The basal forebrain:

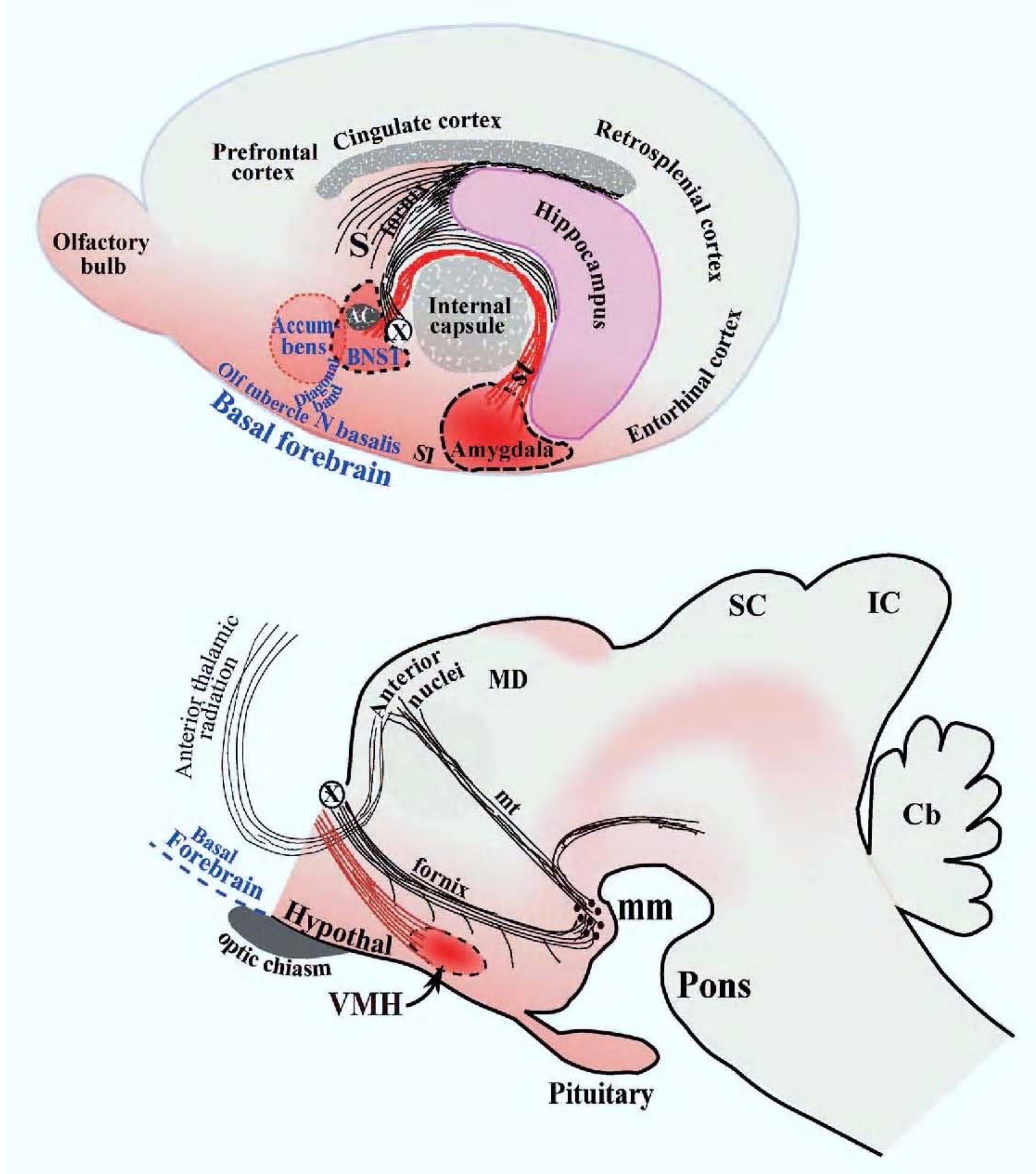
Questions, chapter 29:

7) What is the "basal forebrain", and what is its involvement in Alzheimer's Disease?

The acetylcholine-containing neurons of the nucleus basalis of Meynart degenerate in Alzheimer's.

Next slide: Cerebral hemisphere, medial view

Basal Forebrain structures



Courtesy of MIT Press. Used with permission.
Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Fig 29.9

Frontal sections: the limbic system of rodent

Basal forebrain structures: Ventral striatum, including

*** Nuc. Accumbens**

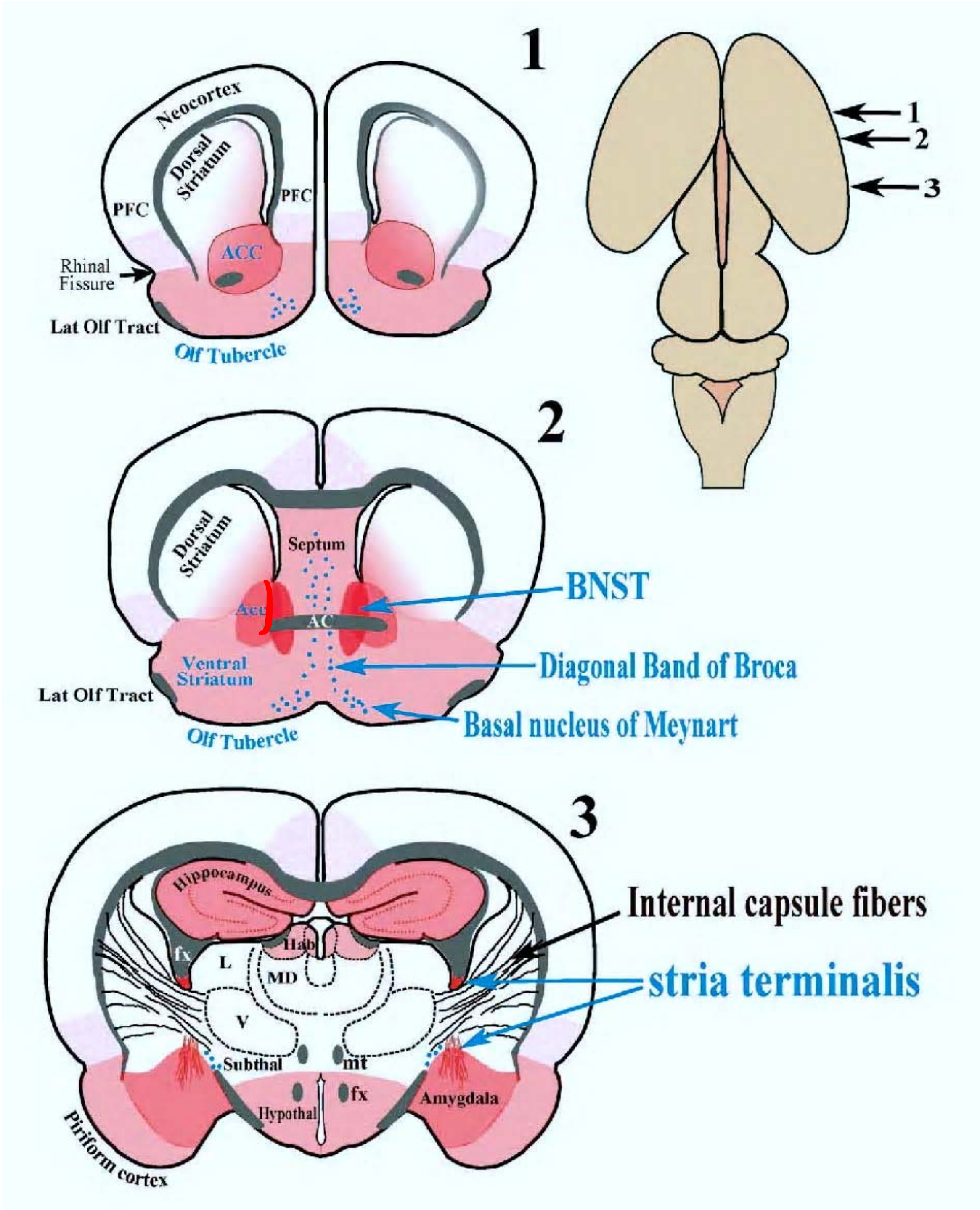
*** Bed Nuc. of the Stria Terminalis**

*** Olfactory tubercle**

*** Basal nuc. of Meynart**

*** Diagonal band of Broca**

Blue dots: ACh containing neurons



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Questions, chapter 29:

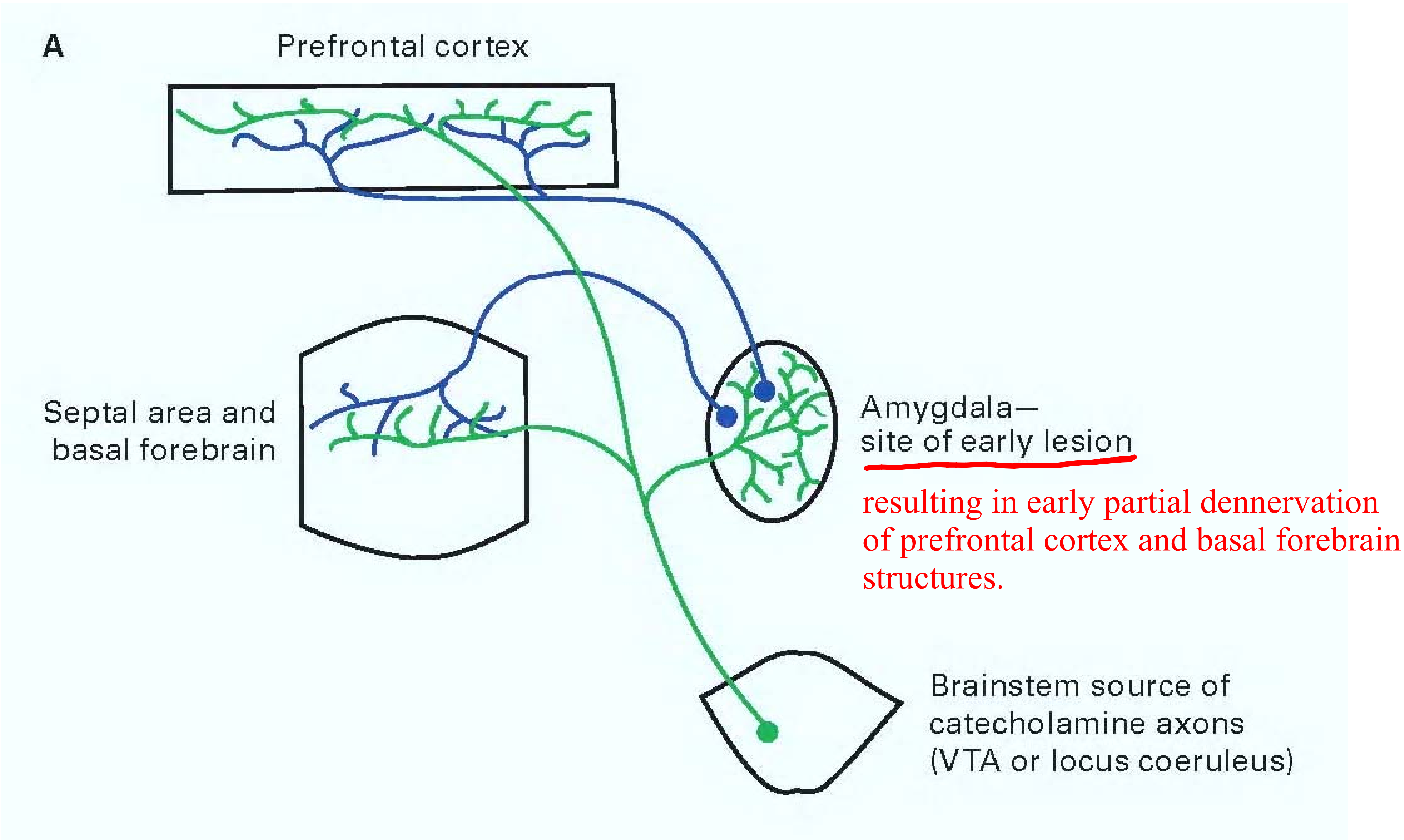
8) What kind of abnormal brain connections may be a cause of some types of schizophrenia? What could cause such abnormal connections to form?

