

# **A sketch of the central nervous system and its origins**

G. E. Schneider 2014

**Part 9: Hypothalamus & Limbic System**

**MIT 9.14 Class 32**

**Limbic forebrain and amygdala**

**(Limbic system 5)**

*Chapter 29*

# Terms:

“Rhinnencephalon”

*(see Brodal, p. 433-434, note 1)*

“Limbic lobe”; “Limbic system”

*(see following slide)*

(From previous classes)

## **Describe Papez' Circuit (Papez, 1937). What did Papez claim about it?**

- **Per Brodal deleted his description of Papez' work from the 3<sup>rd</sup> edition of his textbook, opting for less history in order to limit the length of the book.**

Other reasons? Some did not see enough evidence to group the structures together. They put less weight on the connections argument than experimental neuroanatomists did.

- **James Papez at Cornell described evidence that what was known as the “rhinencephalon” is not actually dominated by the olfactory system. Instead, he proposed, it includes a circuit of interconnected cell groups concerned with feelings and emotional expressions.**

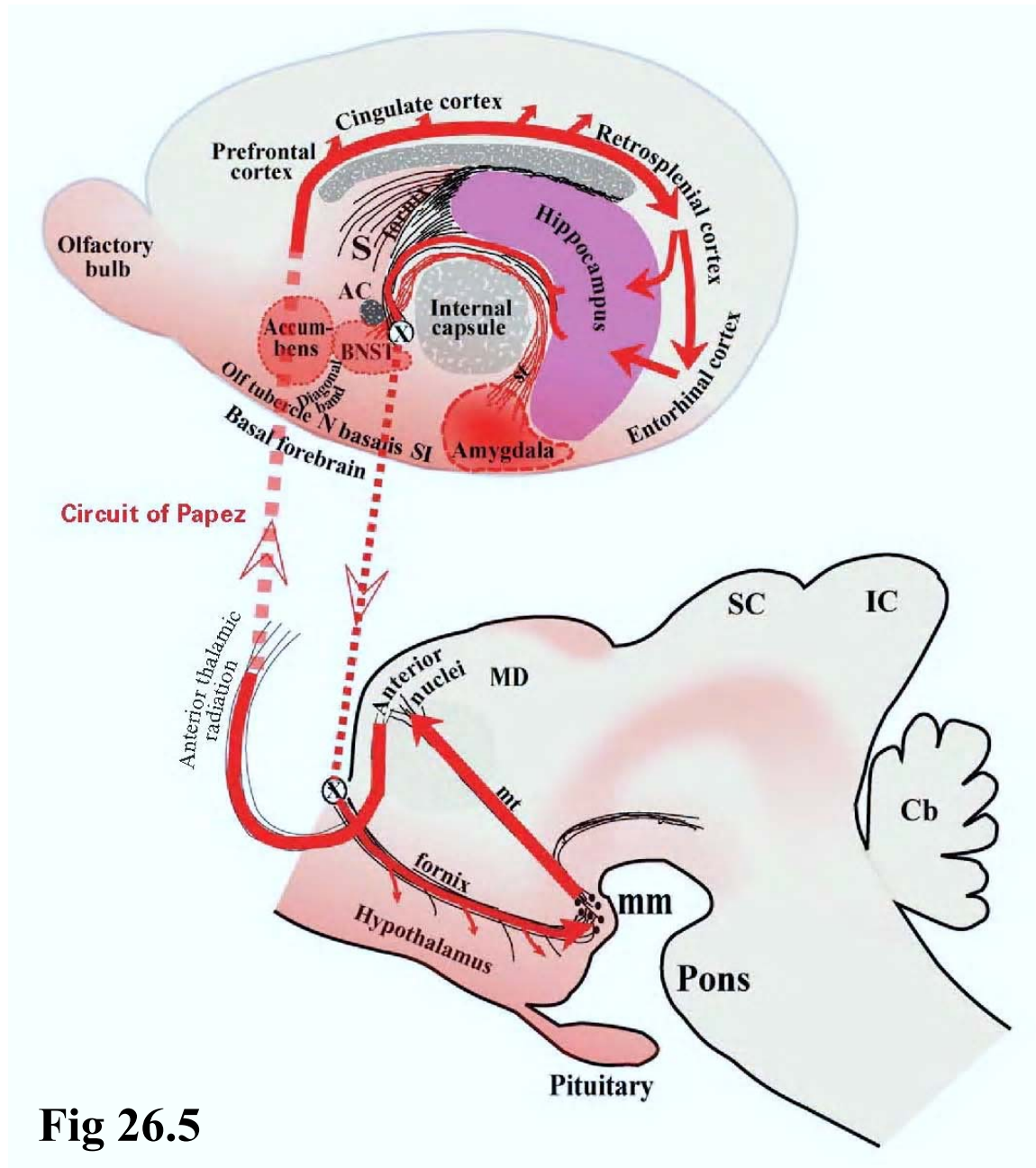
- **This led to new thinking, and resulted in Paul McLean's giving the name "limbic system" to those structures in 1952, resurrecting the term used by Broca when he described "the great limbic lobe".**
- **More recently it was discovered that the functions of this system extend beyond mood and emotion: they play a major role in spatial cognition and in the formation of specific memories for places and events.**

**This has led to a revival of interest in Papez' circuit.**

## [Review]

You have seen the next slide before—it is a useful reference figure. It shows the cerebral hemisphere of small smooth-brained mammal, medial view, with a sketch of **Papez' circuit**: a small selection of connections from a large interconnected network.

