CORTICAL-SUBCORTICAL NETWORKS AND A DUAL TIERED MODEL OF COGNITION – THEORY AND PRACTICE

LFK

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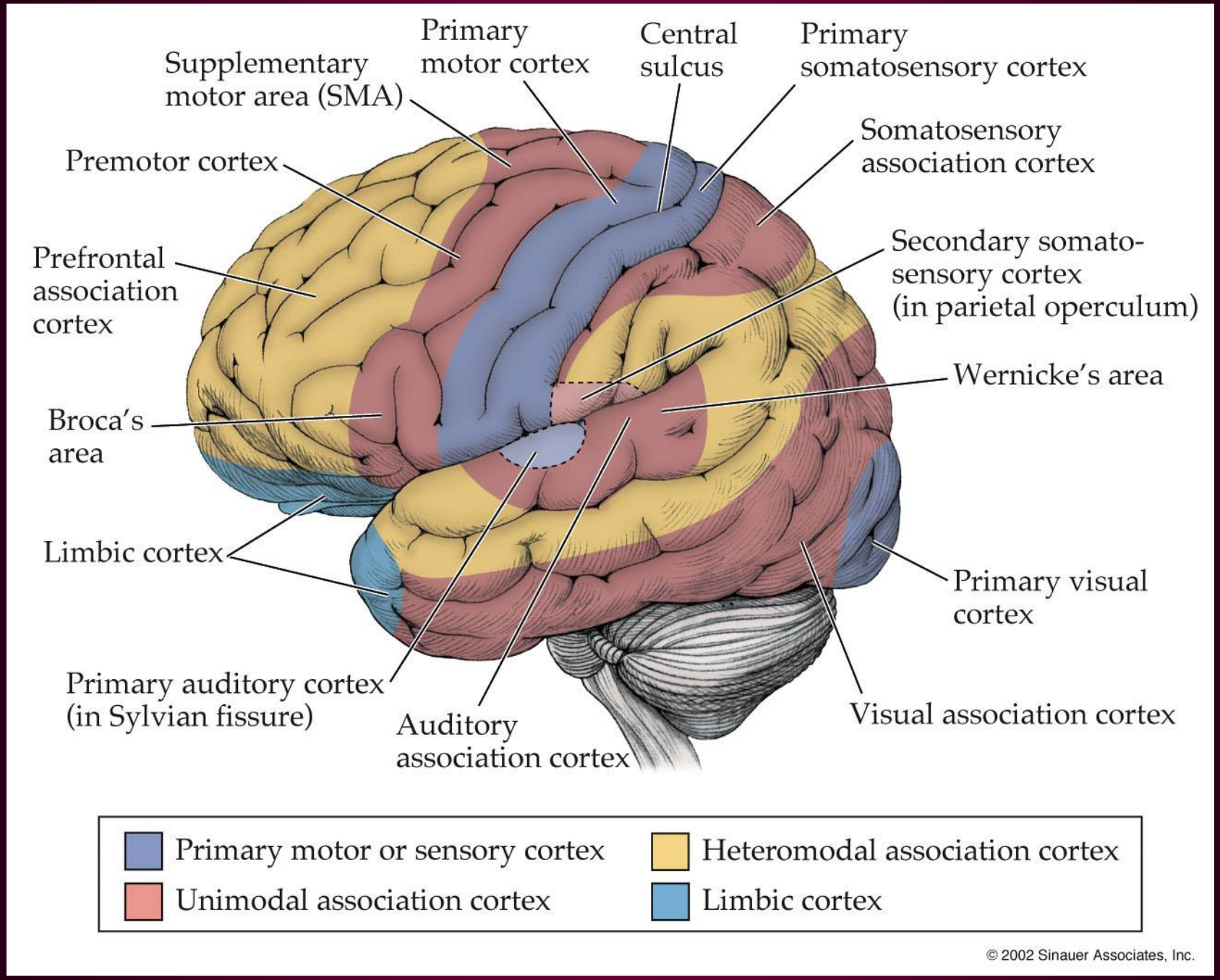
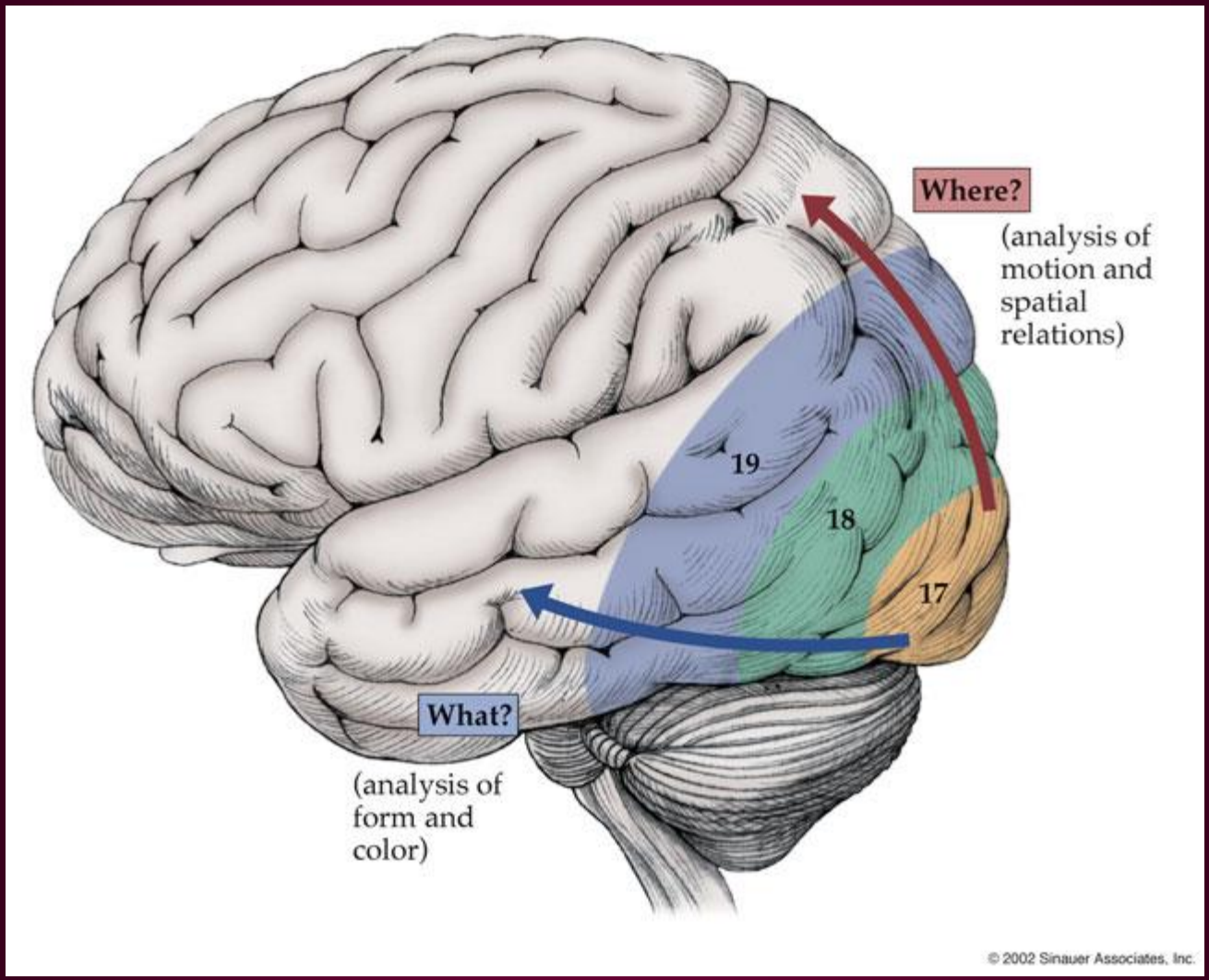
Cortical and Subcortical Structures

- The cortico-centric model
- The basal ganglia and cerebellum are often presented as co-processors of movement.
- Neuropsychological test interpretation and the horizontal organization of the brain.

- Lateralized hemispheric differences in information processing.
- Anterior and posterior differences in cognitive processing.




Where?
(analysis of motion and spatial relations)
19
18
17
What?
(analysis of form and color)
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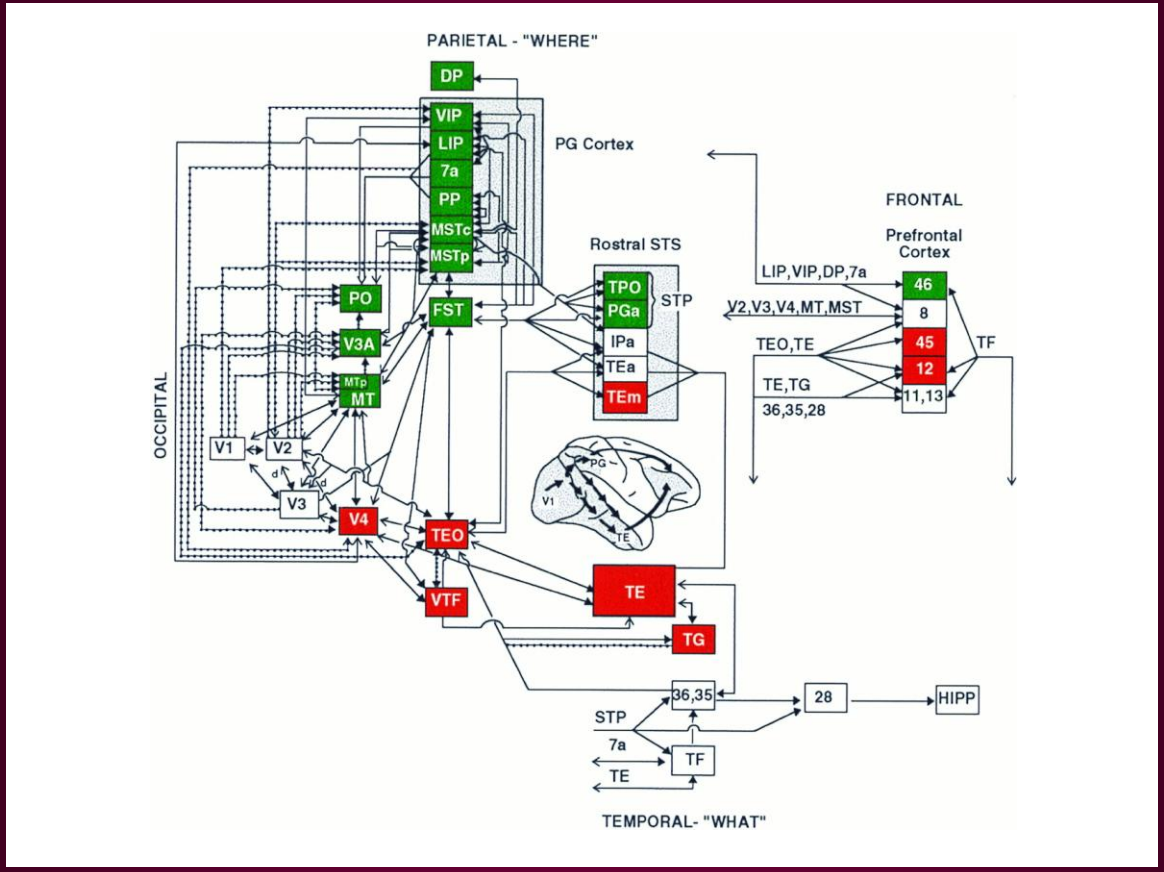
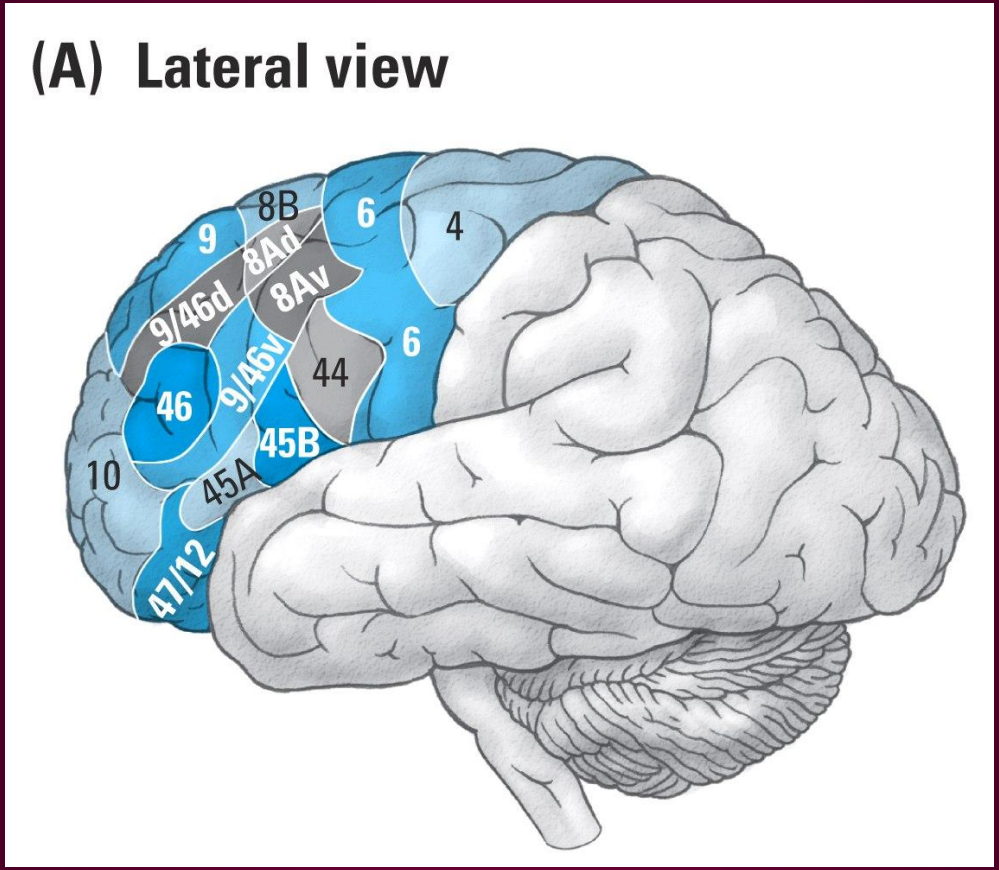