Source of such an idea:

– ***Prenatal lesion hypothesis of the etiology of some types of schizophrenia: Damage to amygdala***

Prenatal damage to amygdala has been found to result in more hospitalization for schizophrenia than postnatal damage to the same structure. My interpretation of how this could lead to altered connections of DA or NE axons is illustrated in the next pictures.

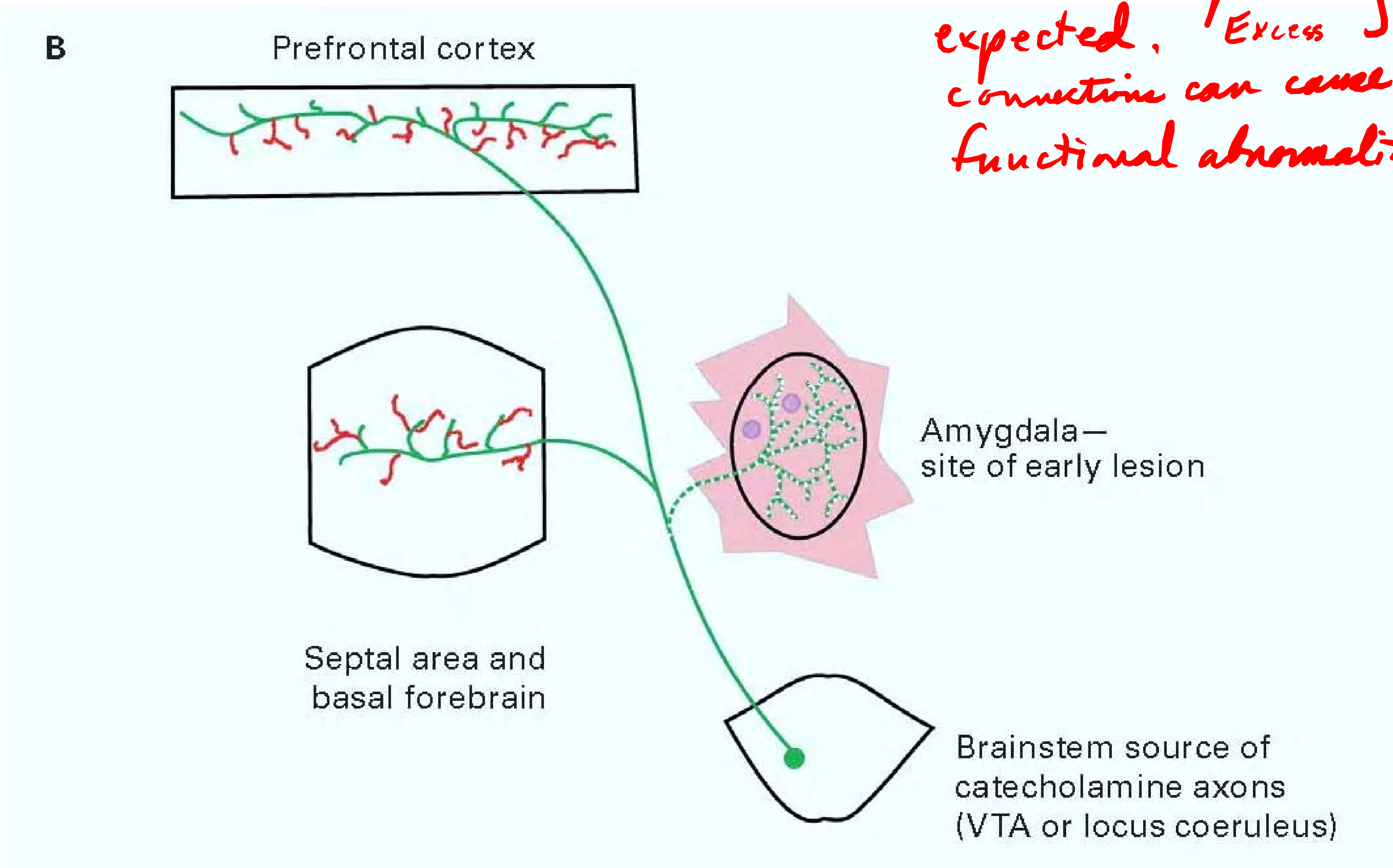
First, remember the research on the visual and olfactory systems that showed much greater plasticity--axonal sprouting or regeneration--after lesions suffered very early in life compared with lesions later in life.



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Fig 29.12A

Red: collateral sprouting expected. [Excess] connections can cause functional abnormalities



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Fig 29.12B

Evidence for such a lesion in some schizophrenic patients

Figure removed due to copyright restrictions. Please see course textbook or:
Hyde, Thomas M., and Daniel R. Weinberger. "The Brain in Schizophrenia."
In *Seminars in Neurology*, no. 3 (1990): 276-86.

note the enlarged ventricles in affected twin

Figure removed due to copyright restrictions. Please see course textbook or:
Shenton, Martha E., Ron Kikinis, et al. "Abnormalities of the Left Temporal Lobe and thought Disorder in Schizophrenia: A Quantitative Magnetic Resonance Imaging Study." *New England Journal of Medicine* 327, no. 9 (1992): 604-12.

Fig 29-11

Schizophrenia: ventricle to brain volume ratios

Enlarged ventricles are evidence of early brain damage.

Figure removed due to copyright restrictions.

[In schizophrenics with evidence of early brain damage, the amygdala is frequently reduced in size, a consequent of early damage.]

REMINDER: from earlier class on "Brain States"

Ascending monoamine neurotransmitter systems

(Zigmond 48.3)

Figure removed due to copyright restrictions. Please see figure 48.3 of:
Zigmond, Michael J., Floyd E. Bloom, et al. "Fundamental Neuroscience." (1999).

Antipsychotic Drugs

Figure removed due to copyright restrictions.

Note the binding to dopamine and norepinephrine receptors by these drugs.

(Such binding reduces synaptic activity by blocking the postsynaptic

A sketch of the central nervous system and its origins

G. E. Schneider 2014

Part 10: Corpus striatum

MIT 9.14 Classes 33-35

Corpus striatum,

the major subpallial structure underlying behavior control by the endbrain

Chapters 30-31

Review

Evolution of corpus stiatum: Next, we review pathways supporting this story

1. Beginnings: a link between olfactory inputs and motor control: The link becomes “Ventral striatum”.

2. Non-olfactory inputs invade the striatal integrating mechanisms (*via* paleothalamic structures).

3. Early expansions of endbrain: Striatal and pallial.

4. Pre-mammalian & then mammalian expansions of cortex and striatum: For the striatum, the earlier outputs and inputs remain as connections with neocortex expand.

Figure 1. Postulated beginnings in primitive chordates

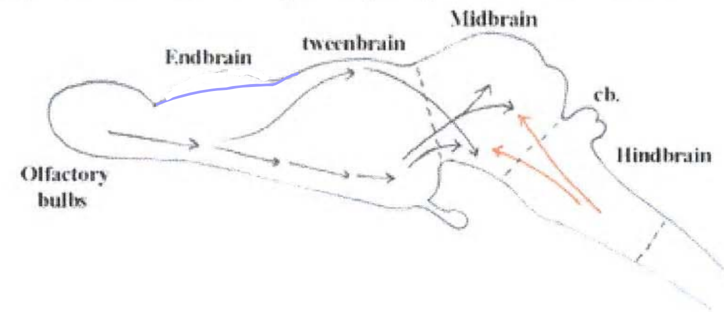


Figure 2. Other inputs reached the striatum

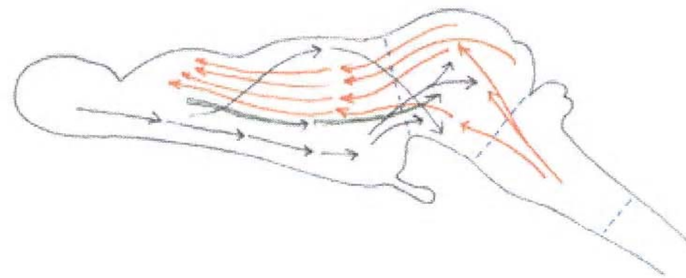


Figure 3. Early expansion of striatal and adjacent " limbic" areas

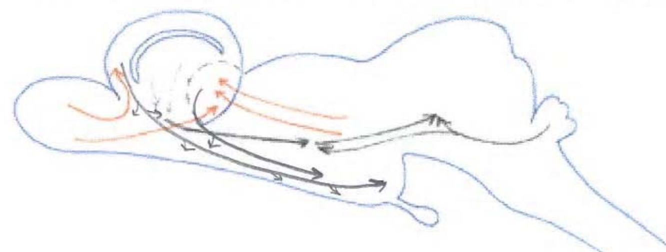
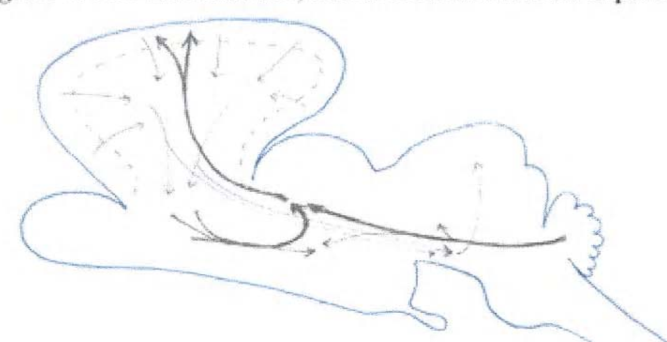


Figure 4. Pre-mammalian, and then mammalian expansions



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

What are the primitive outputs?

