG can switch on selected motor resources

3. There must be evidence of a flow of information between command centres, BG, and associated motor centres
Evidence for this hypothesis: 2

If the action selection hypothesis is true then we require that …

4. The BG must understand be able to extract the ‘salience’ of each request
   • Assuming that this is done in BG and is not sent separately (otherwise we have a repeat of the ‘wiring argument’)

5. There must be evidence of neuronal selection mechanisms in BG

Subsequent slides will be related back to these points by labels of the form E#
The main input nucleus is neostriatum (or sometimes simply the striatum) composed of the putamen and caudate nuclei.

The striatum is by far the largest nucleus in the basal ganglia and receives input from all over the brain including: all of cerebral cortex (except primary sensory areas) and subcortical nuclei such as the superior colliculus (via the intralaminar thalamus).

Also shown is the globus pallidus (see next slide for details).
Disinhibition gating hypothesis 1: basic mechanism

- Cortex
- Thalamus
- BG
- striatum
- GPi/SNr
- subcortical motor nuclei

Output nuclei of the BG
GPi = globus pallidus internal segment
SNr = substantia nigra pars reticulata

Alexander, et al. 1990
Disinhibition gating hypothesis 2: data with glutamate injections in striatum

VM = ventromedial thalamus

SC = superior colliculus (midbrain sensory and motor motor nucleus)

Alexander, et al. 1990
Representing discrete actions 1: cortico-basal ganglia loops

Five main loops according to primary cortical input area

- **Motor** (supplementary motor area – SMA)
- **Oculomotor** (frontal eye fields – FEF)
- **Prefrontal 1** (dorsolateral prefrontal cortex – dlPFC)
- **Prefrontal 2** (lateral orbitofrontal prefrontal cortex – LOF)
- **limbic** (anterior cingulate area – ACA)
Representing discrete actions 2: topography in BG

Different body parts represented by different parts of BG and related structures

We conclude (from this slide and the last) that BG represents actions in discrete *channels*
Representing discrete actions 1: sub-cortical-basal ganglia loops

Sub-cortical structures include:

Superior colliculus (SC)

Pedunculopontine tegmental area (or simply peduncularpontine nucleus - PPN)

Periaqueductal gray (PAG)
Disinhibition gating and channels

Predisposing conditions

Ctx1: action1

Thalamus

BG

Motor resources for action 1

Ctx2: action2

Thalamus

BG

Motor resources for action 2

Probably some shared resources

E2 & E3
Interlude – the anatomy

Coronal section

Output nuclei

Globus pallidus

Putamen

Head of caudate

Tail of caudate

Amygdala

Thalamus
Salience extraction in striatum

Medium spiny neurons
Spines up close…

textbook

Paul Bolam’s lab
Selection mechanisms in BG 1: basic idea

Cortical inputs

Note: ‘striatum’ is both excitatory and inhibitory
Resolved later...

Output (GPI/SNr)

E5

Model neuron

inhibition
excitation
Selection mechanisms in BG 2: realistic Instantiation in basal ganglia

Assumes diffuse projections from STN = subthalamic nucleus

Mink and Thach, 1993
Focussed and diffuse connectivity

- Medium spiny neuron
- STN neuron
Striatal structure and BG architecture

- Mainly D1 dopamine receptors
- Mainly D2 dopamine receptors

NB – red/blue do NOT signify excitation/inhibition here
Instantiation in basal ganglia: 2

Selection pathway

Striatum (D1) → Cortex/thalamus → EP/SNr → STN → BG output

Striatum (D2) → Cortex/thalamus → GPe → STN

Function?
New functional architecture: selection and control pathways

Interpret GP efferents as control signals for modulating selection pathway

Gurney et al, 2001

Selection pathway

Control pathway
Simulation - basic selection dynamics

Channel 1

Channel 2

Channel 3

Saliency
EP/SNr output
Comparison with prevailing model: ‘Direct’ and ‘Indirect’ pathways

- Never instantiated quantitatively
- No global selection
Summary

- Action selection is a key computational problem for all animals.
- Central switching appears to be an optimal solution.
- The BG appears well placed to do this in vertebrates because:
  - It receives widespread input (cortical and subcortical).
  - Tonic inhibition and its selective release appear to be a mechanism for gating motor programmes.
  - Functional loops and topography support the idea of action ‘channels’.
  - Medium spiny neurons could act to extract salience.
  - There is a multitude of selection mechanisms in BG, including that supported by the innervation of SNr/GPi from striatum and STN.
- Under our hypothesis, disorders of the basal ganglia are understood as disorders of action selection.
Suggested reading

● The chapter in Squire et al (Fundamental Neuroscience)

● The review by Mink (1996)

● Our paper outlining the action selection hypothesis (Redgrave et al 1999)
References