PARIETAL - "WHERE"
DP
VIP
LIP
7a
PP
MSTc
MSTp
PG Cortex
Rostral STS
TPO
PGa
IPa
TEa
TEm
STP
PO
FST
V3A
MTp
MT
OCCIPITAL
V1
V2
V3
V4
TEO
VTF
TE
TG
36,35
28
HIPP
STP
7a
TE
TF
FRONTAL
Prefrontal Cortex
LIP,VIP,DP,7a
V2,V3,V4,MT,MST
TEO,TE
TE,TG
36,35,28
46
8
45
12
11,13
TF
TEMPORAL- "WHAT"

Squire, 2005



Kolb & Whishaw, 2008

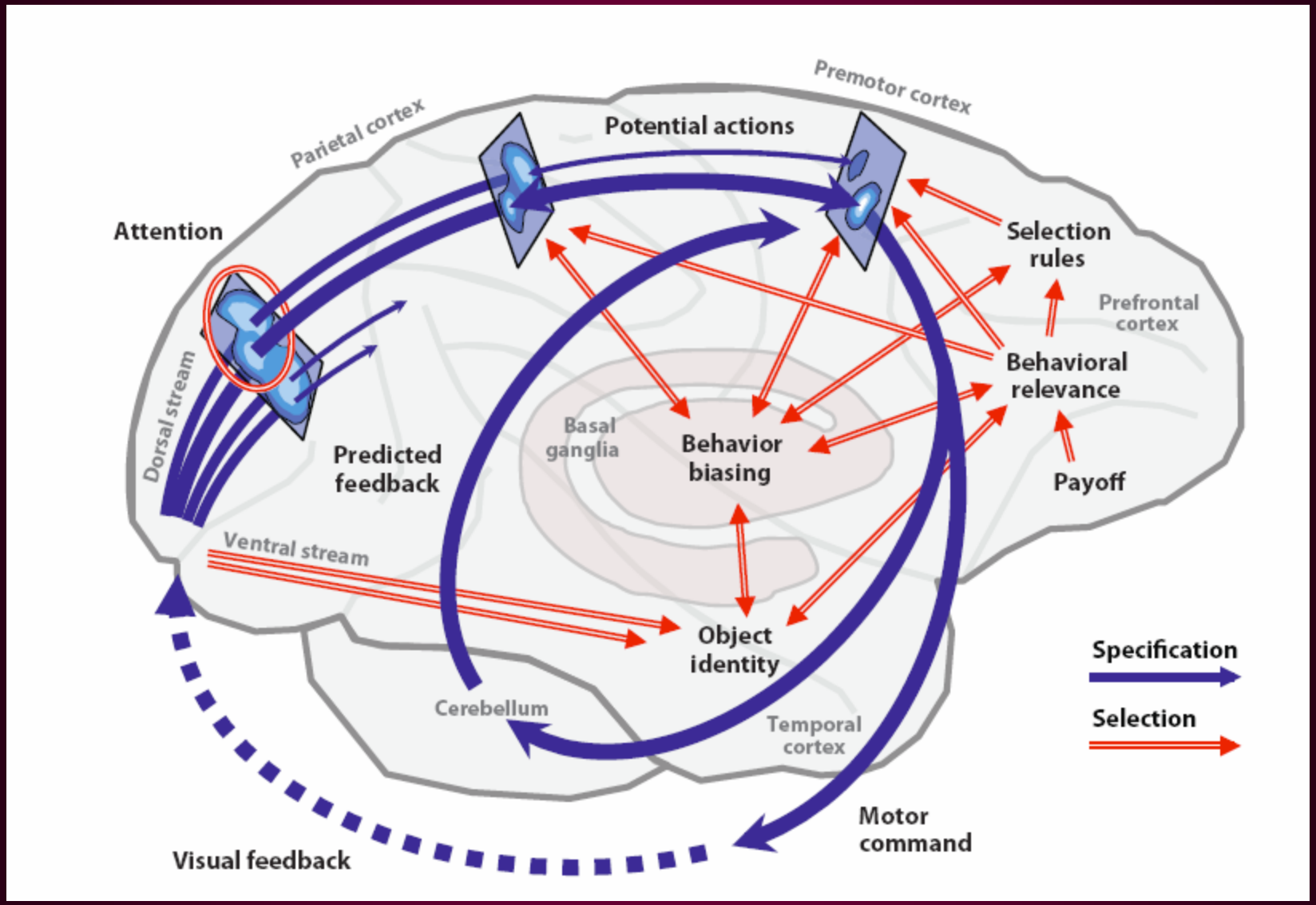
Current Neuropsychological Evaluation

- Neuropsychology is very adept at measuring the functioning of the medial temporal lobe memory system (posterior cortices)
- Neuropsychology is adept at assessing aspects of frontal system functioning, especially DLPFC processes
- Neuropsychology does not assess the ability to benefit from interacting with the environment;

different types of “memory” are not assessed - this is a huge drawback

Models of Cognition

- Perception-cognition/thought-movement
- First we perceive
- Then we think (about what to do)
- Then we act (we engage a motor program)
- But in “real life,” do things really work that way?


Premotor cortex
Parietal cortex
Potential actions
Attention
Selection rules
Prefrontal cortex
Behavioral relevance
Dorsal stream
Predicted feedback
Basal ganglia
Behavior biasing
Payoff
Ventral stream
Object identity
Specification
Selection
Cerebellum
Temporal cortex
Motor command
Visual feedback

Cisek, 2007

Movement, Cognition, and Perception

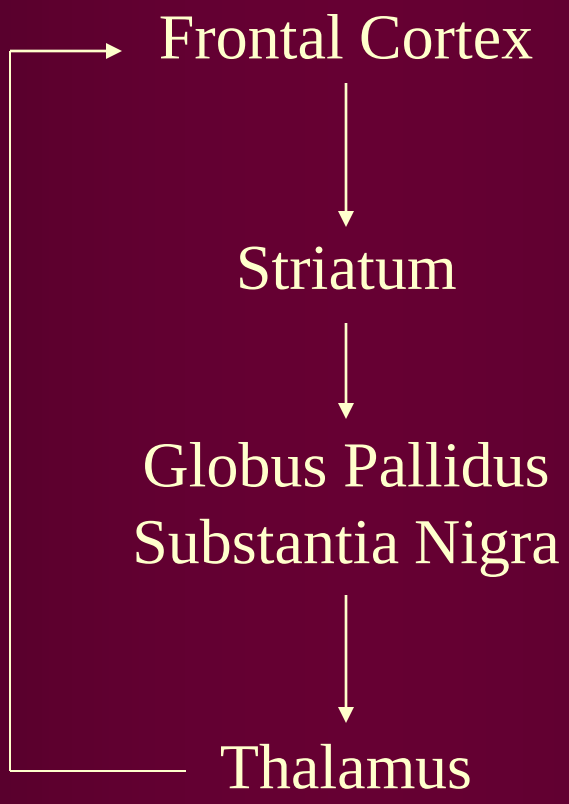
- Sometimes we perceive, think, and move
- Sometimes we perceive and move without thinking - we do things without conscious awareness, just because things need to be done
- Sometimes we move in order to perceive
- Movement is focal. Accepting this idea requires a different understanding of functional neuroanatomy
- We are born to move!

Vertical Brain Organization

- There are two vertically organized re-entrant brain systems that interface the cortex and the descending systems:
- The cortico-striatal system
- The cerebro-cerebellar system

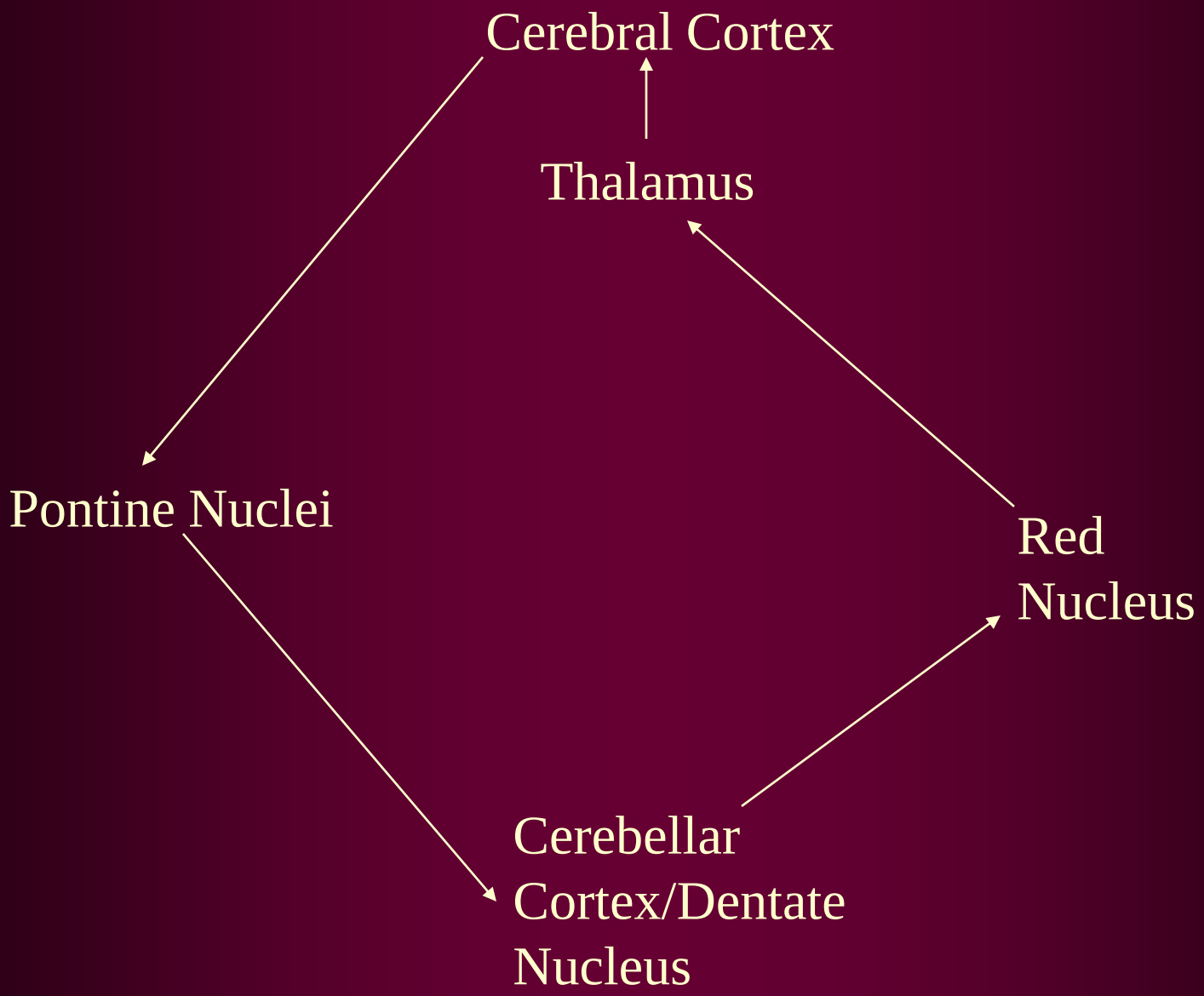
NEW WORKSHOP TITLE

- THINKING OUTSIDE THE BOX!
- This requires a significant modification to the cortico-centric model of cognition and behavior
- If ontogeny recapitulates phylogeny, then is the cortico-centric model of neuropsychology inaccurate and misleading?



Chapter 1 Figure 1

Simplified version of Frontal-subcortical circuit



Chapter 1 Figure 2

Simplified version of Cerebro-cerebellar circuit

NEW WORKSHOP TITLE

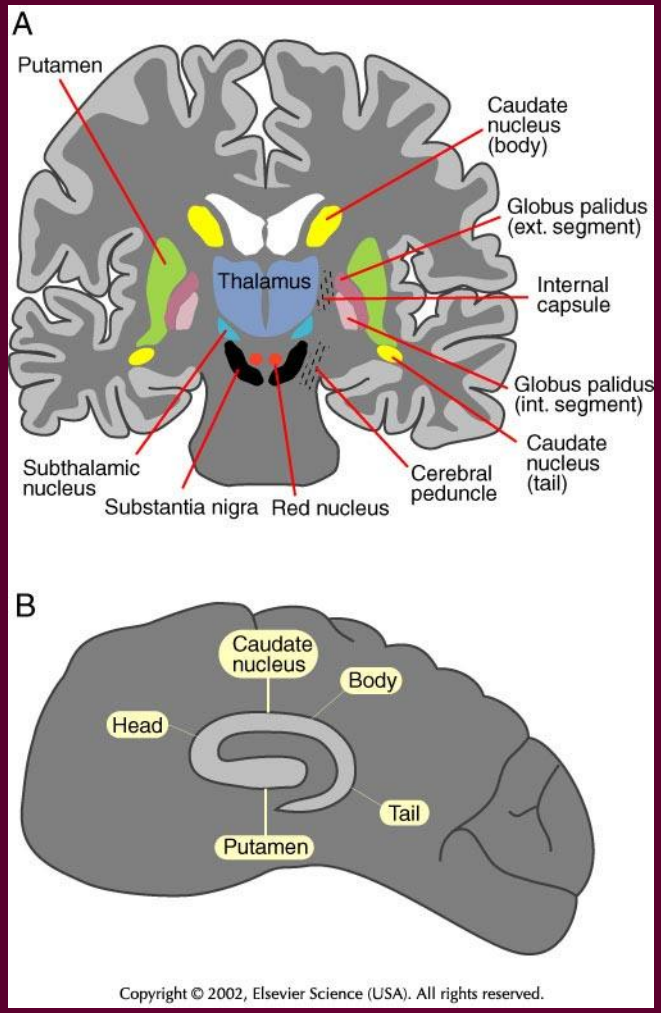
- FOLLOW THE YELLOW BRICK ROAD
- If we follow the connectional profiles of vertical brain organization, then the integrated functional neuroanatomy that might be proposed by the "Wizard of Oz" does not provide support for many of the inferences that are derived from neuropsychological tests
- What do our tests assess? What are we neglecting?