- To hypothalamus & subthalamus, including what became the hypothalamic & subthalamic locomotor areas; also to epithalamus (especially the habenula)
  - Influences on endocrine system & motivational states controlling inherited action patterns, *via* midbrain
- To midbrain for influencing three types of motor control:
  1) Locomotion (towards or away from something)
  2) Orienting of head and eyes
  3) Grasping with mouth or forelimb

(Connections to midbrain were probably not direct at the beginning.)

Review

Evolution of corpus striatum:
basic outline of a story

1. Beginnings: a link between olfactory inputs and motor control: The link becomes "Ventral striatum". **It was a <u>modifiable</u> link (capable of experience-induced change).**

2. Non-olfactory inputs invade the striatal integrating mechanisms (via paleothalamic structures).

3. Early expansions of endbrain: striatal and pallial.

4. Pre-mammalian & then mammalian expansions of cortex and striatum: For the striatum, the earlier outputs and inputs remain as connections with neocortex expand.

Figure 1. Postulated beginnings in primitive chordates

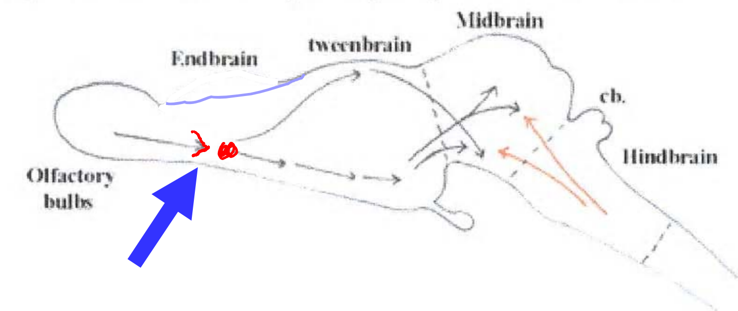


Figure 2. Other inputs reached the striatum

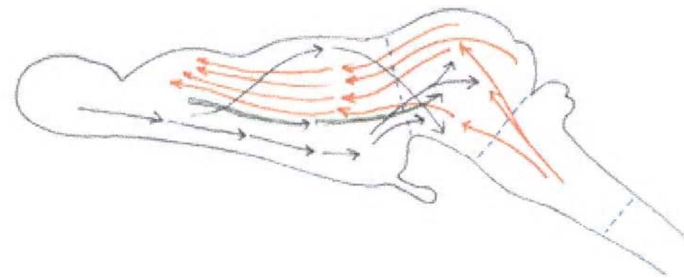


Figure 3. Early expansion of striatal and adjacent " limbic" areas

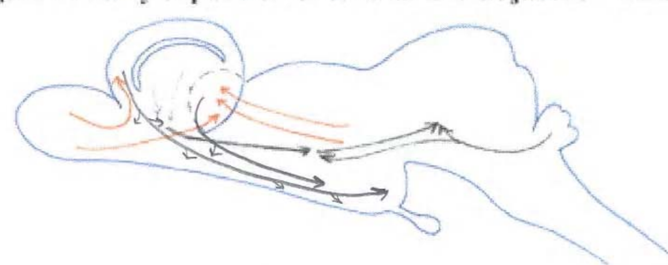
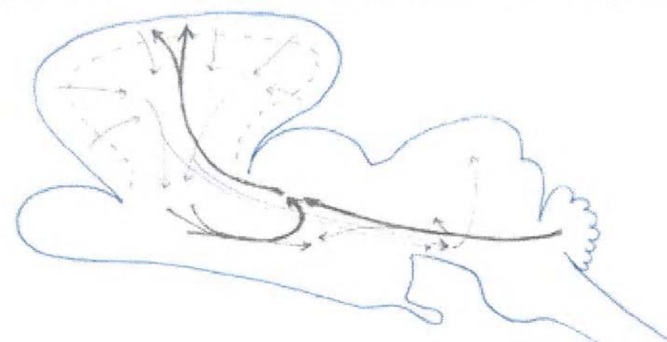


Figure 4. Pre-mammalian, and then mammalian expansions



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

From Class 25 (Forebrain intro., see chapter 24)

Plasticity of the links to the output systems: **How?**

- Feedback from sensory systems monitoring the consequences of the outputs. This feedback could activate reward mechanisms:
  - Reward mechanisms *via* the dopamine pathways from brainstem into striatum:
    - **From posterior tuberculum** and hypothalamus in most vertebrates (lampreys, cartilaginous fishes, ray-finned fishes, lungfishes, amphibians)
    - **From ventral tegmental area and substantia nigra** in the amniotes* and in sharks, skates and rays.

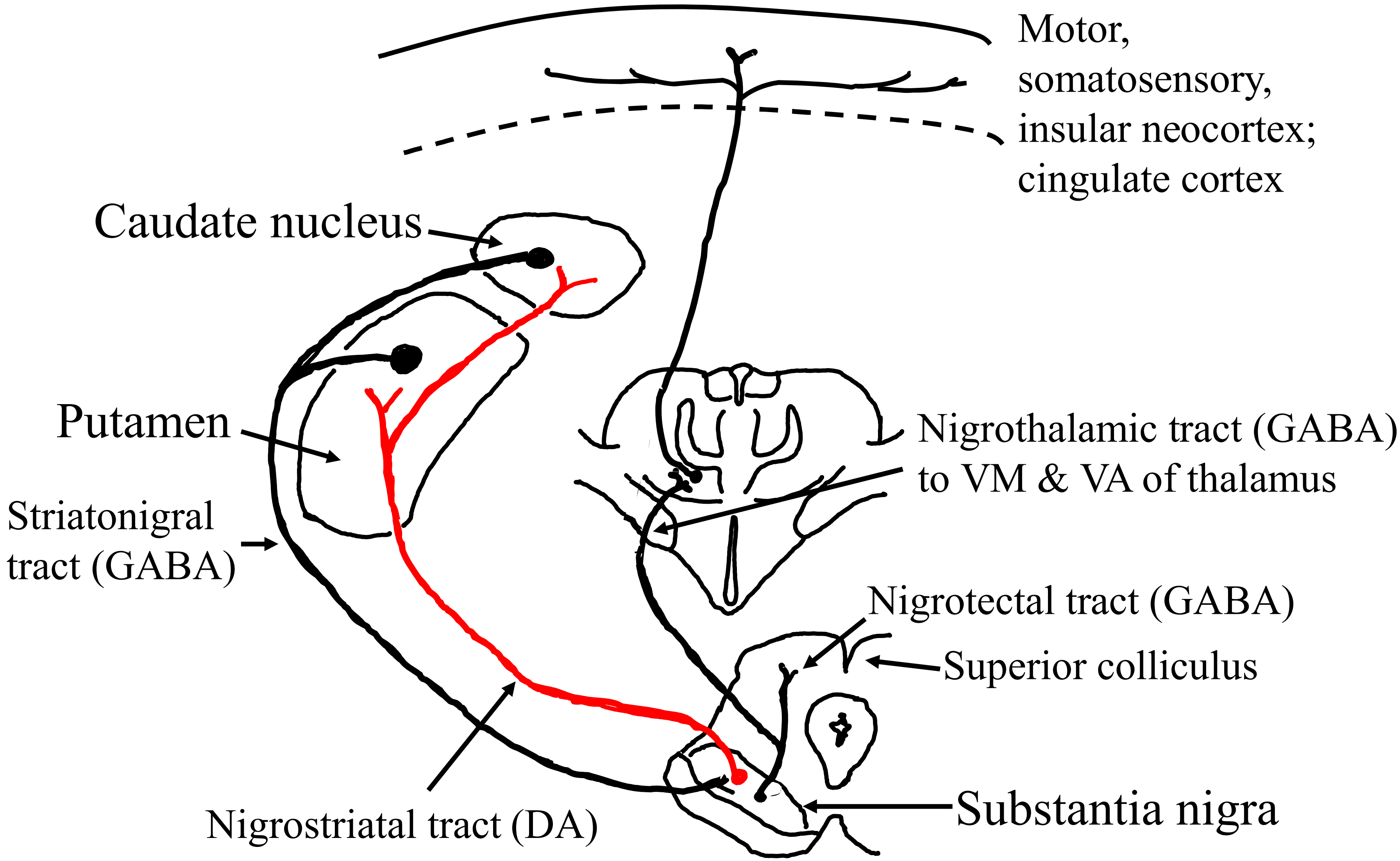
* mammals, birds, reptiles

- An input to these dopamine cells comes from the taste system—an obvious source of feedback.
  - This feedback may have been one of the earliest to evolve
  - Other inputs are numerous and have become more dominant in many species.

In present-day mammals, the substantia nigra is a major recipient of the striatal outputs

- The nigra (*pars compacta*) is the major source of dopamine axons destined for the dorsal striatum, whereas the VTA is the major source for the ventral striatum.
- The nigra *(pars reticulata)* projects to superior colliculus, thereby influencing orienting movements.
- It also projects to the thalamic nuclei that project widely to motor and somatosensory neocortex, to the insula and to the cingulate cortex.

These connections to and from the substantia nigra are depicted on the next slide.