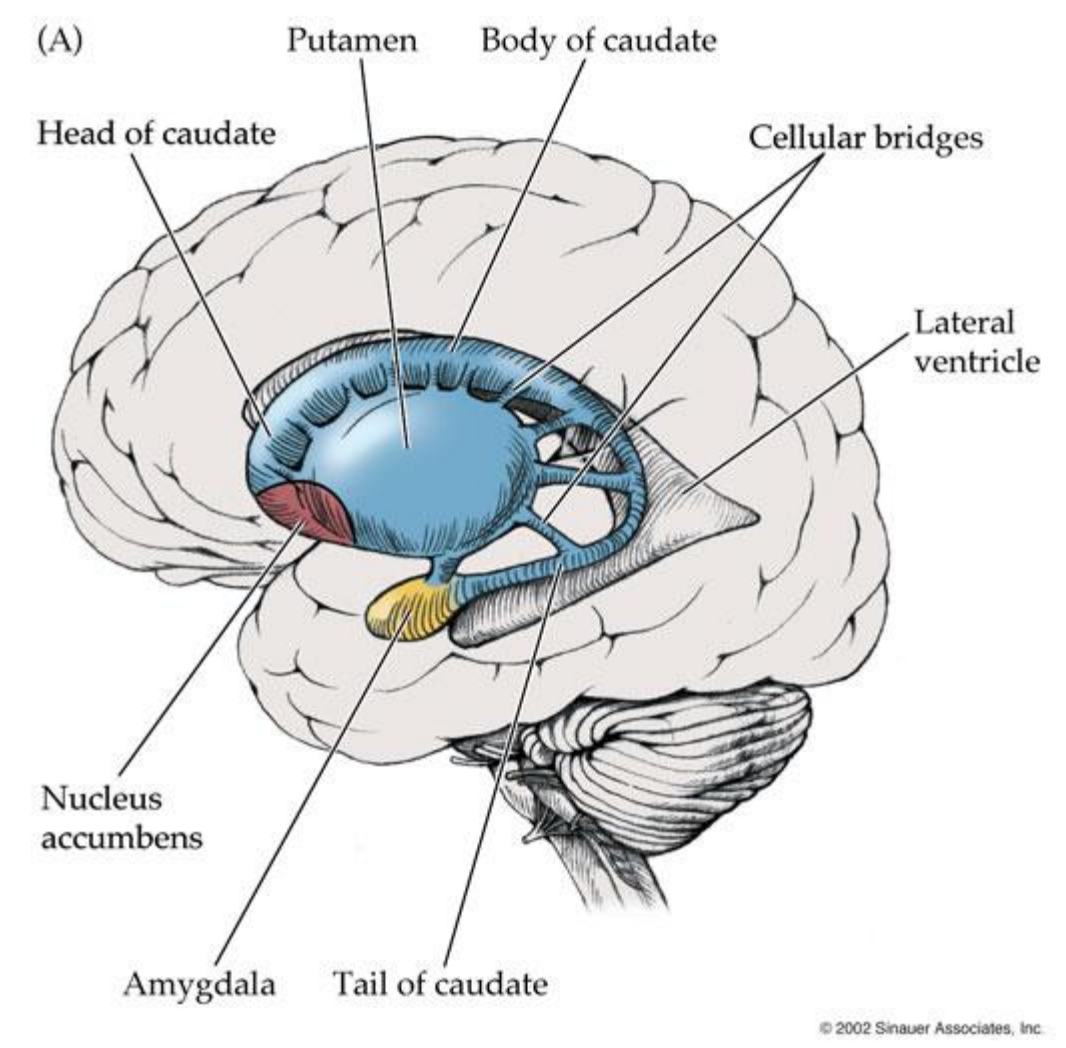
The Purposes of this Workshop

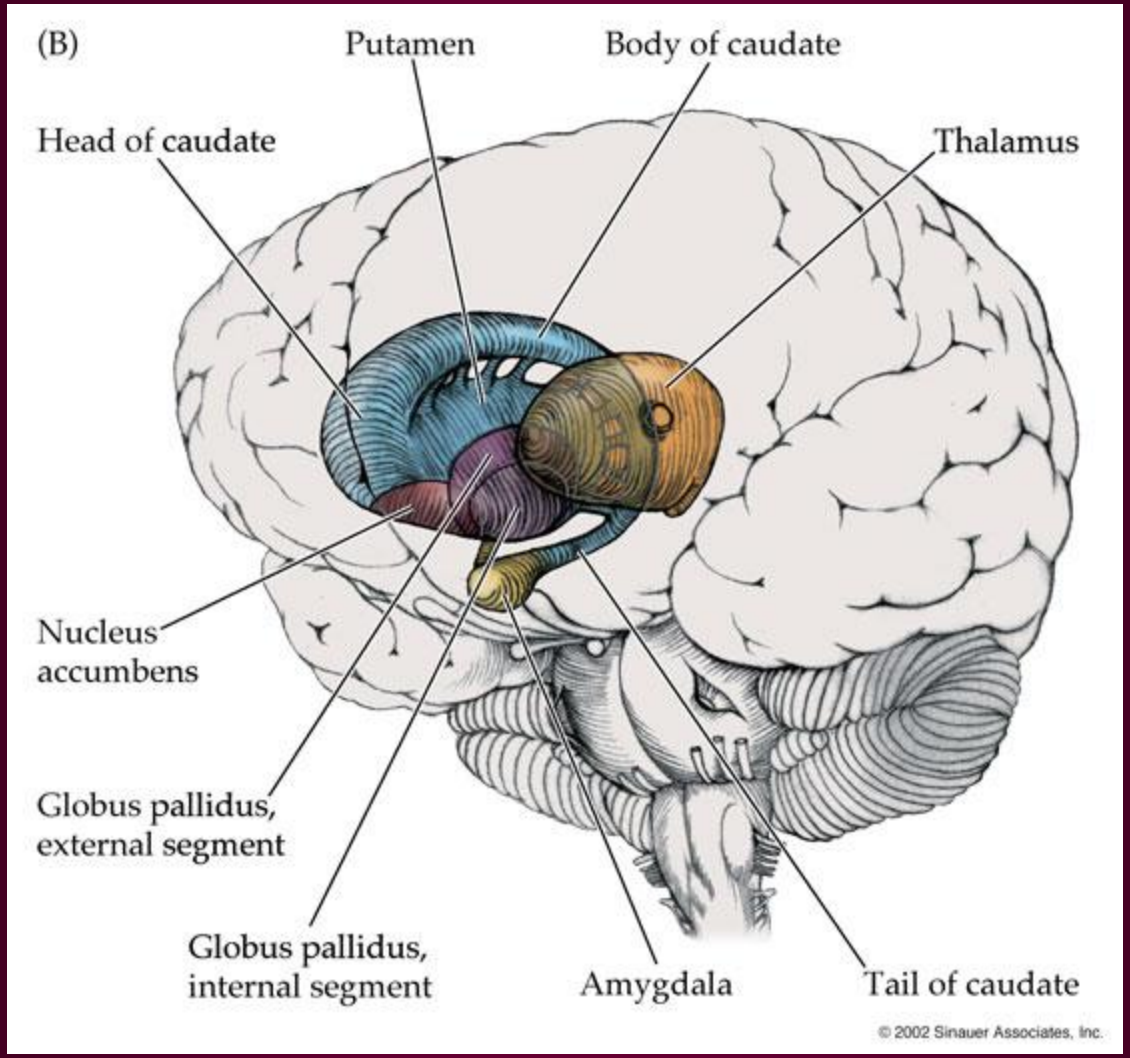
- To provide an understanding of the structure and function of the basal ganglia
- To provide an understanding of the structure and function of the cerebellum
- To provide an understanding of cortical-subcortical interactions
- To propose an anatomy of a dual tiered model of brain function
- To present this information in a practical way

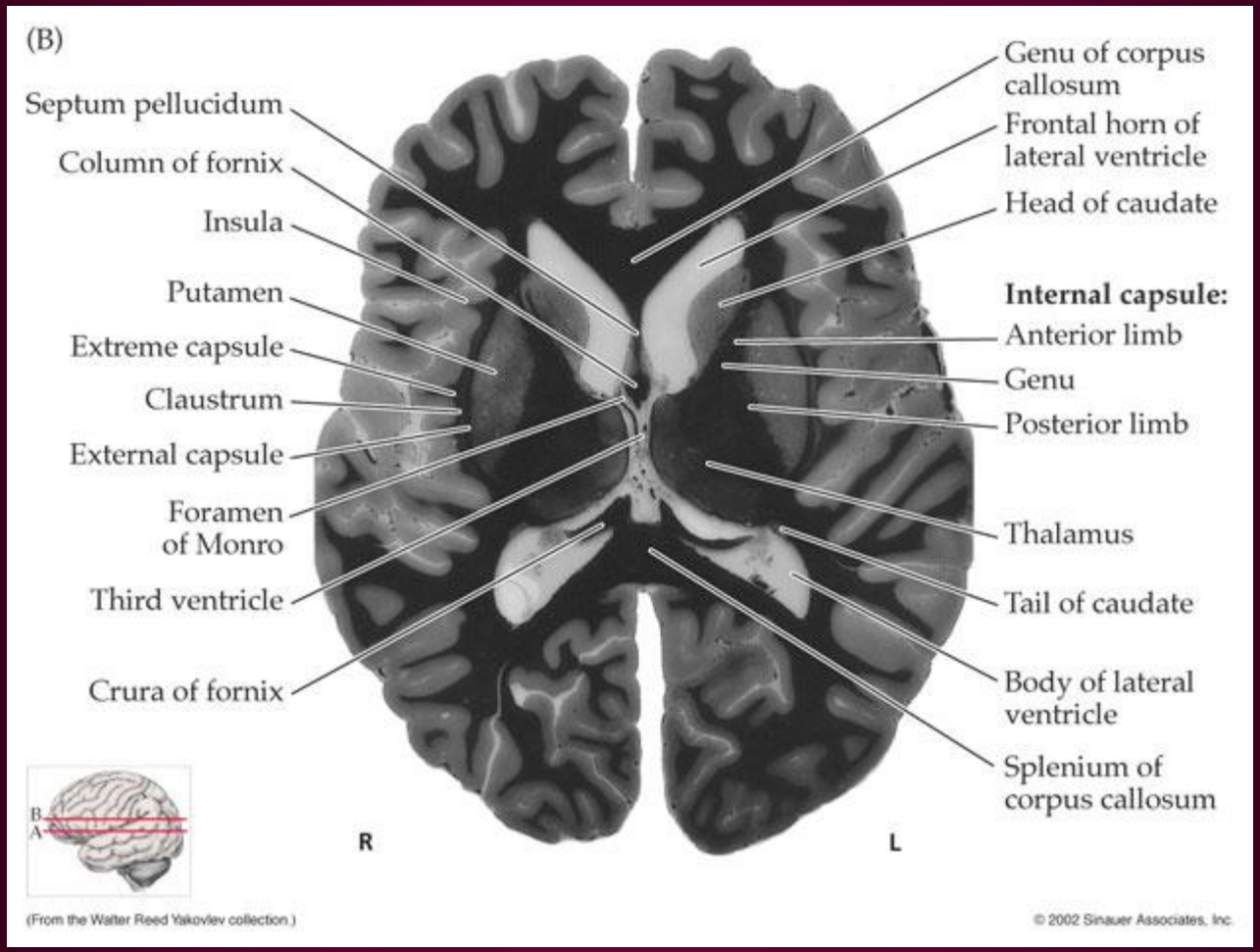
Basal Ganglia Subdivisions

Basal ganglia structure	Primary subdivision	Secondary subdivision	Tertiary subdivision
Striatum	Dorsal striatum Ventral striatum	Caudate Putamen Nucleus accumbens	 Core Shell
		Septum Olfactory tubercle	
Globus pallidus	External segment Internal segment	 Outer portion Inner portion	
	Ventral pallidum		
Substantia nigra	Pars compacta Pars reticulata	 Pars lateralis	
Subthalamic nucleus			




(A)
Putamen
Body of caudate
Head of caudate
Cellular bridges
Lateral ventricle
Nucleus accumbens
Amygdala
Tail of caudate
© 2002 Sinauer Associates, Inc.


(B)
Putamen
Body of caudate
Head of caudate
Thalamus
Nucleus accumbens
Globus pallidus, external segment
Globus pallidus, internal segment
Amygdala
Tail of caudate
© 2002 Sinauer Associates, Inc.


(B)
Septum pellucidum
Column of fornix
Insula
Putamen
Extreme capsule
Claustrum
External capsule
Foramen of Monro
Third ventricle
Crura of fornix
Genu of corpus callosum
Frontal horn of lateral ventricle
Head of caudate
Internal capsule:
Anterior limb
Genu
Posterior limb
Thalamus
Tail of caudate
Body of lateral ventricle
Splenium of corpus callosum
B
A
R
L
(From the Walter Reed Yakovlev collection.)
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Evolutionary Underpinnings

- A general evolutionary model – survival through interaction with the environment
- Object recognition and object location
- Motor or action programs-what to do and how to do it
- Intention programs-when to do it; when to act

Intention Programs

- Knowing when to start a behavior
- Knowing when not to start a behavior
- Knowing when to persist with a behavior
- Knowing when to stop a behavior

Types of Processing

- Stimulus-based processing (this includes reflexes, habits, skills, and procedures)
- Higher-order processing
- We usually do things automatically, just because they need to be done
- If circumstances change, higher-order processing, cognitive control mechanisms allow for “adjustments”

Adaptive Advantages of Stimulus-based Processing

- Simplicity of design
- Biologically cost effective
- High speed of reaction
- Exploitation of predictable features of the environment
- Under the proper conditions, the behavior always works

Disadvantages of Stimulus-based Processing

- Limitations to the number of viable trigger stimuli
- Problems of competition between triggers
- Little or no spontaniety or autonomy
- No capacity to generate/synthesize new behavior under novel environmental conditions
- No ability to “move in order to perceive”

Higher-Order Processing

- Managing novelty and ambiguity
- Problem-solving – setting the context for stimulus-based control
- Autonomy – programming goal-directed behavior

Disadvantages of Higher-Order Controls

- This system has one huge drawback – it is SLOW!
- Stimulus-based control – a system which is fast, accurate, efficient, but “dumb.”
- Higher-order control – a system which is smart, extremely flexible and creative, but slow.