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

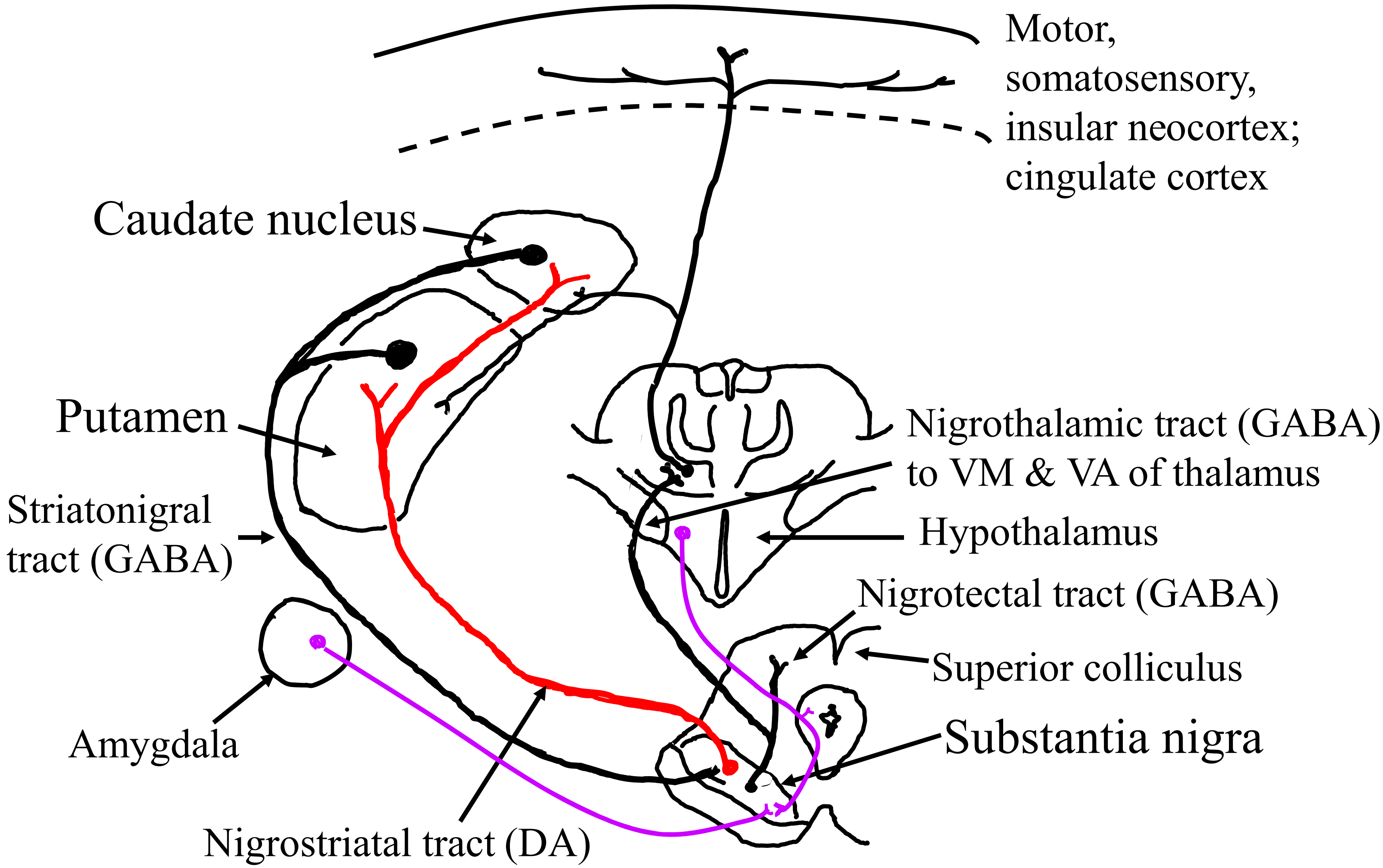
Some of the main connections of substantia nigra in mammals: the dopamine pathway shown was probably preceded in evolution by the DA pathway from VTA to ventral striatum.

A question naturally arises:

If the nigra is signalling reward/punishment to the striatum, how does it get the necessary feedback?

- Studies of nigral inputs as well as outputs have shown additional connections.
- Examples:
  - Connections from central nucleus of amygdala
  - Connections from hypothalamus (both anterior and posterolateral)
  - Thus, non-limbic and limbic system inputs appear to meet here
- The nigra is also reciprocally connected to the midbrain locomotor region, and it projects back to the striatum.

See the next slide:



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Some of the main connections of substantia nigra in mammals: the dopamine pathway shown (in red) was probably preceded in evolution by the DA pathway from VTA to ventral striatum. Connections with the pedunculopontine nucleus of the midbrain locomotor region are not shown.

Review

Evolution of corpus striatum: *back to the story*

1. Beginnings: a link between olfactory inputs and motor control: The link becomes "Ventral striatum".

2. Non-olfactory inputs invade the striatal integrating mechanisms (via paleothalamic structures): Dorsal striatum begins to expand*

3. Early expansions of endbrain: striatal and pallial.

4. Pre-mammalian & then mammalian expansions of cortex and striatum: For the striatum, the earlier outputs and inputs remain as connections with neocortex expand.

Figure 1. Postulated beginnings in primitive chordates

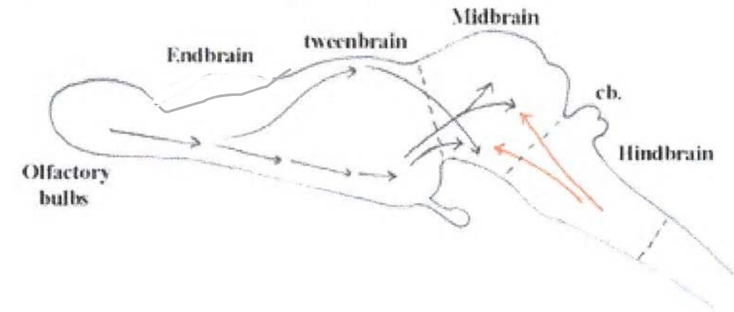


Figure 2. **Other inputs reached the striatum**

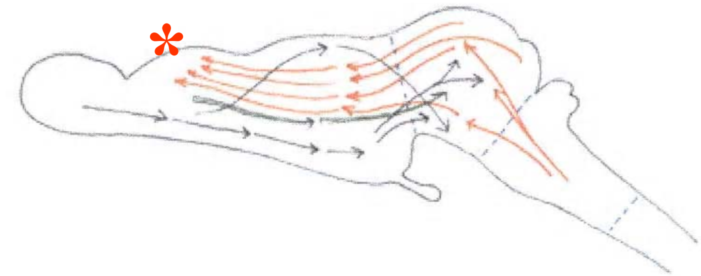


Figure 3. Early expansion of striatal and adjacent " limbic" areas

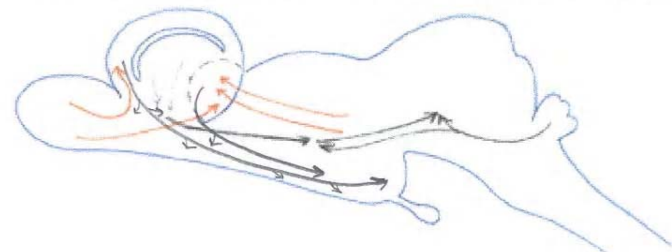
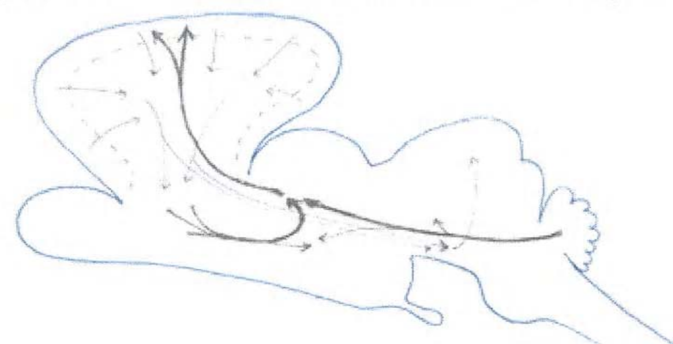


Figure 4. Pre-mammalian, and then mammalian expansions



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

The primitive sensory pathways to striatum remain in modern mammals:

Major afferents of dorsal striatum:

- DA axons from the substantia nigra
- **Sensory inputs via the paleothalamus**
- Inputs via the neocortex

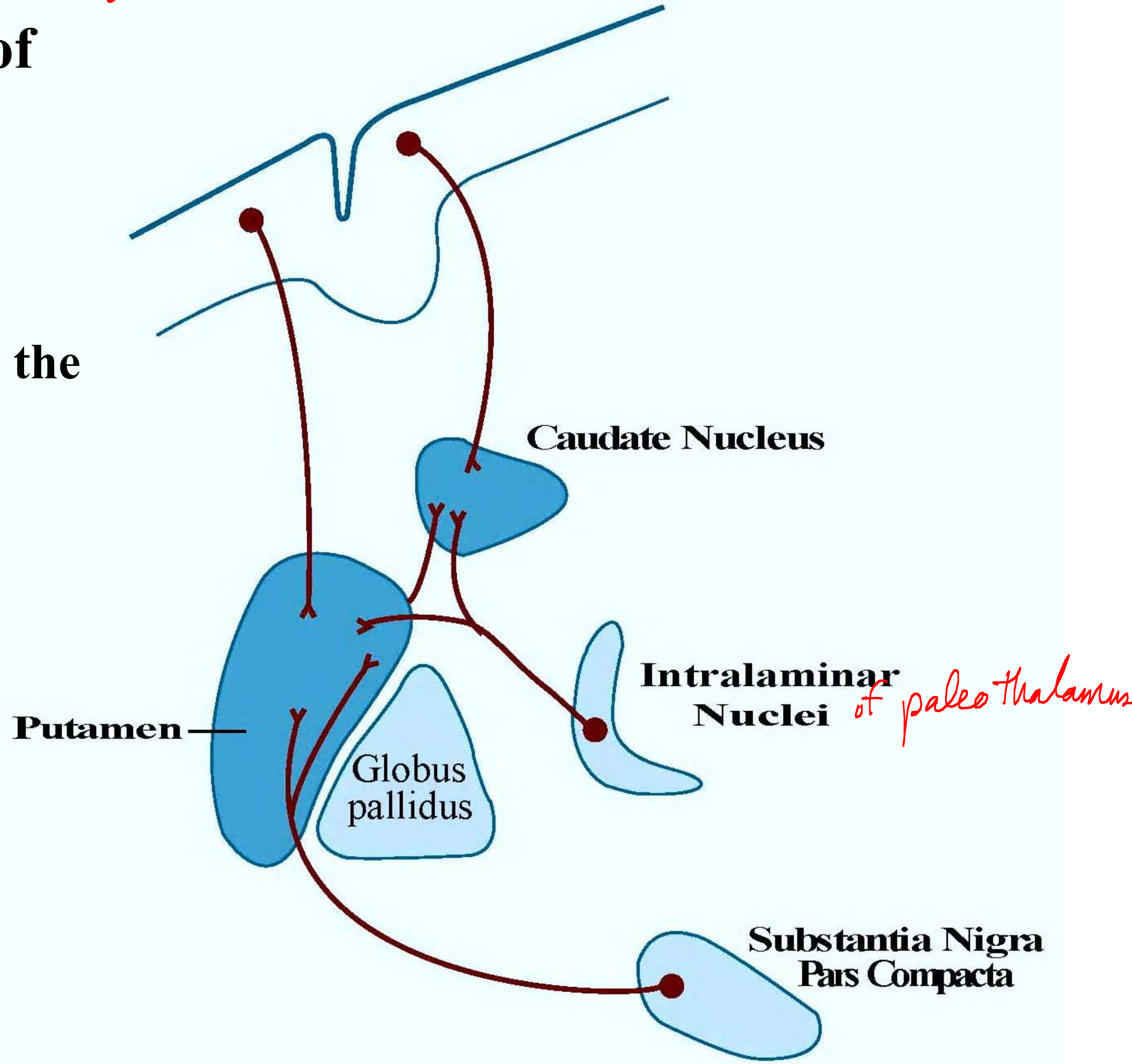


Fig 30-2

Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Major afferents of striatum come from neocortex and from “old” thalamus

Figure removed due to copyright restrictions. Please see:
Brodal, Per. *The Central Nervous System, Structure and Function*. 3rd ed. Oxford University Press, 2003. ISBN: 9780195165609.