The Frontostriatal System

- Nature's response to adaptive pressure is the frontostriatal system
- Both systems coexist
- Both systems interact in order to learn and benefit from interacting with the environment
- Bonus – solutions to "novel" problem-solving situations can be automated for future application.
- Adaptation is characterized by alternating episodes of automatic processing with higher-order control

Ideal Higher-Order Control Processing

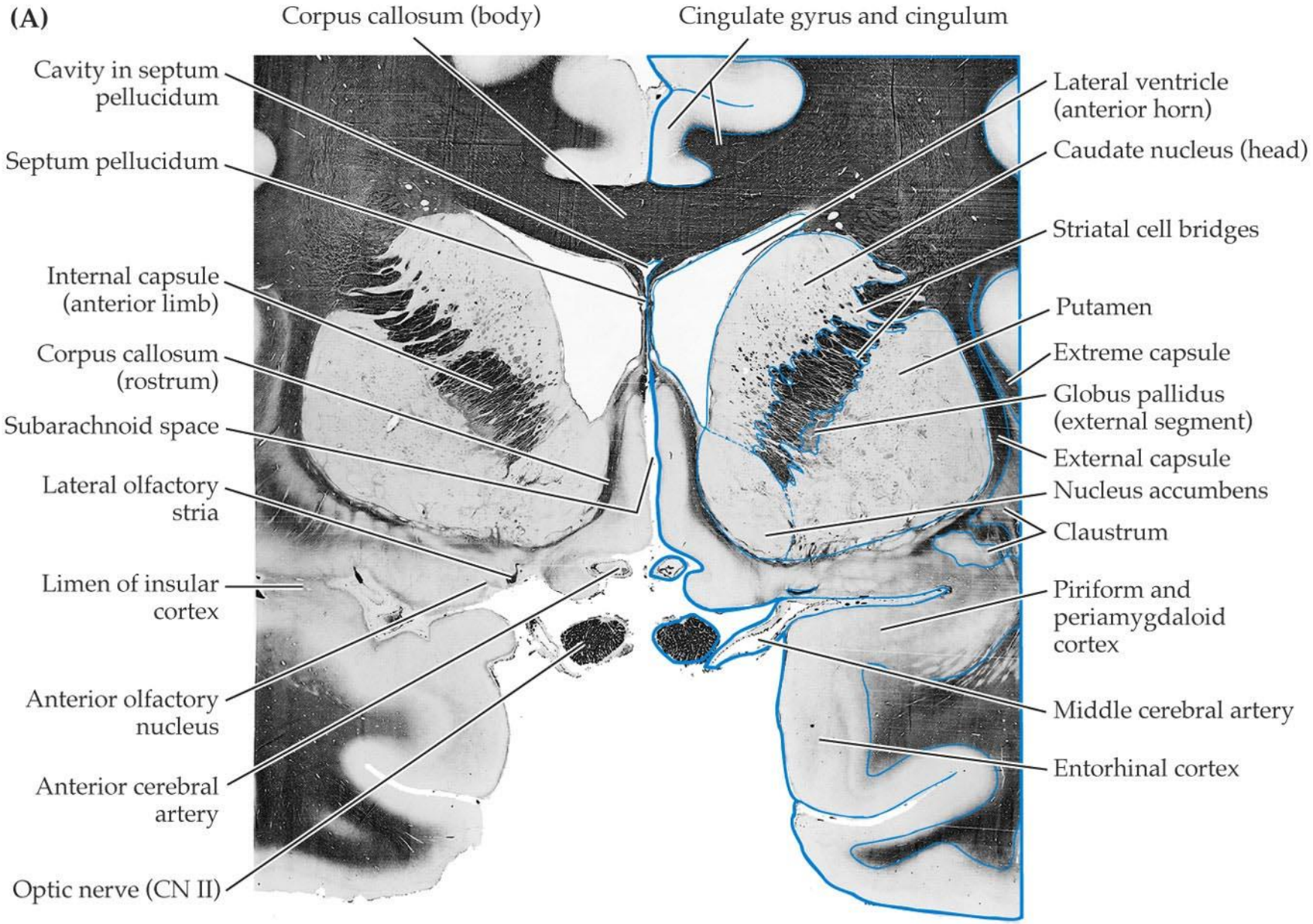
- Provide solutions in situations where stimulus-based control is unable to do so or has failed.
- Allow for a “best guess” or extrapolation based upon aspects of stimulus input or context.
- Determine goal-directed action by synthesizing certain response links and inhibiting others.
- To automate solutions to previously “novel” situations for future application.This is the “heart” of the matter – operating on the basis of acquired associations

What Functions Do The Basal Ganglia Serve?

- The BG promote the learning of procedures, habits, and cognitive skills-instrumental learning
- Highly specialized regions subserve movement, cognitive skills, and affective/emotional predispositions
- The linking of automatic movement with voluntary movement
- Intention (when) programs
- The BG are a selection mechanism

Phylogeny and the Basal Ganglia

- The forebrain components of the BG are well conserved across vertebrates
- The Nucleus Accumbens and the Globus Pallidus
- The Caudate and the Putamen
- The Basal Ganglia and the Cortex
- The connectional profiles we will discuss are phylogenetically very old.
- Implications for Executive Functions



(From Martin JH. 1996. *Neuroanatomy: Text and Atlas,* 2nd Ed. McGraw-Hill, New York.)

A Major Evolutionary Trend

- The striatum always receives sensory input from the largest and presumably most important sensory region of the brain.
- In amphibians, inputs originate from the dorsal thalamus.
- In reptiles, inputs originate from the ventral area of the olfactory cortex.

- In mammals, striatal inputs invariably arrive from the neocortex.
- In climbing up the phylogenetic scale, the striatum receives more and more highly processed and highly specialized sensory inputs.
- A major evolutionary trend is the progressive involvement of the cortex in the processing of the thalamic sensory information projected to the striatum.

- Mammals always direct output from the basal ganglia back to the thalamus and from there, back to cortex, maintaining segregated, parallel circuits.
- During the course of phylogenetic development, the neocortex was slowly and gradually grafted upon this system.

Why Is This of Critical Importance?

- The neocortex operates according to a principle of excitation.
- A complex organism cannot function only according to principles of excitation
- The basal ganglia are the first and only region of the brain that are capable of massive and selective inhibitory control
- Cortical-basal ganglia interactions control the processes of excitation versus inhibition, enabling focused attention and behavior.

Interim Conclusions

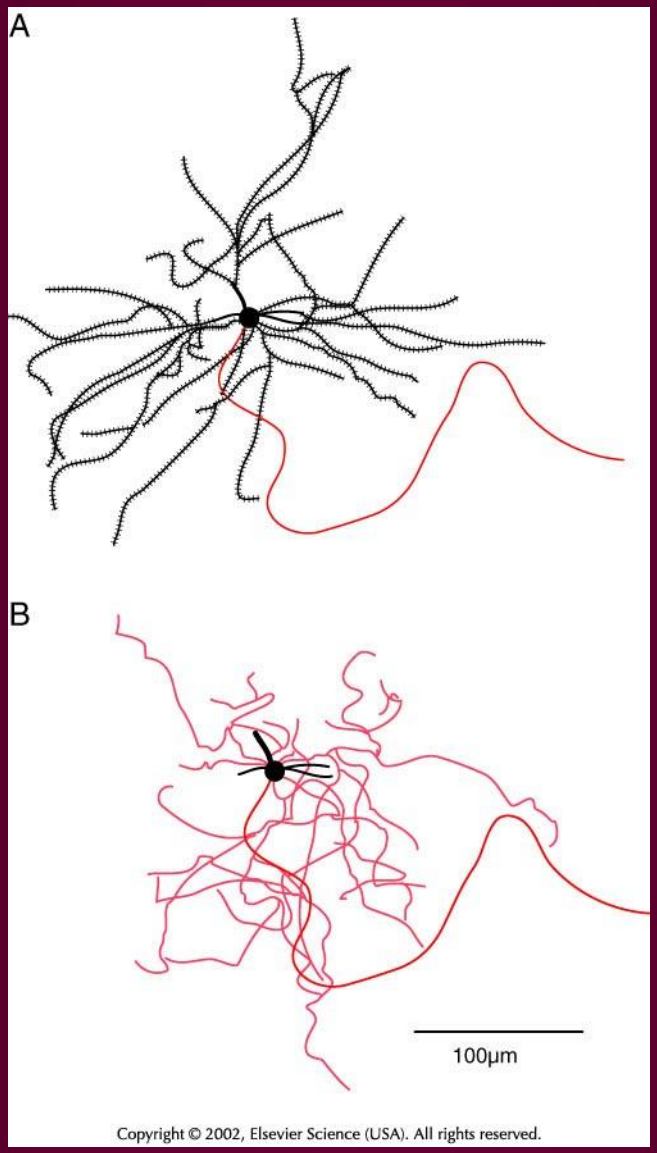
- The basal ganglia have always played a critical role in executive control
- The basal ganglia assist in allowing the organism to make choices and decisions which are in the best interest of the organism as a whole.
- The basal ganglia continue to serve a critical role within the executive functioning system.
- The basal ganglia are the vertebrate brain solution to the selection problem

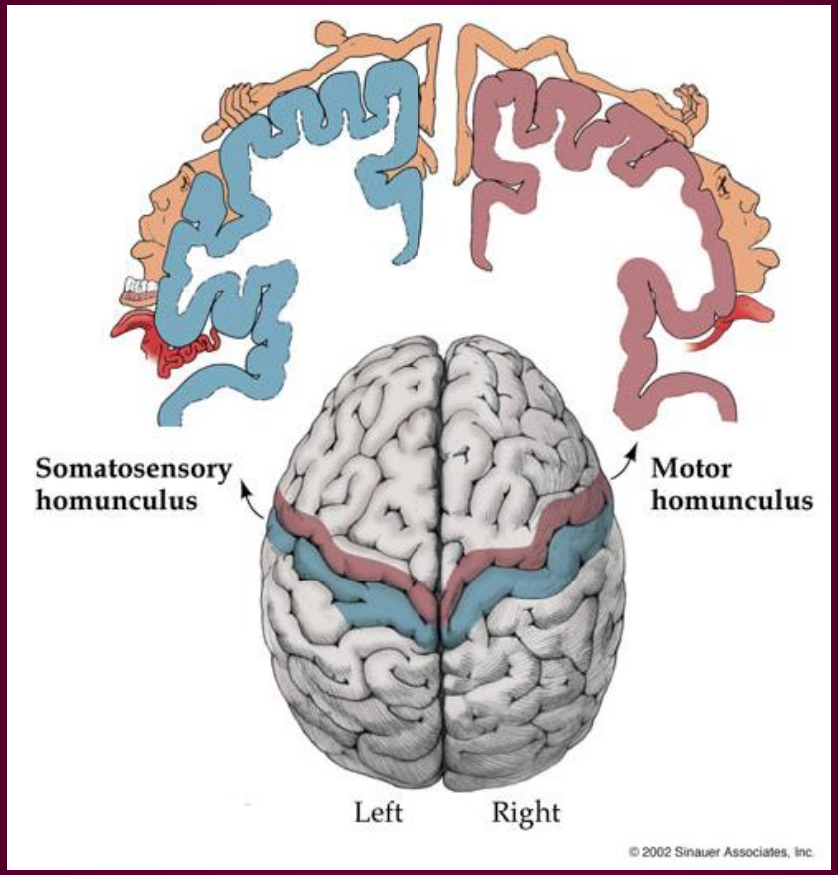
Basal Ganglia Input Structures

- Caudate
- Putamen
- Nucleus Accumbens
- These input structures receive direct projections from nearly the entire cerebral cortex

Matrix / Striosome Compartments

Graybiel, 2001




Somatosensory homunculus
Motor homunculus
Left
Right
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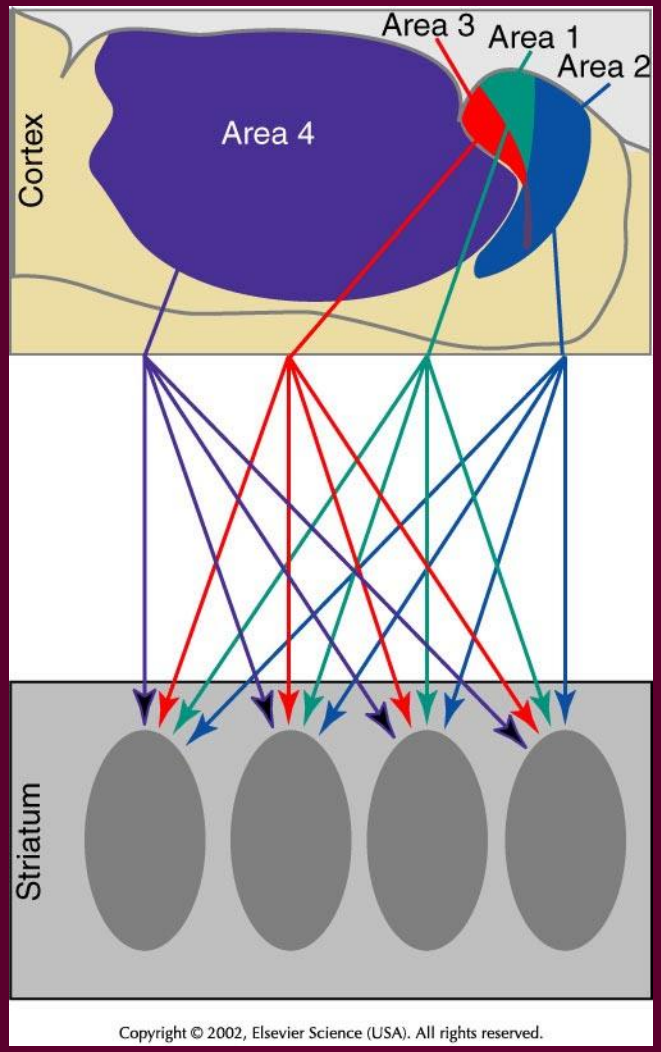