The **centromedian** nuc. is the largest of the intra-laminar nuclei in large primates. All of the intralaminar nuclei (paleo-thalamic structures) project to the striatum, often with collaterals to the neocortex as well. They receive multisensory inputs from midbrain tectum, hindbrain (e.g., vestibular), spinal cord (somatosensory). *Next: example*

Axons from ‘tweenbrain to striatum in rat

Parent, Bourassa & Deschenes, in The Basal Ganglia (Plenum, 1996)

Figure removed due to copyright restrictions. Please see:
Deschenes, M., J. Bourassa, and A. Parent. "Striatal and Cortical Projections of Single Neurons from the Central Lateral Thalamic Nucleus in the Rat." *Neuroscience* 72, no. 3 (1996): 679-87.

Parent, Bourassa & Deschenes, in *The Basal Ganglia (*Plenum, 1996)

Figure removed due to copyright restrictions. Please see:
Deschenes, M., J. Bourassa, and A. Parent. "Striatal and Cortical Projections of Single Neurons from the Central Lateral Thalamic Nucleus in the Rat." *Neuroscience* 72, no. 3 (1996): 679-87.

Parent, Bourassa & Deschenes, in *The Basal Ganglia* (Plenum, 1996)

Review

Evolution of corpus striatum, *continued*

1. Beginnings: a link between olfactory inputs and motor control: The link becomes "Ventral striatum".

2. Non-olfactory inputs invade the striatal integrating mechanisms (via paleothalamic structures).

3. Early expansions of endbrain: striatal and pallial.

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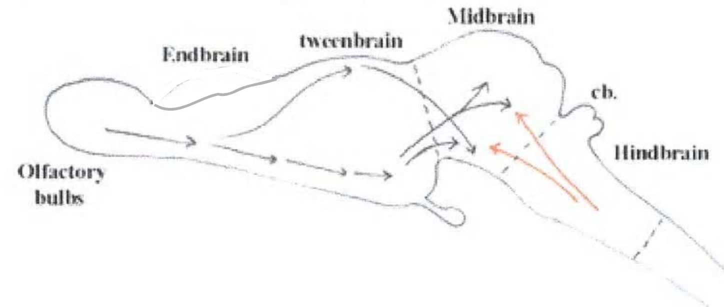
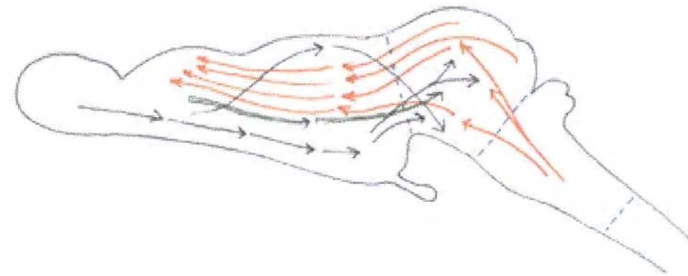


Figure 2. Other inputs reached the striatum



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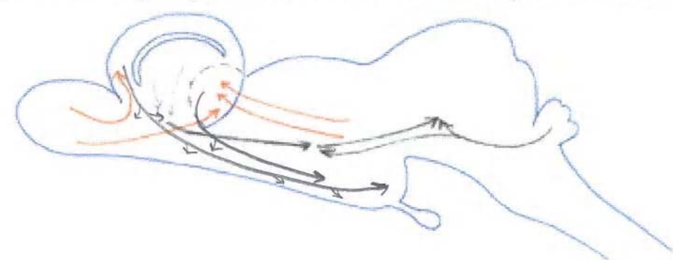
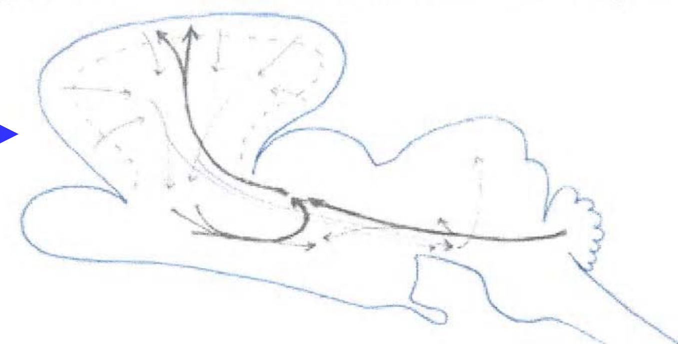


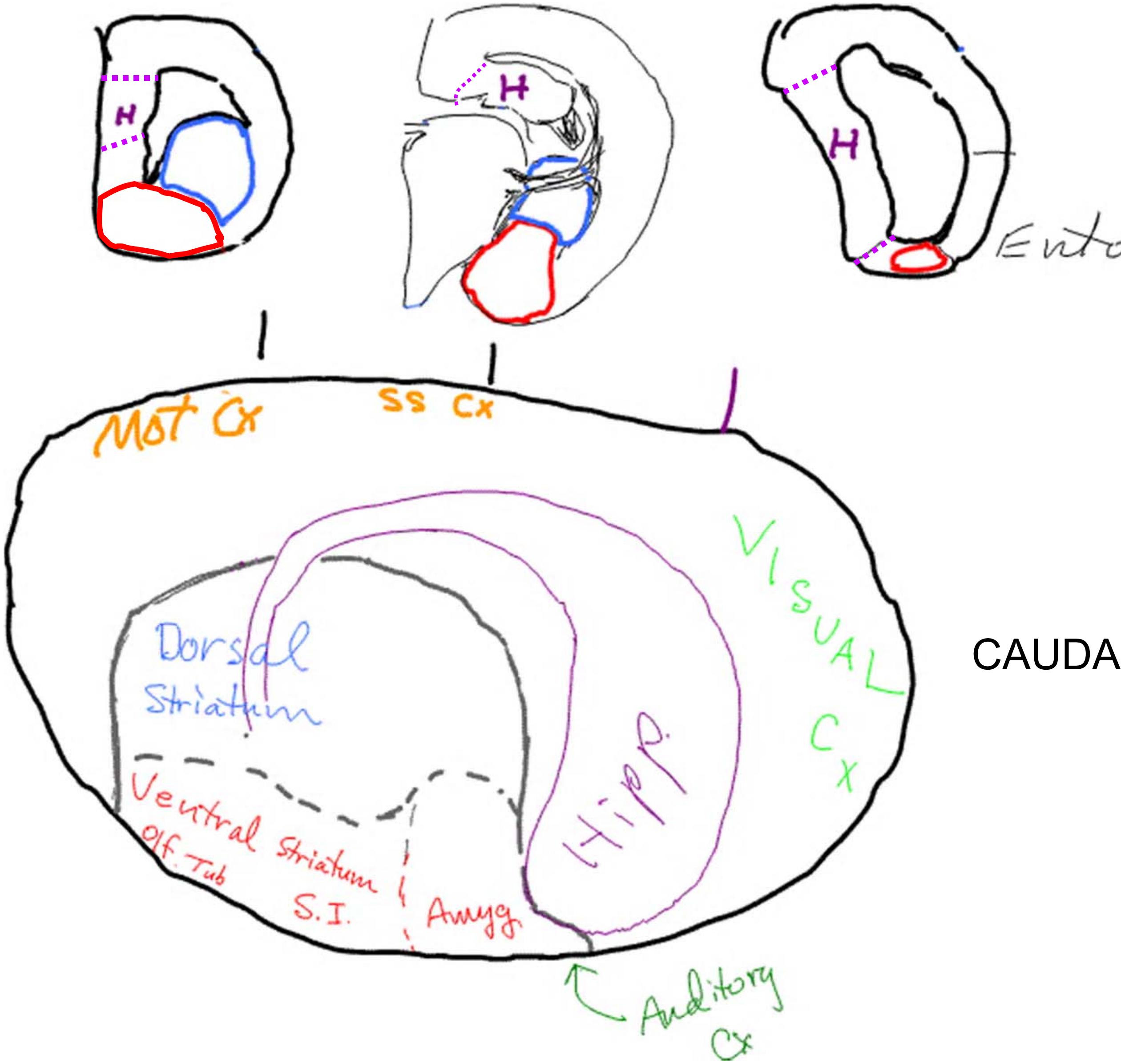
Figure 4. Pre-mammalian, and then mammalian expansions



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Positions in the hemisphere: Dorsal striatum, ventral striatum including Amygdala, and Hippocampus

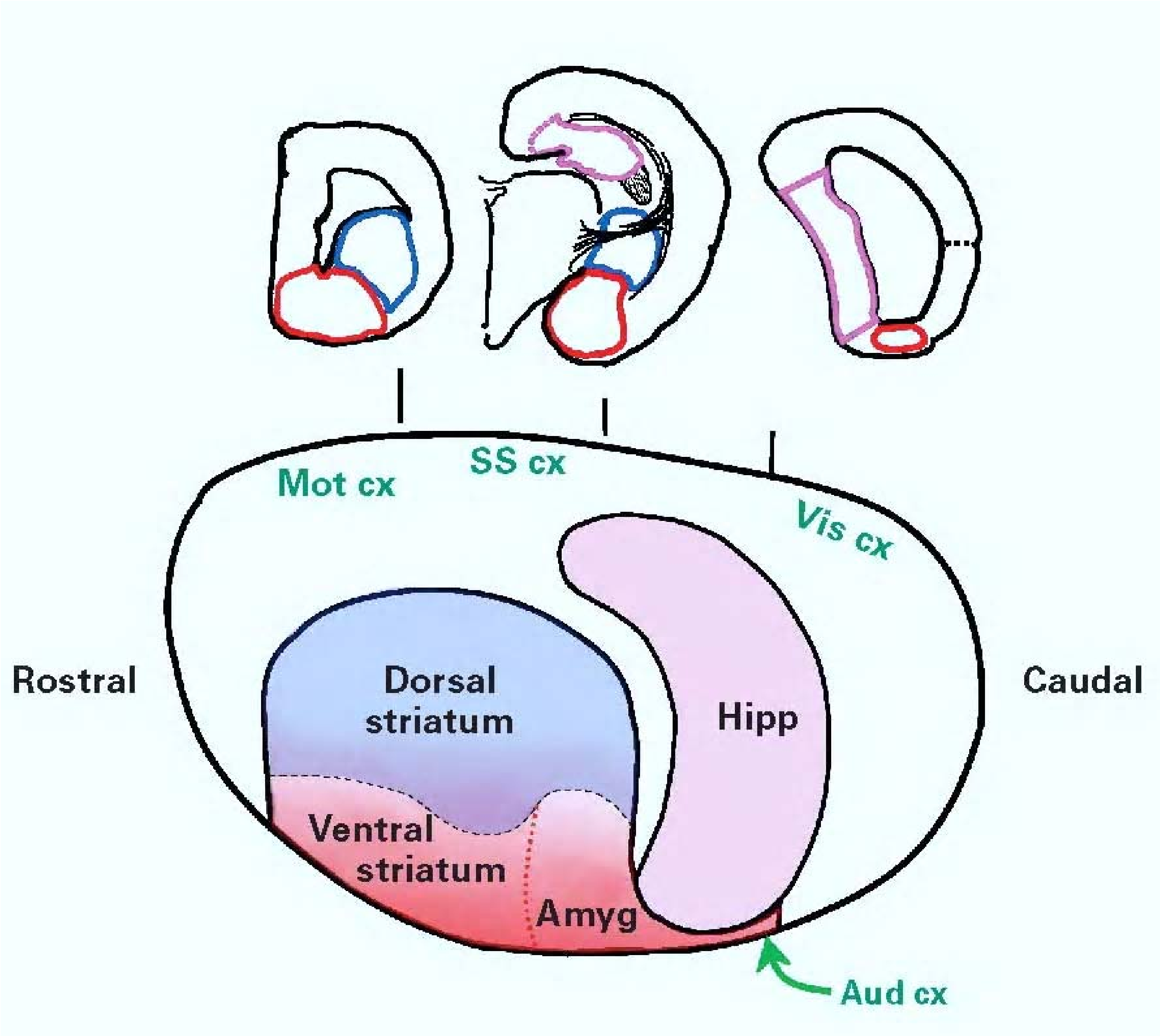
ROSTRAL



CAUDAL

(View from medial side)

Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Fig 30.4

Questions, chapter 30

1) What are two major outputs of the corpus striatum via the globus pallidus (dorsal pallidum)? Which one of them is the larger one in mammals? (This explains the meaning of the statement that the major output of the extrapyramidal system is the pyramidal system.)

   Larger: to VA + VL of thalamus
   Smaller: to midbrain locomotor area

2) Contrast the major source of sensory inputs to the striatum in amphibians and in mammals.

   thalamus — neocortex

3) What is the limbic striatum? How does it differ from the non-limbic striatum? What are several of the structures that it includes? (See also chapter 29.)

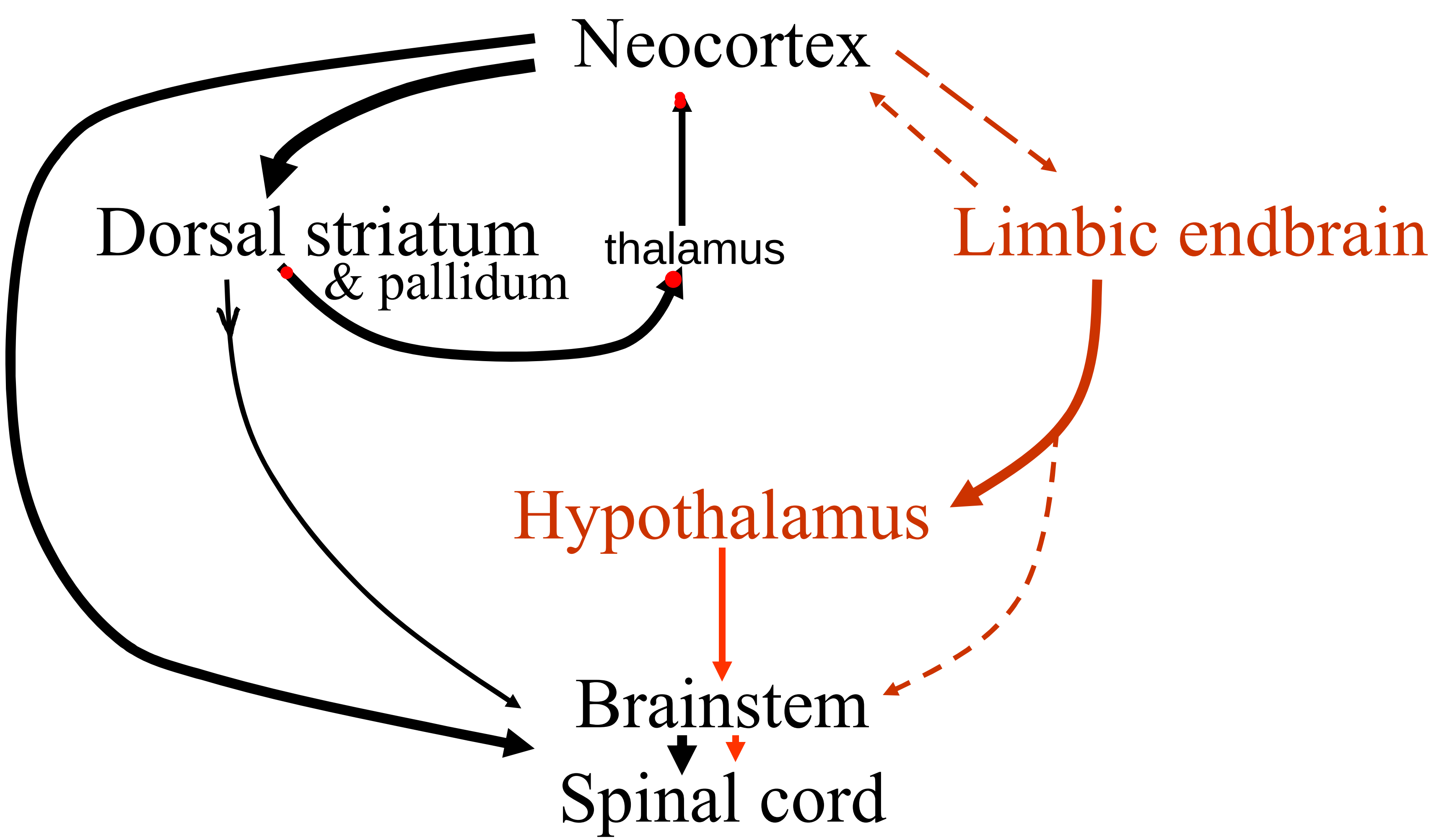
Outputs of the mammalian striatum

What is meant by the statement, "the major output of the extrapyramidal system is the pyramidal system"?

The striatum is the major endbrain structure of the "extrapyramidal system." That statement refers to a major output of the dorsal striatum. (Shown on next slide)

It also has other outputs.

Mammalian endbrain connections: outputs



However:

- This characterization is based on the neuroanatomy of modern mammals, especially higher primates
- It does not represent the **earlier** stages of chordate evolution.
  - Connections remain from those earlier stages, not shown in the simplified dagram.

Textbook views

- Parts of the striatum closely connected to the limbic system used to be commonly neglected. (Sometimes this is still the case.)
  - These parts are called the ventral striatum and ventral pallidum.
  - They are more primitive in evolution, but they retain crucial functions in present-day advanced mammals
  - First clear conceptualization: Lennart Heimer and Richard Wilson at M.I.T., working in Nauta's lab, 1975.
- **In the following slide, we re-organize the schema, adding connections of the limbic striatum.**

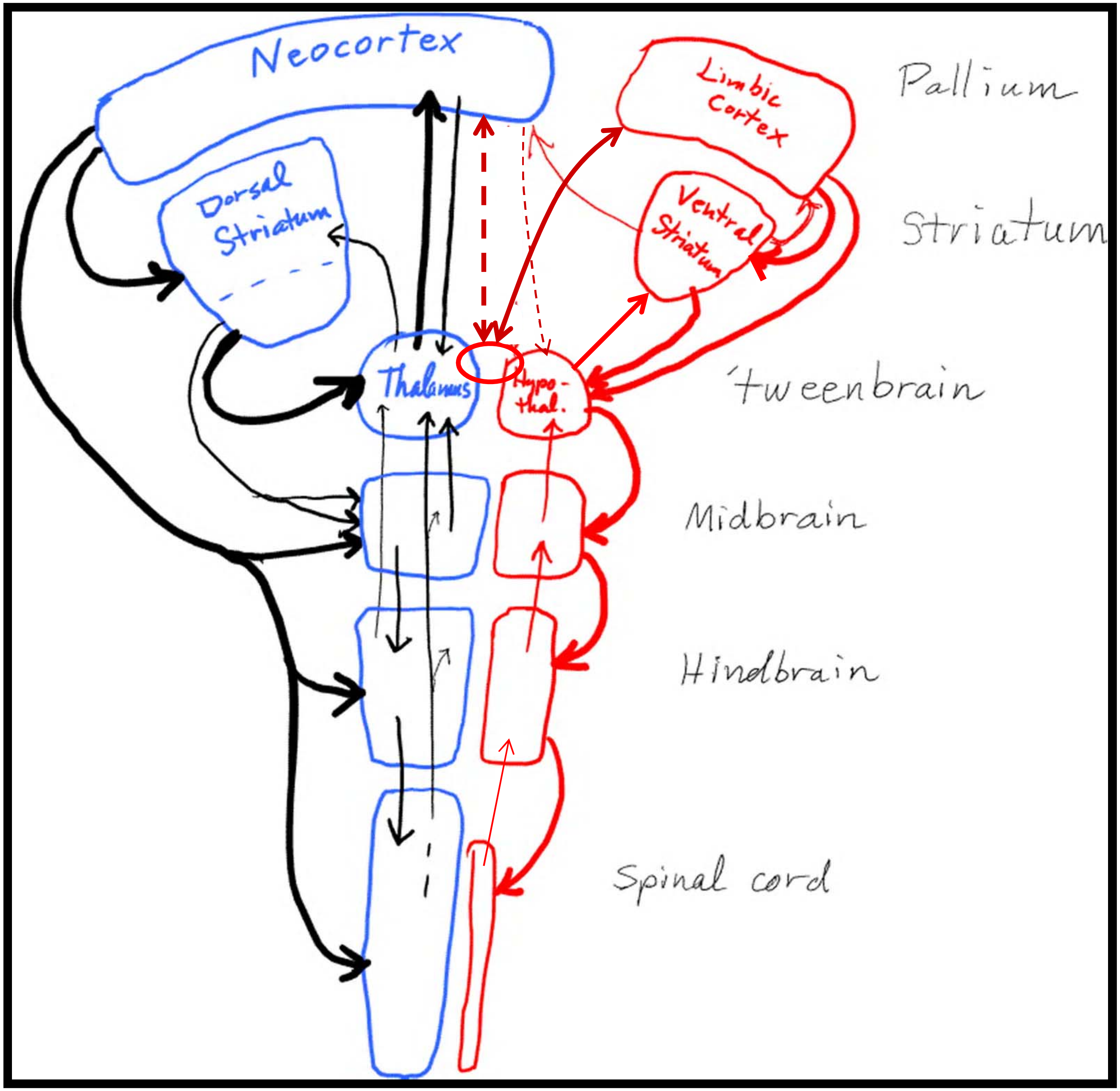
Some Major Endbrain Connections:

Note especially the dorsal and ventral striatum where the links are believed to be plastic.