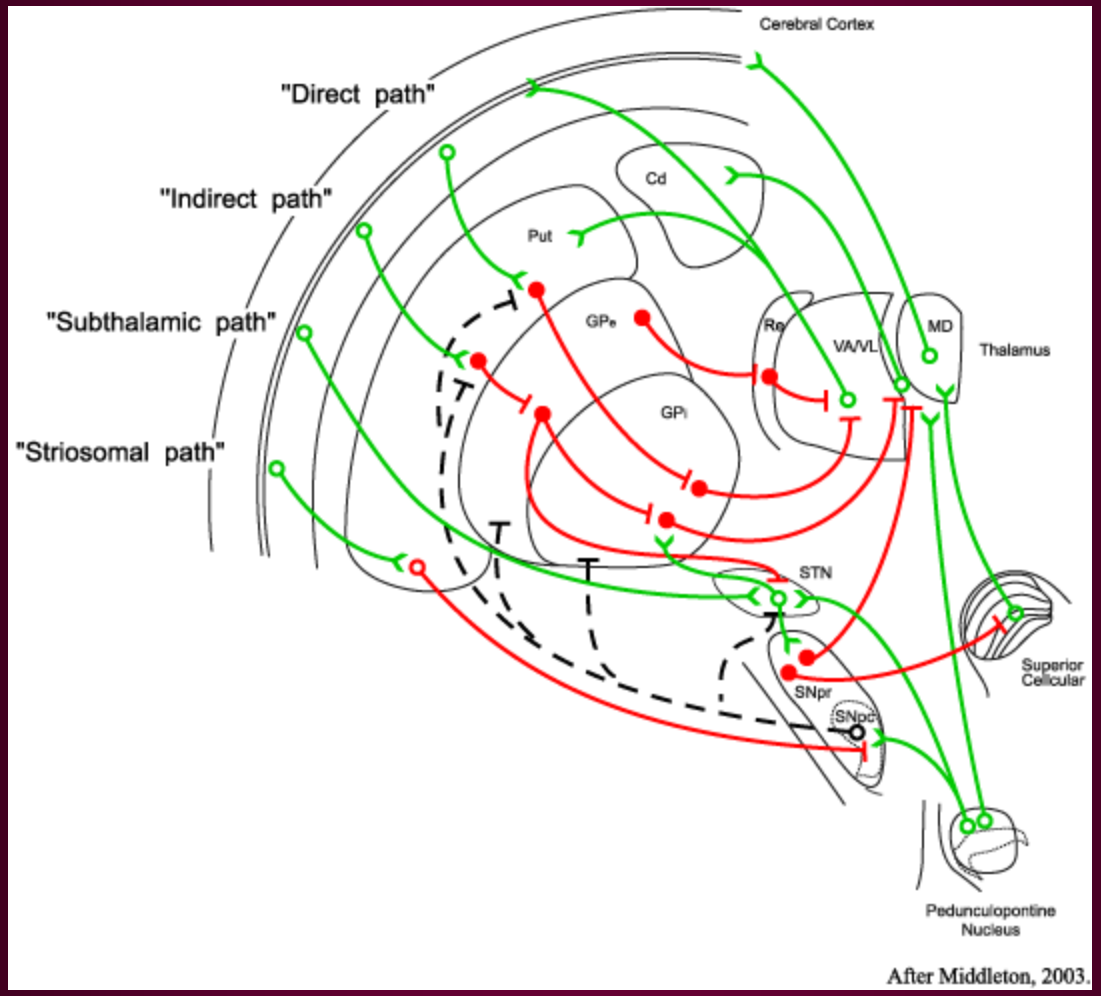
Basal Ganglia Intermediate Structures

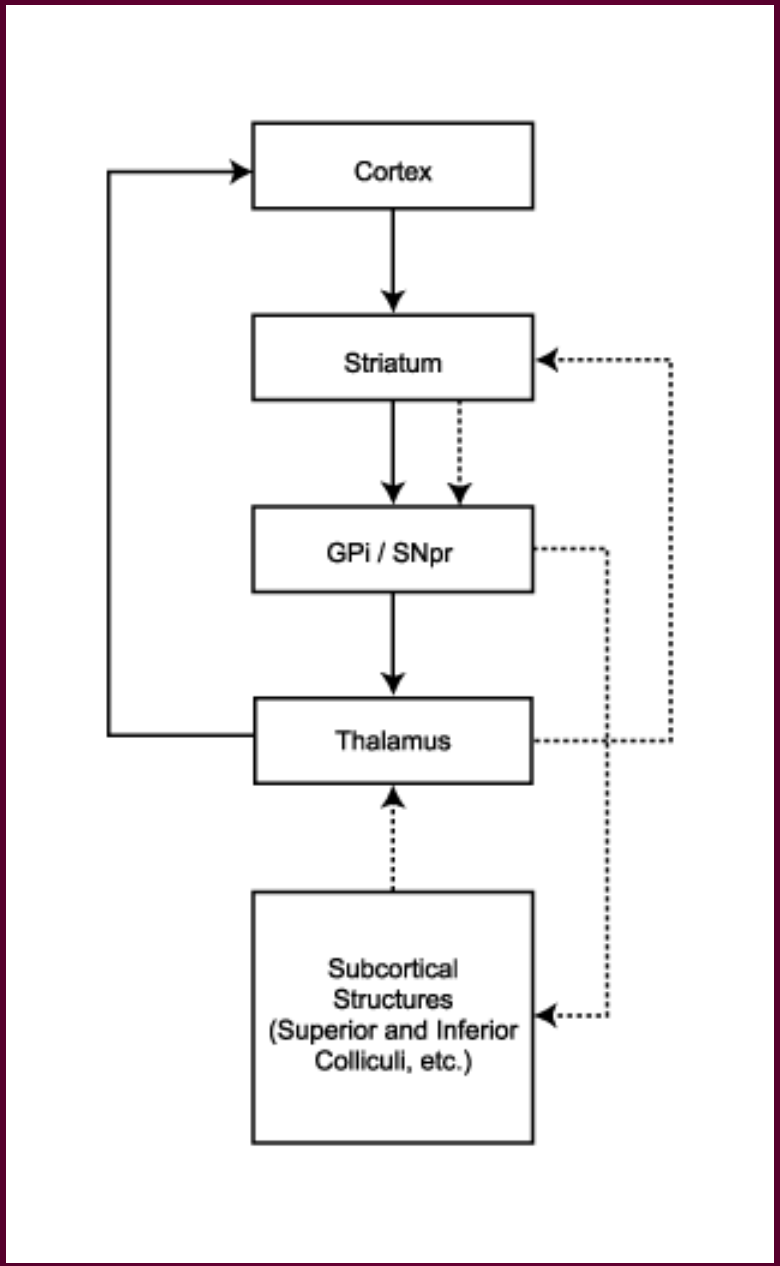
- Subthalamic Nucleus
- Globus Pallidus Externa
- Substantia Nigra Pars Compacta
- These nuclei project most heavily to other basal ganglia nuclei

Basal Ganglia Output Structures

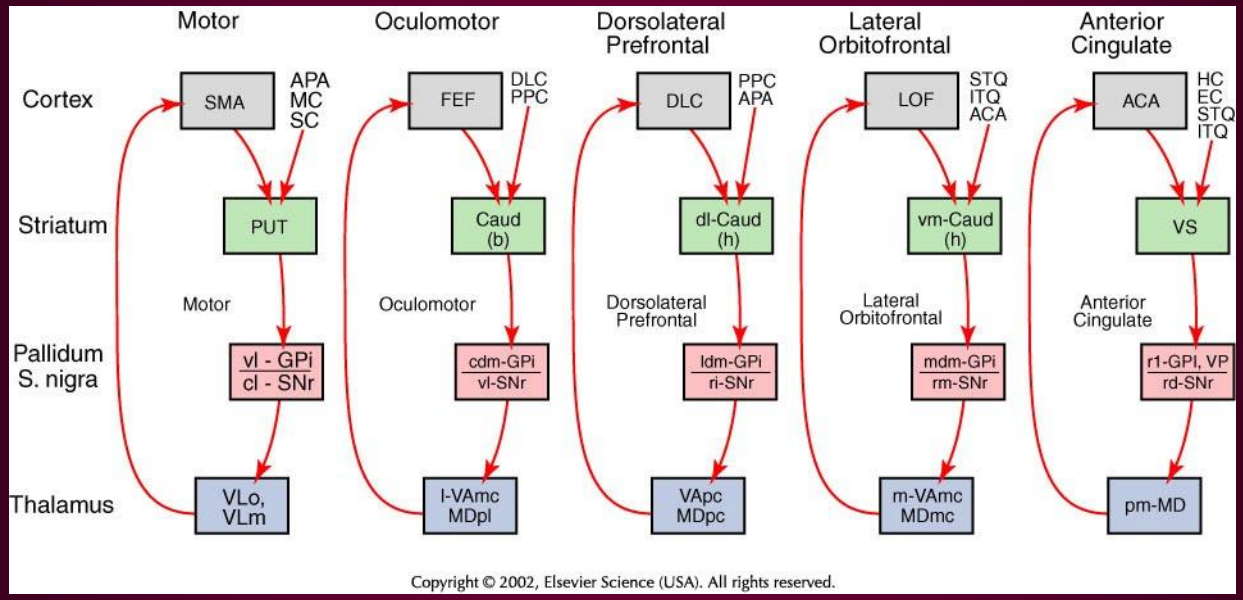
- Globus Pallidus Interna
- Substantia Nigra Pars Reticulata
- Ventral Pallidum
- These output nuclei send projections to the thalamus (VA/VL/DM/IL), which project back upon cerebral cortex