(Diffuse systems are omitted—as well as many others)

These connections are the same on both sides.

Fig 30-5



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

The nature of the connections shown in figure 30.5:

- What is most unique on the somatic side?
- What is most unique on the limbic side?

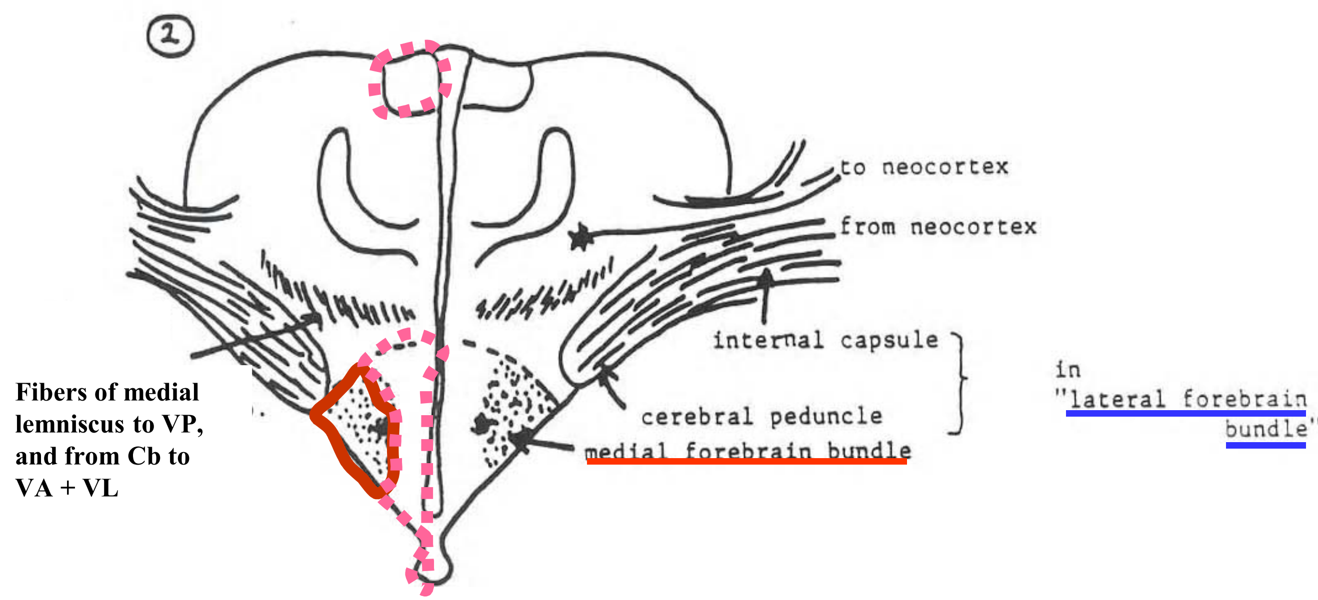
Review:

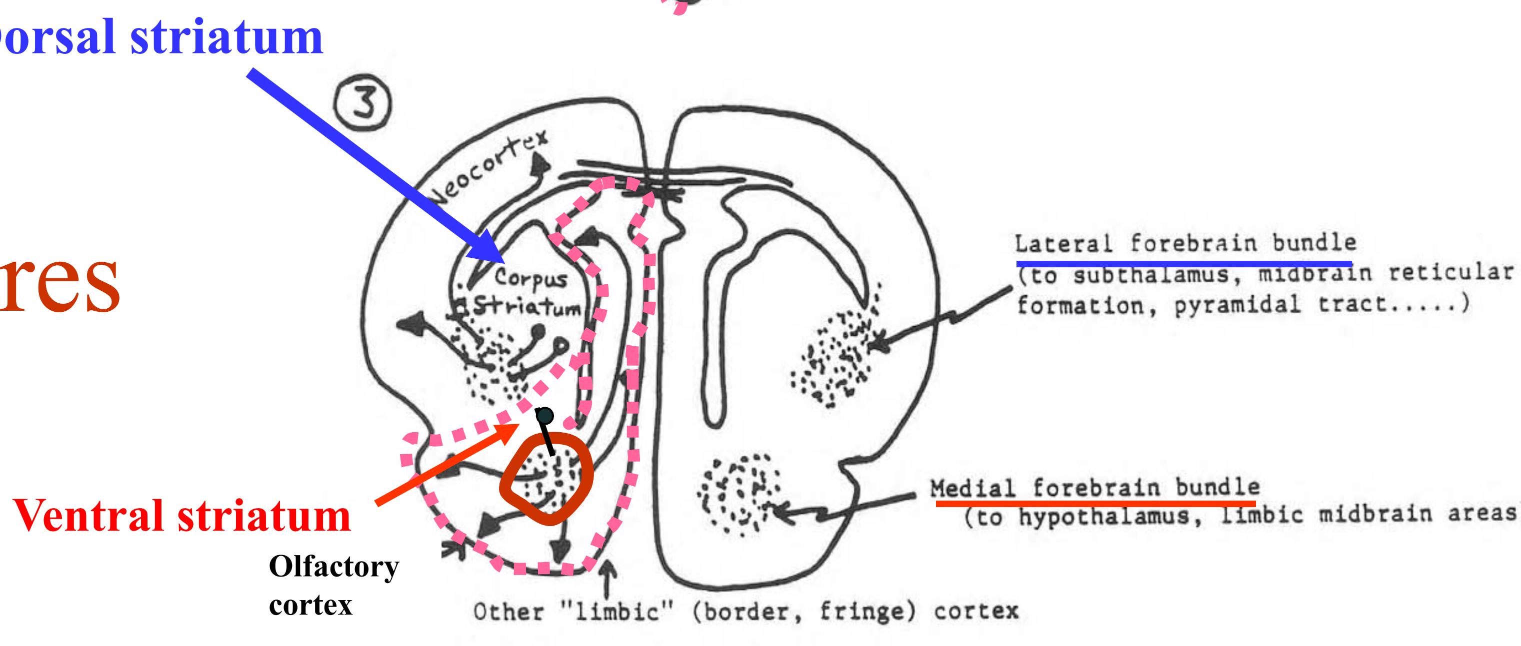
A less diagrammatic view of some of these connections:

- The lateral forebrain bundle and the medial forebrain bundle
- Note the position of the dorsal striatum

'tween-
brain
and
endbrain

limbic
structures
MFB





Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

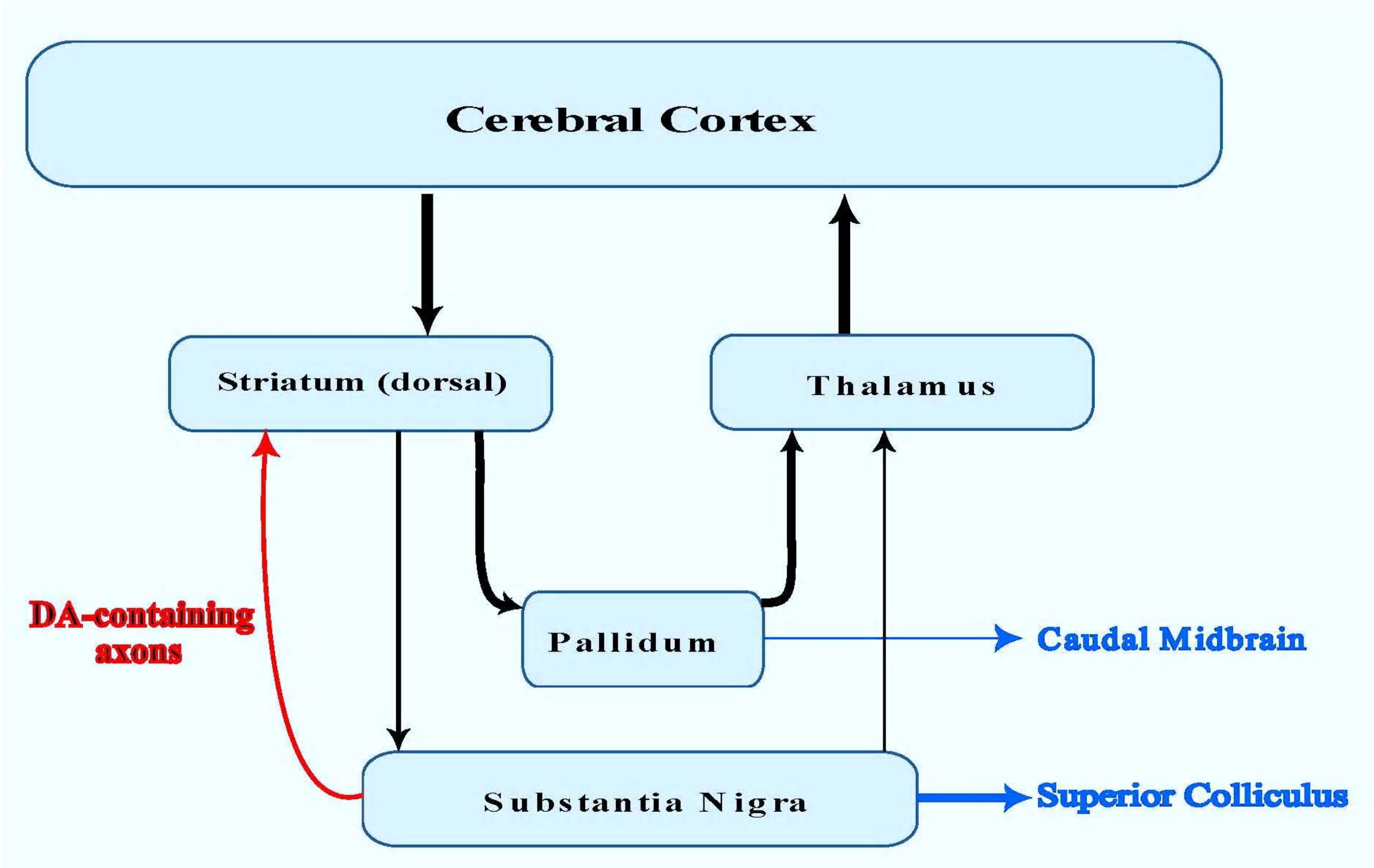
REVIEW:

Origins and course of 2 major pathways:

- ***Lateral forebrain bundle***
  - **Dorsal striatum & pallidum outputs**
  - Neocortical white matter
  - Internal capsule
  - Cerebral peduncle
  - Pyramidal tract
- ***Medial forebrain bundle***
  - Olfactory cortex
  - Limbic cortex
  - Subcortical limbic endbrain structures: **amygdala, basal forebrain (ventral striatum & pallidum)**
  - lateral hypothalamic area
  - limbic midbrain areas

Another simplified view, separating the striatum and pallidum

- Focus is on striatal connections with neocortex and with midbrain
- Omits many of the diencephalic connections (those to the hypothalamus and subthalamus)



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Caudal midbrain: Midbrain Locomotor Region, for approach and avoidance movements

Superior colliculus, for orienting and escape movements

Questions, chapter 30

4) What is the “ansa lenticularis”?