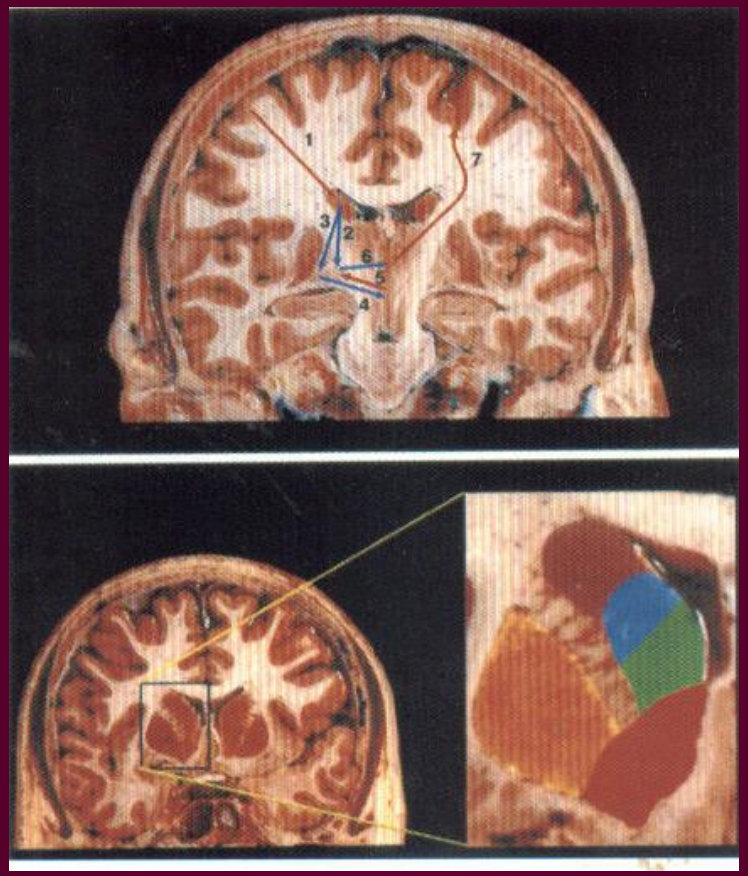
Cortical – Basal Ganglia Circuitry





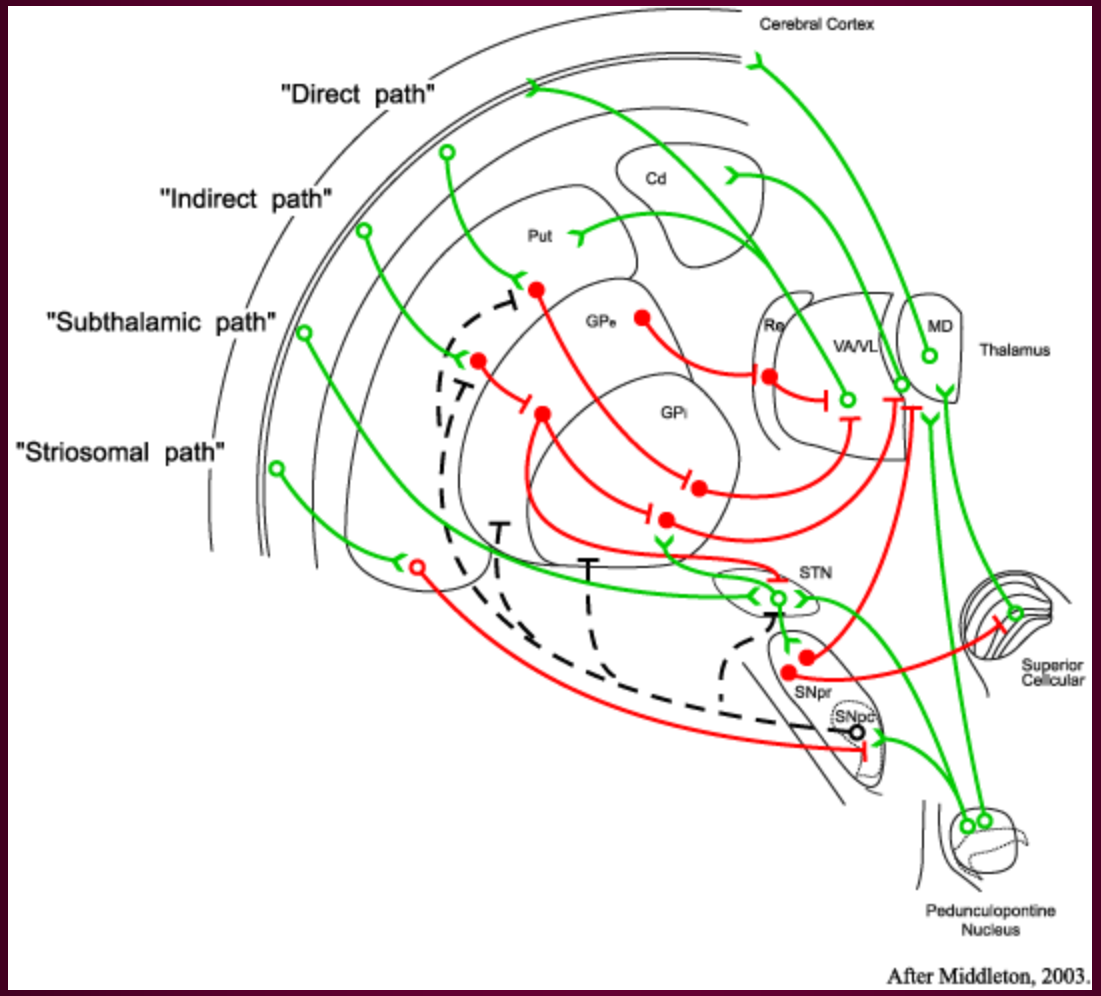
Koziol & Budding, 2009





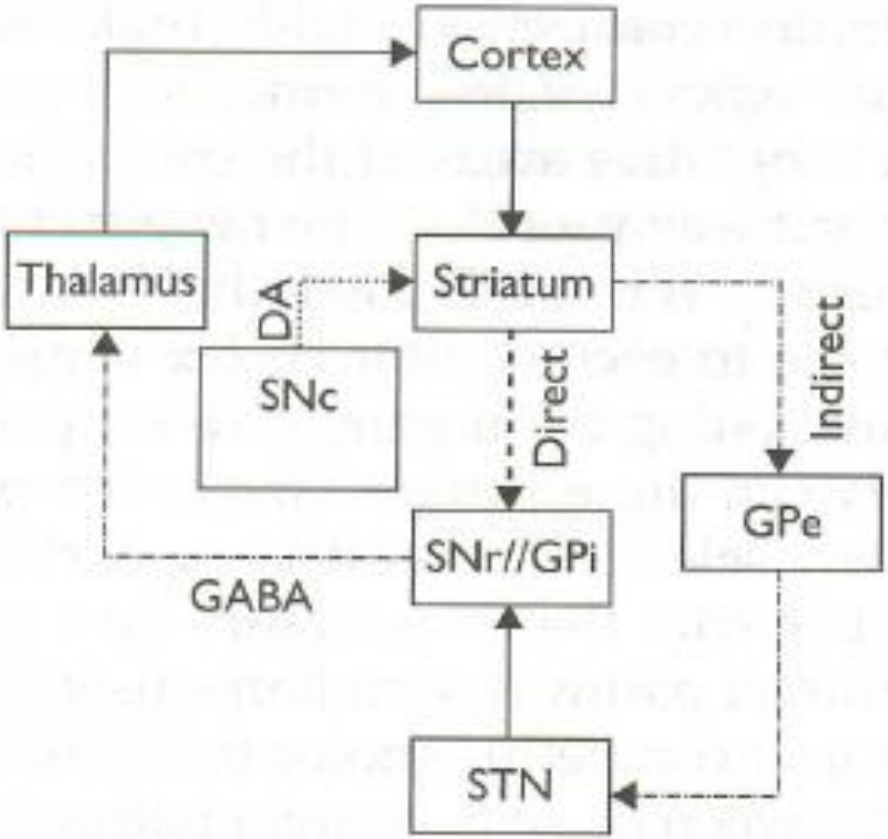
Salloway, Malloy, & Duffy,2001

Cortical – Basal Ganglia Circuitry

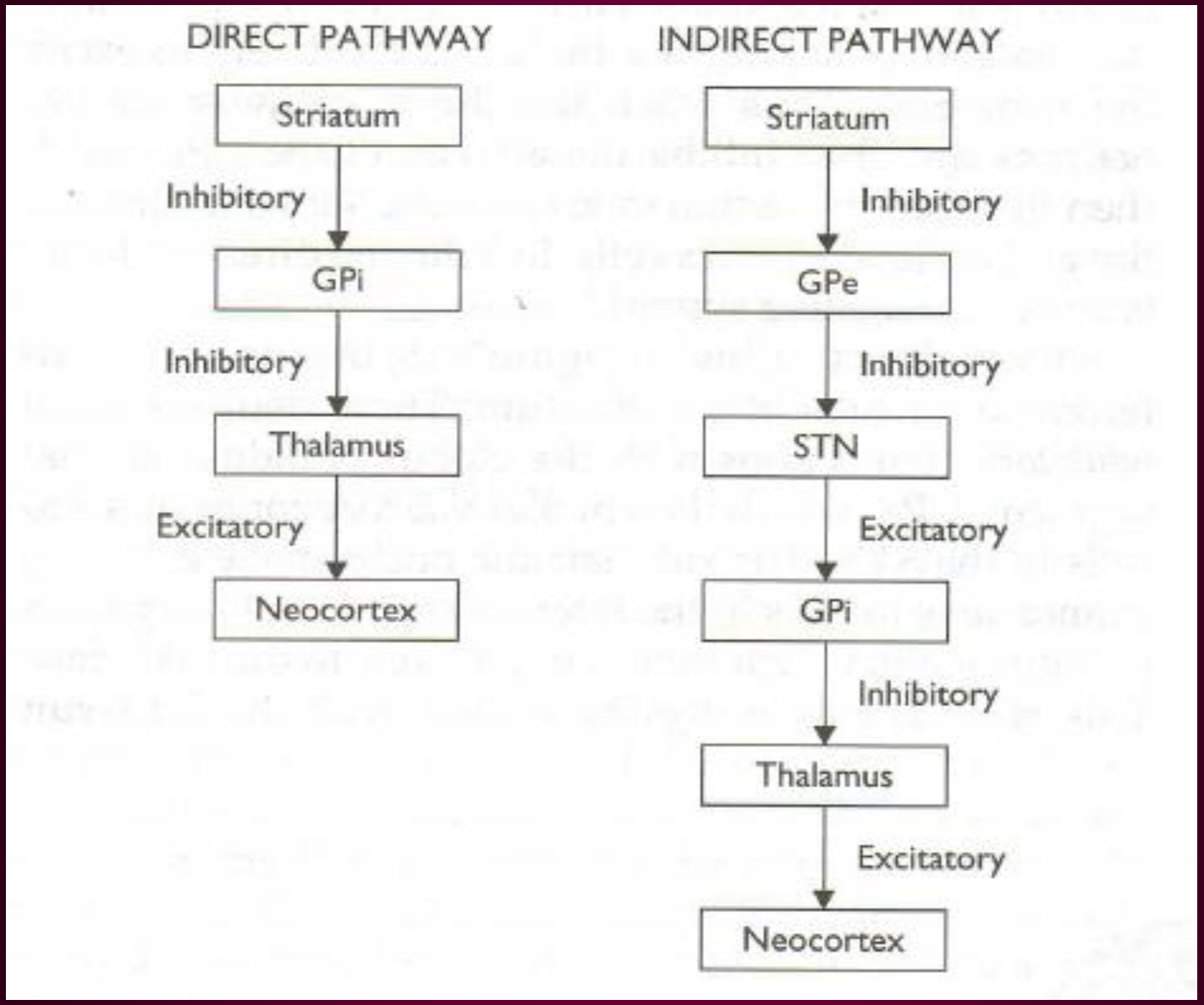


The Direct and Indirect Pathways

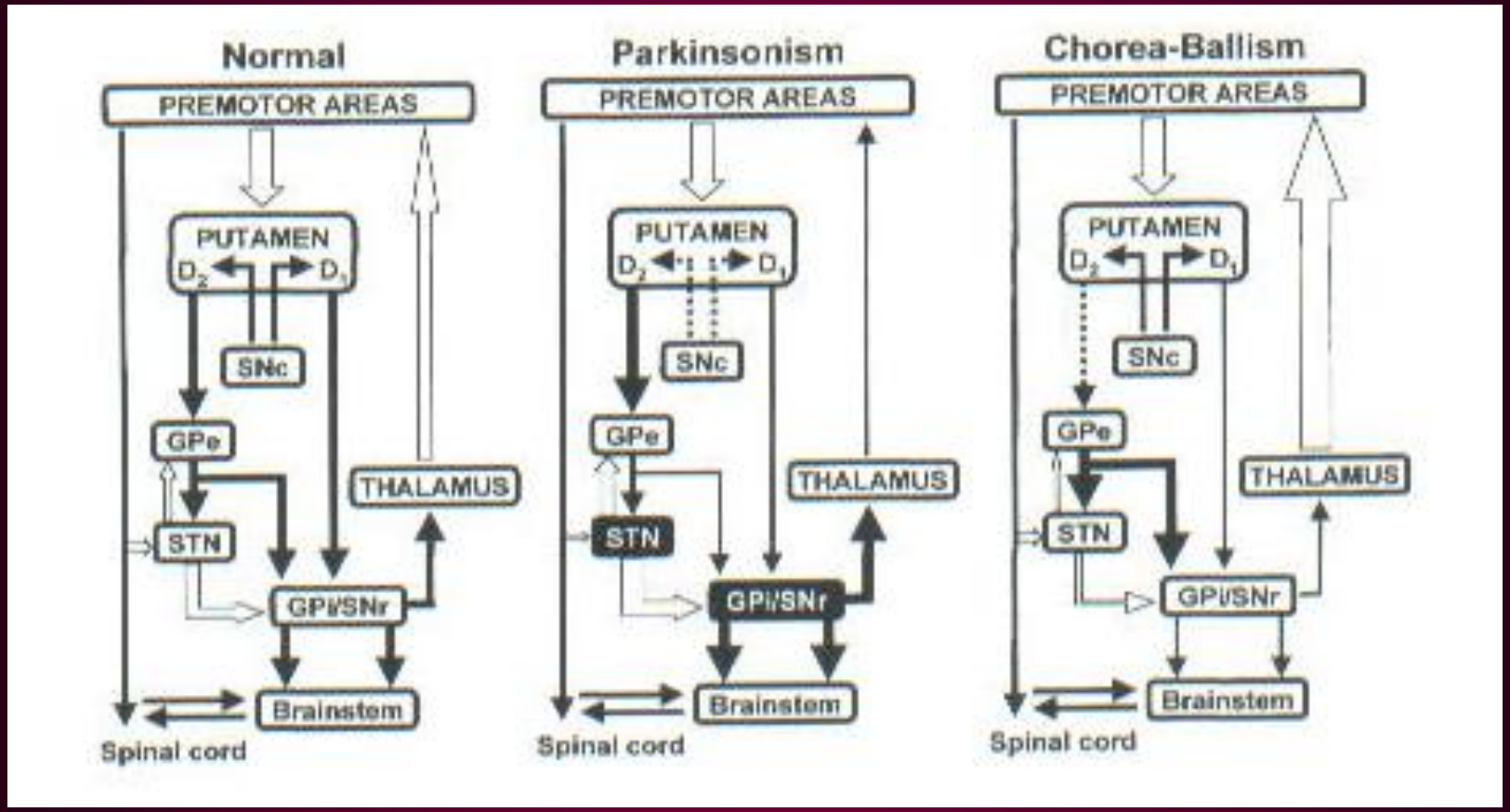
- Most cortical projections into the striatum have two pathways
- The Direct Pathway
- The Indirect Pathway
- These pathways project to the Matrix compartment



Springer, 2011



Springer, 2011



Parent & Cicchetti, 1998

The Hyperdirect Pathway

- The Subthalamic Nucleus – STN
- The Subthalamic/Hyperdirect Pathway
- Projections originate from frontal regions
- Quickly suppresses Thalamic activity

The Striosomal Pathway

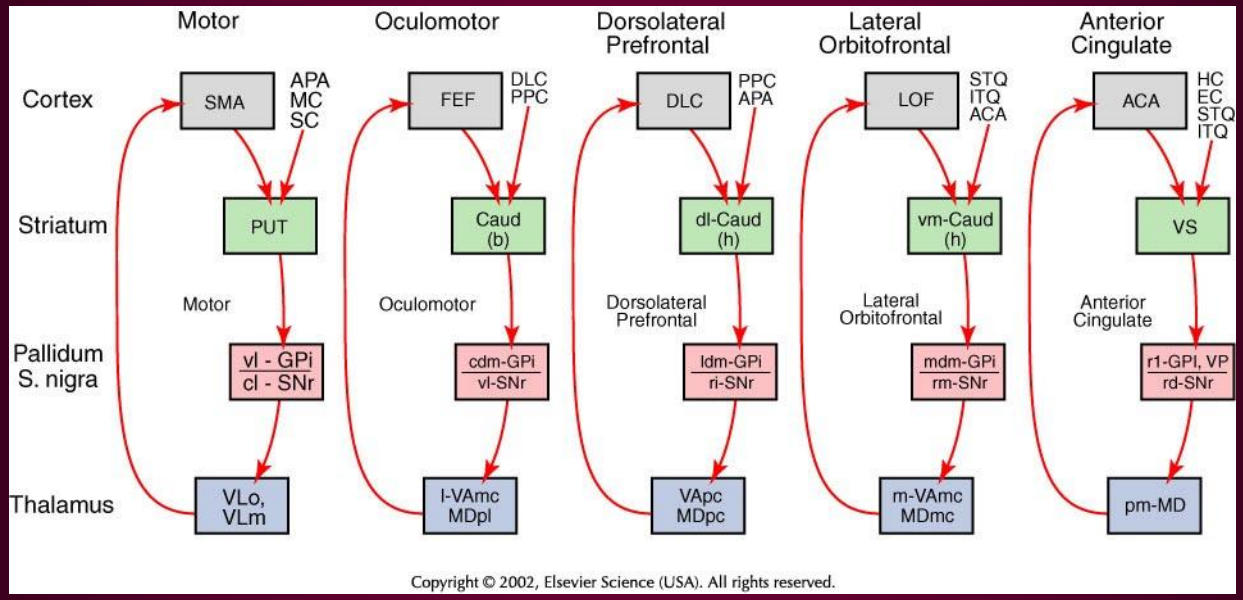
- Projections originate primarily from Orbitofrontal and Temporal limbic regions
- Project to the Striatal “Patches” or Striosomes
- This pathway projects to the SNpc

Matrix / Striosome Compartments

Graybiel, 2001

Excitation and Inhibition

- The Cortex – primarily functions according to principles of excitation
- The Basal Ganglia – a selection mechanism that balances excitation with inhibition
- Without these pathways, the vertebrate brain cannot decide/select what to attend do and what to do!



Information Integration and Learning

- The segregated, parallel connectional profile explains how attention and behavior can be sustained or maintained.
- However, we live in a constantly changing environment in which attention and behavior must be adjusted or changed to meet the demands of the internal/external environment as conditions develop.

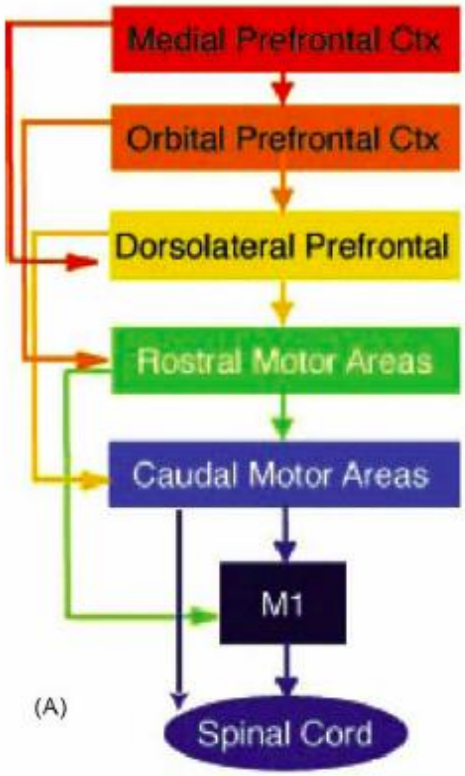
- Parallel and segregated processing through the identified circuits does not address this critical issue.
- Information must flow between circuits for generating new or changing previously learned behaviors.

Basal Ganglia Integrative Networks

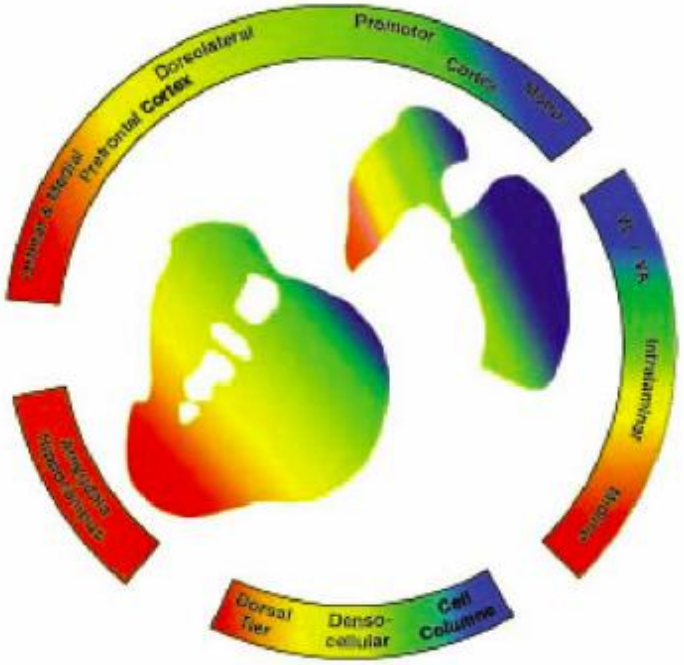
- Cortico-striatal pathways are characterized by focal, circumscribed, and topographically organized projections
- However, there is some overlap between terminal fields from these different functional regions.
- There are regions where focal projections from cognitive and reward-related prefrontal areas converge.

Matrix / Striosome Compartments

Graybiel, 2001


Medial Prefrontal Ctx
Orbital Prefrontal Ctx
Dorsolateral Prefrontal
Rostral Motor Areas
Caudal Motor Areas
M1
Spinal Cord

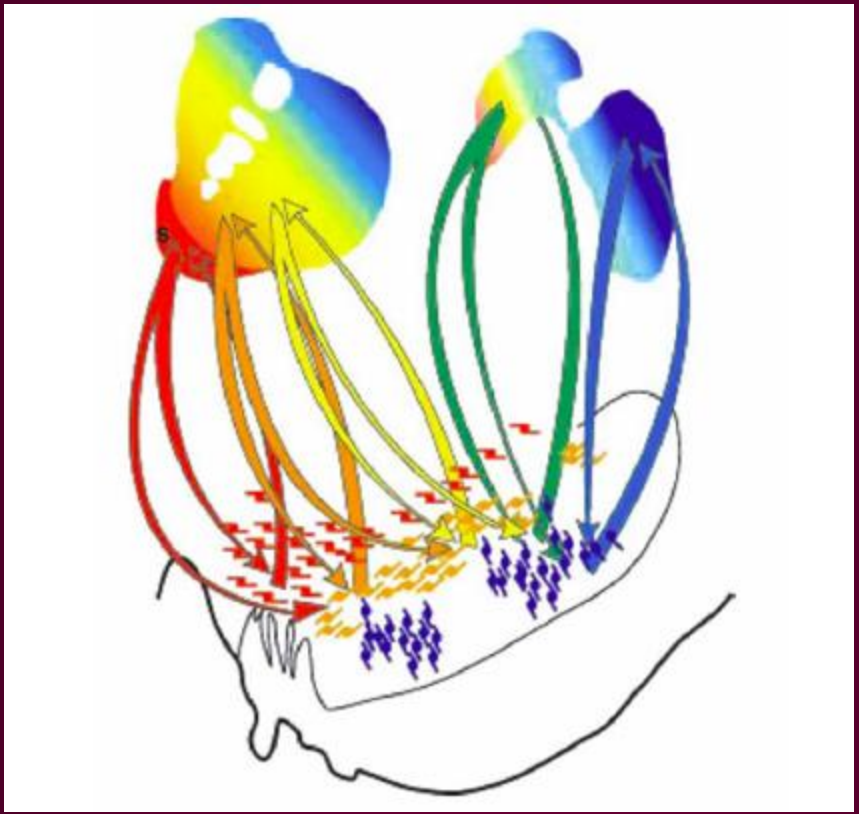
(A)


Dorsolateral Prefrontal Cortex
Premotor Cortex
Intralaminar
Cell Columns
Dorsal Tier
Dorsolateral

(B)

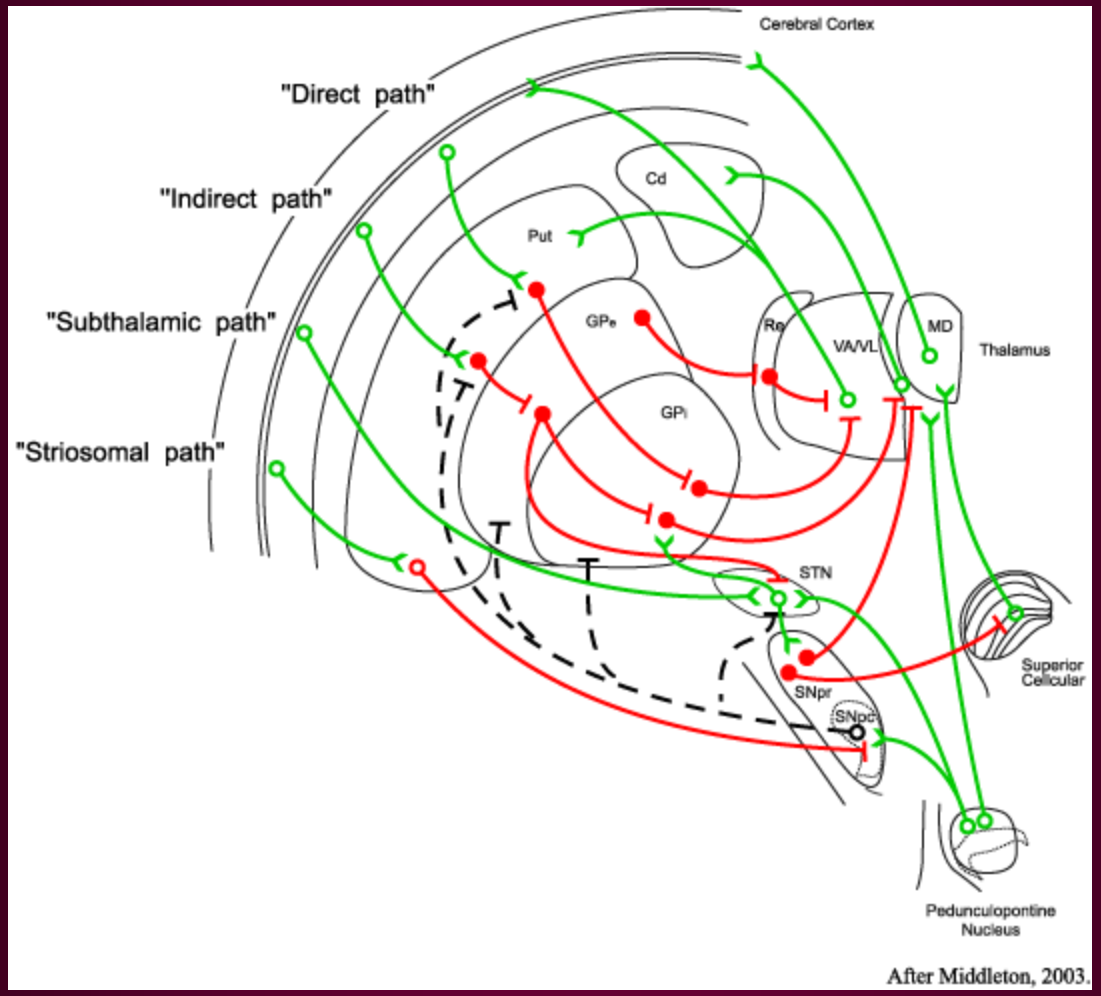
- Although the Gpi is also topographically organized according to functional domains, information integration occurs by convergence at the borders between functional domains.
- Within the Gpe, projection fibers extend well into other functional domains besides through the domain border areas.

- A striato-nigro-striatal projection system has also been identified.
- This midbrain, SN system includes reciprocal connections with cognitive, limbic/motivational, and motor regions of the striatum.
- This establishes a mechanism for integrating cognition and motivation for influencing motor decision-making processes.

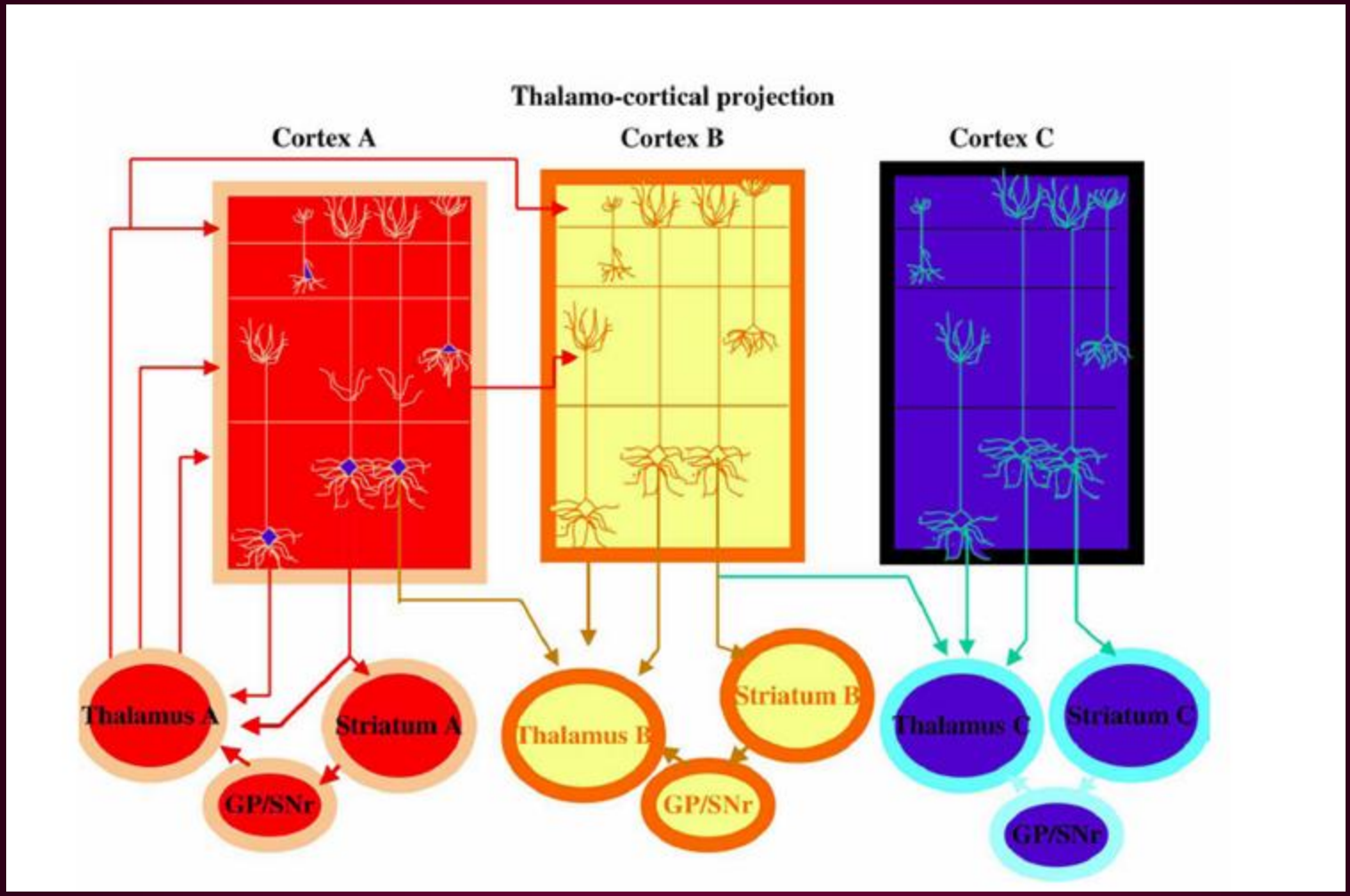


Haber, 2010

Cortical – Basal Ganglia Circuitry



- The thalamo-cortical pathway is not simply a “relay station” for thalamus to activate cortex.
- The thalamus has additional, non-reciprocal connections projecting to nearly all cortical layers, besides those parallel and segregated regions from which the cortico-striatal “loop” originated.