What is the "ansa lenticularis"?

The "handle" of the lentiform nucleus, curving back into the VA-VL from the globus pallidus (GP).

Figure removed due to copyright restrictions. Please see course textbook or:
Nauta, Walle J. H., and Michael Feirtag. Fundamental Neuroanatomy. Freeman, 1986. ISBN: 9780716717232.

Fig 30-12

Nauta & Feirtag, fig.48

Figure removed due to copyright restrictions.
Please see figure 48 of: Nauta, Walle J. H., and Michael Feirtag.
F*undamental Neuroanatomy*. Freeman, 1986. ISBN: 9780716717232.

Note the two projections from the pallidum

Questions, chapter 30

5) What are the major "satellites" of the striatum? Which of these has direct outputs to midbrain structures that are important in controlling orienting movements and locomotion?

Substantia nigra
Subthalamic nucleus

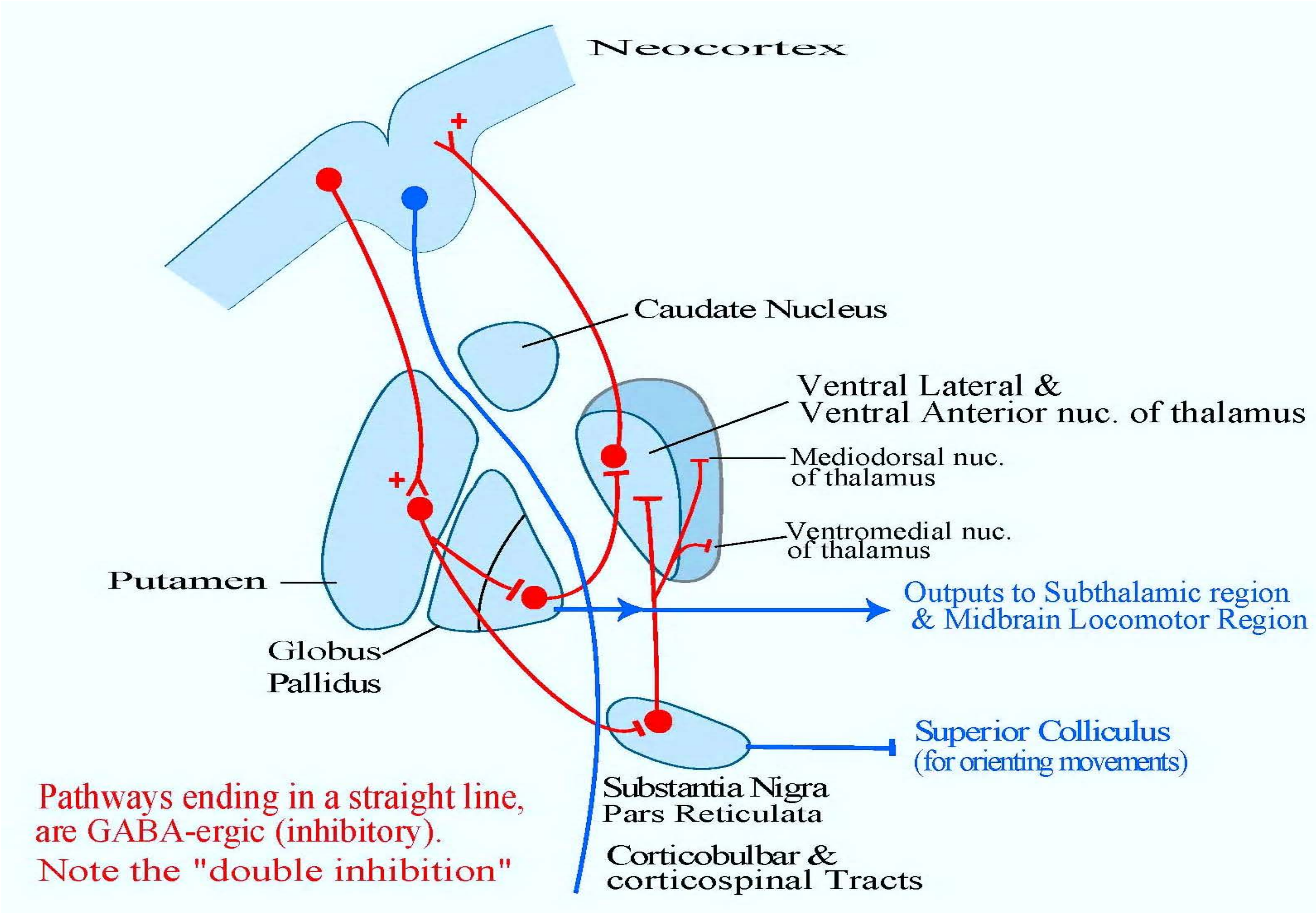
6) Contrast the pathways to motor cortex and the pathways to the superior colliculus from the dorsal striatum (caudate-putamen).

see slides →

7) What is meant by "double inhibition" in pathways through the striatum and its satellites? What neurotransmitter is involved?

see slides →

Illustration of some major connections of the dorsal striatum and globus pallidus that affect the control of movement

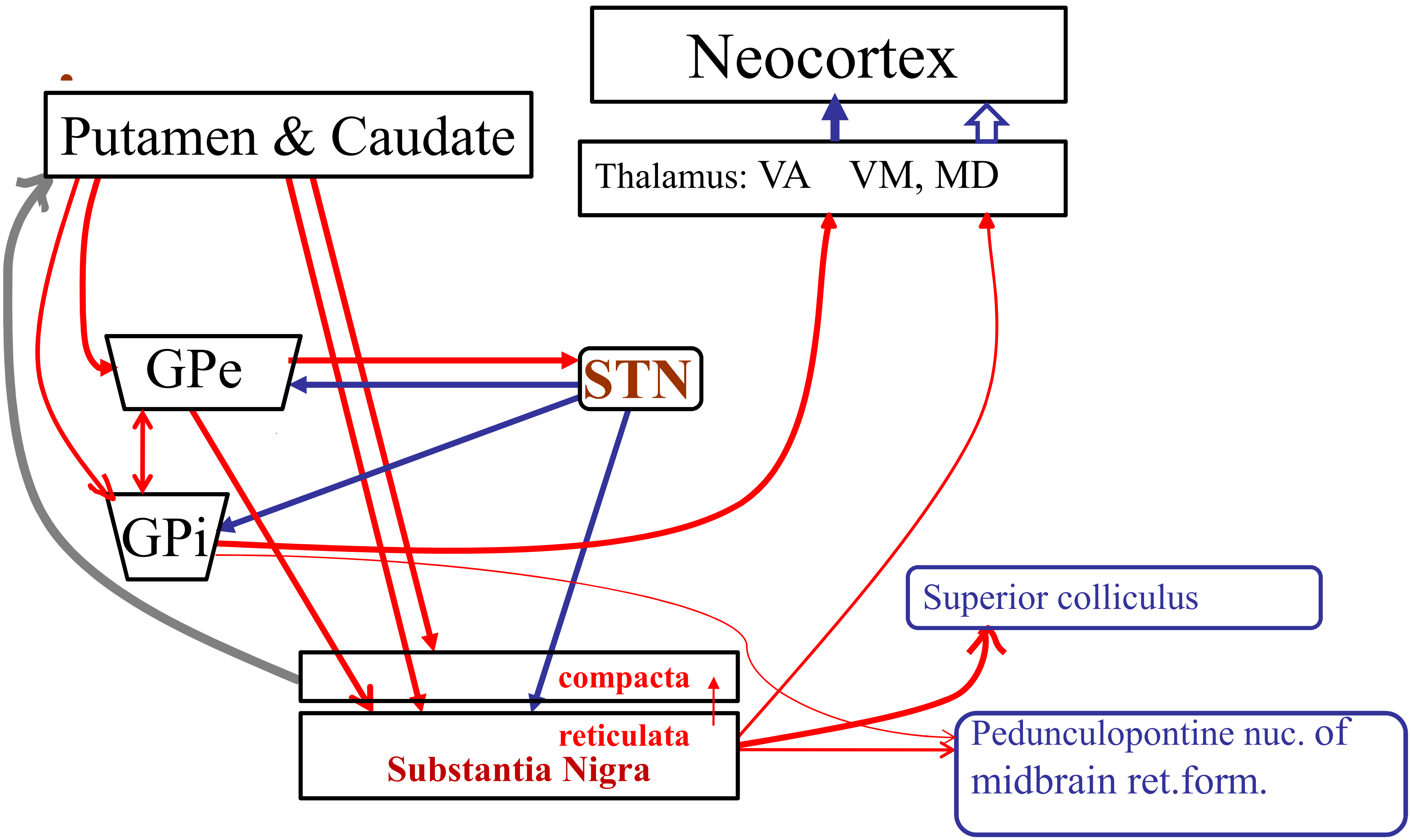


Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.

Fig 30-8

Explaining some disorders requires knowledge of striatal “satellites”

In addition to the **Substantia Nigra**, the **Subthalamic nucleus** is a major satellite.



Schneider, G. E. *Brain structure and its Origins: In the Development and in Evolution of Behavior and the Mind*. MIT Press, 2014. ISBN: 9780262026734.47

Satellites of the corpus striatum: substantia nigra & subthalamic nucleus (STN):
Inhibitory connections (using GABA) in red, excitatory (using GLU) in blue.

Fig 30-9

9.14 Brain Structure and Its Origins
Spring 2014