Thalamo-cortical projection
Cortex A
Cortex B
Cortex C
Thalamus A
Striatum A
GP/SNr
Thalamus B
Striatum B
GP/SNr
Thalamus C
Striatum C
GP/SNr

Haber, 2010

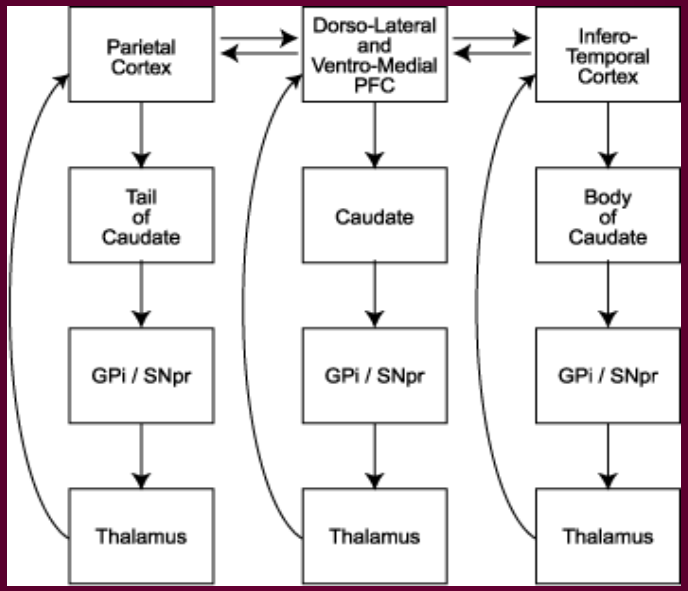
- Therefore, cognitive/associative, motivational/reward, and motor control functions are not discretely, distinctly, and completely segregated within cortico-striatal networks.
- Specific integrative networks function in concert with parallel circuitry.
- This allows for behavior to be focused and maintained, as well as modified and changed, and for new behaviors to be learned.

The Basal Ganglia and Working Memory

- Working memory consists of two contradictory demands
- Representations in working memory must be robust
- Representations in working memory must be flexible
- Working memory and motor programs

Cognitive Control

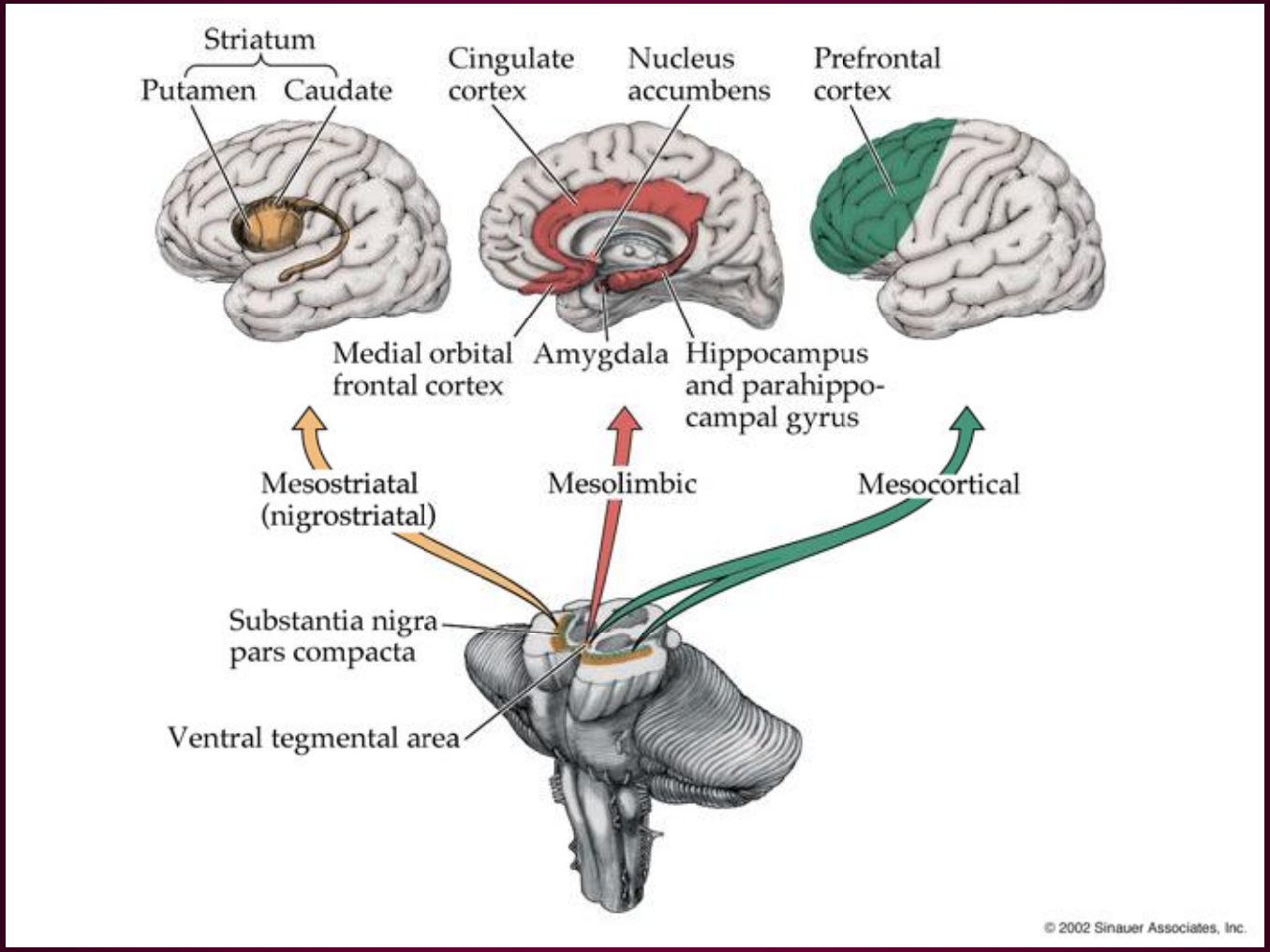
- Cognitive control is higher-order processing
- Working memory is cognitive control
- Cognition evolved and developed for the purpose of controlling the motor system
- Child development is the process of acquiring increasing control over the motor system



Koziol & Budding, 2010

The BASAL GANGLIA AND INSTRUMENTAL LEARNING

- The Basal Ganglia are an instrumental learning system.
- Instrumental learning is based upon Dopaminergic activity
- The roles of D1 and D2 in instrumental learning – sensitivity to the reward-based characteristics of the environment


Striatum
Putamen
Caudate
Cingulate cortex
Nucleus accumbens
Prefrontal cortex
Medial orbital frontal cortex
Amygdala
Hippocampus and parahippo-campal gyrus
Mesostriatal (nigrostriatal)
Mesolimbic
Mesocortical
Substantia nigra pars compacta
Ventral tegmental area
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DOPAMINE AND INSTRUMENTAL LEARNING

- Tonic Dopaminergic levels
- D1 receptors and sensitivity to the positive reward characteristics of the environment
- D2 receptors and sensitivity to the negative reward characteristics of the environment
- Dopaminergic “spikes” versus “dips.”
- Dopaminergic activity also modulates movement

The Basal Ganglia in Human Sequence Learning

- Learning a relative sequence of events across time
- Viewing 4 locations on a screen that correspond to 4 response keys
- Stimuli actually appear in a sequence
- Learning is measured by comparing reaction time to sequenced versus random ordered presentations
- Head of caudate and anterior putamen

Categorization and Classification

- The ability to respond differentially to objects or events that belong to separate classes or categories is termed categorization
- This ability is absolutely essential for adaptation and survival
- Not all complex category learning tasks are the same

Types of Category Learning

- Unstructured categories (my passwords, important phone numbers – MTL)
- Probabilistic learning
- Information-integration learning
- Rule-based category learning

Category Learning

- Category learning with feedback
- S's view stimuli and learn which stimuli belong in which category by trial and error
- PD and HD are impaired on classification learning
- High levels of caudate activity are are found on category learning tasks

Functional Specialization of Striatal Regions

- Learning about rewards involves the affective loop (VS and OFC)
- Learning visual categories involves the visual loop
- Boday/Tail of CN demonstrate increased activity during correct classification, activity increased with time course of learning, and greater activity is exhibited in good versus poor learners.
- Head of CN demonstrates peak activity with positive feedback

Cortical-Striatal Interaction

- Does the cortex “teach” the striatum what to do?
- Activity in the head of the CN peaks early after the beginning of each new task/problem and then drops.
- Activity in PFC reaches peak values later.
- Striatal activity preceeds frontal activity!

- These data are in agreement with theories that suggest the striatum identifies the behavioral context necessary for the frontal lobe to select an appropriate strategy.
- The striatum is important for recognizing the behavioral context and modulating activity in the cortex.

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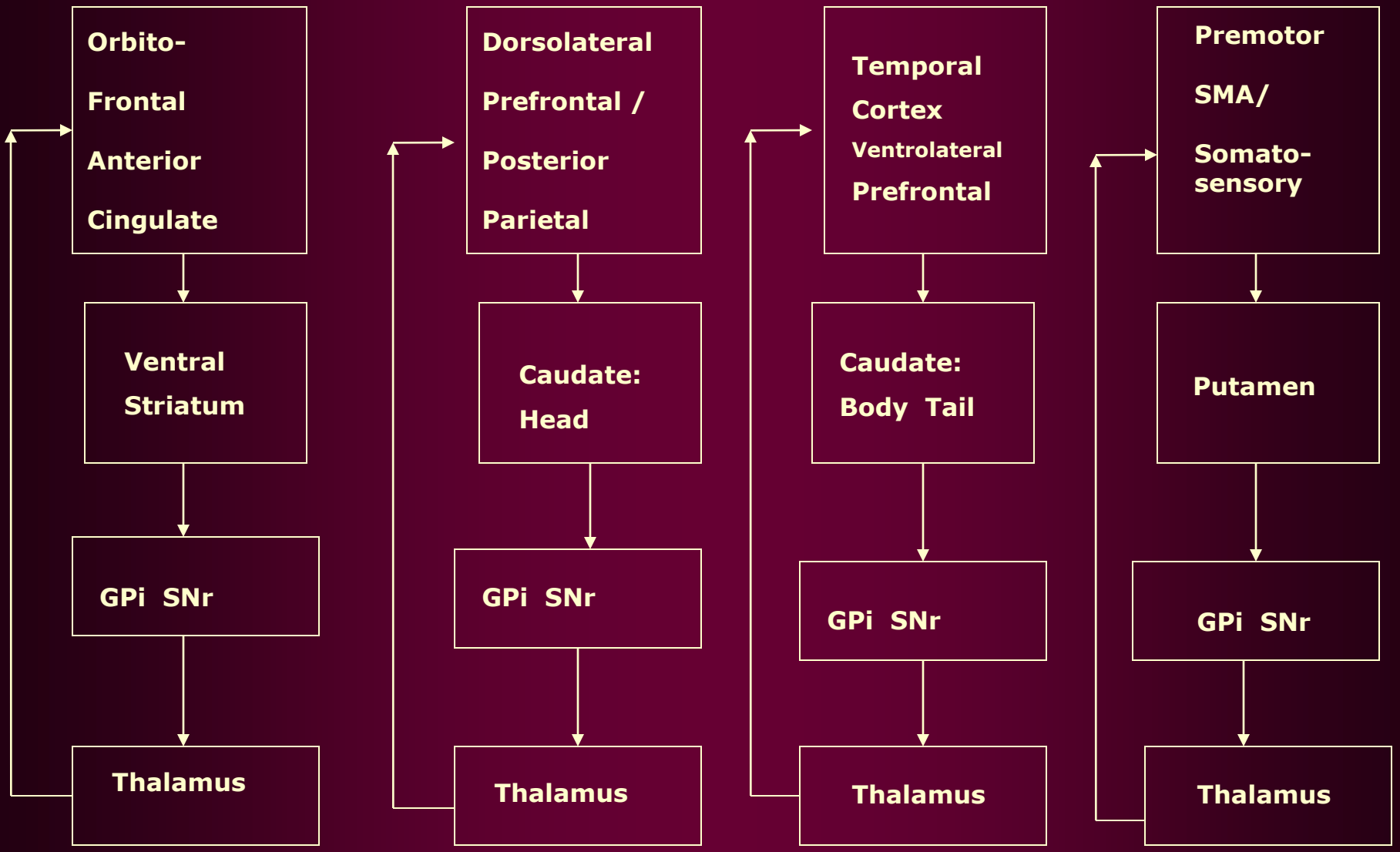
Parallel Corticostriatal Loops



Koziol & Budding, 2010

Interim Summary

- Stimulus-based processes and higher-order processes coexist and interact.
- The basal ganglia link automatic movements with voluntary movements so that behaviors are biologically adaptive.
- This linking includes translating sensory input into motoric “what” and “when.”

- The basal ganglia place a situation in context and select behaviors/mobilize procedures according to that context.
- PFC sets goals and develops new stimulus-based programs when existing programs do not work.
- The basal ganglia operate on the basis of reward-based instrumental learning – acquired associations
- This has direct implications for neuropsychological testing.

Neuropsychological Evaluation

- Sequence learning is not assessed
- Instrumental learning is not assessed; information about a person's sensitivity to the reward characteristics of the environment is not obtained
- The use of practice effect as a source of clinical information instead of practice effect as a source of error