# The Circuit of Papez



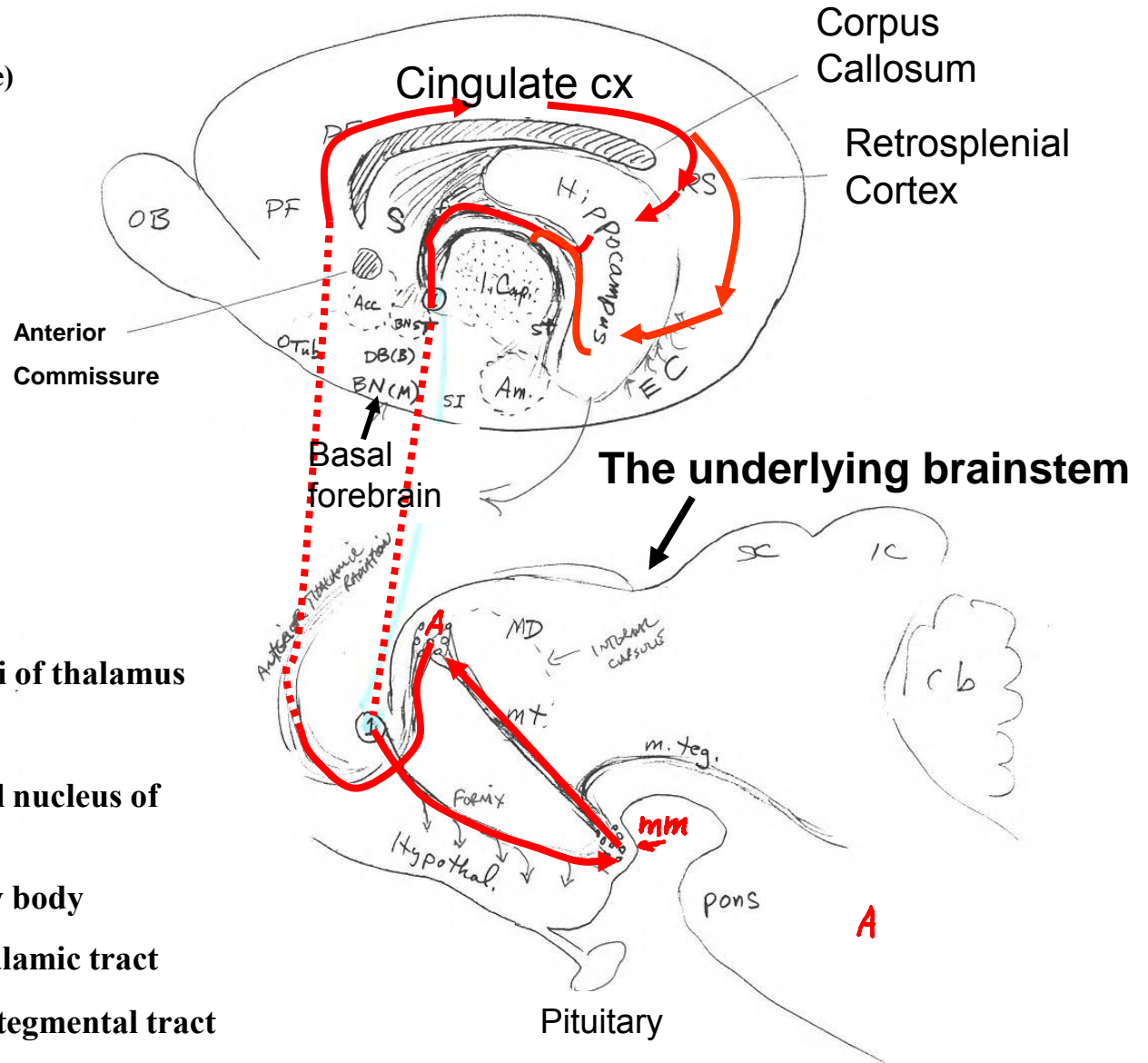
**Fig 26.5**

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

# Papez' Circuit

- OB, olfactory bulb
- PF, prefrontal cortex
- Cing, Cingulate cortex
- RS, retrosplenial cortex (caudal cingulate)
- S, septal area
- fx, fornix
- st, stria terminalis
- DB(B), diagonal band of Broca
- Am, amygdala
- EC, entorhinal cortex
- O Tub, olfactory tubercle
- SI, substantia innominata
- Acc, nuc. Accumbens
- BNST, bed nucleus of the stria terminalis

- A, anterior nuclei of thalamus
- Cb, cerebellum
- MD, mediodorsal nucleus of thalamus
- mm, mammillary body
- mt, mammillothalamic tract
- m teg, mammillotegmental tract
- SC, superior colliculus

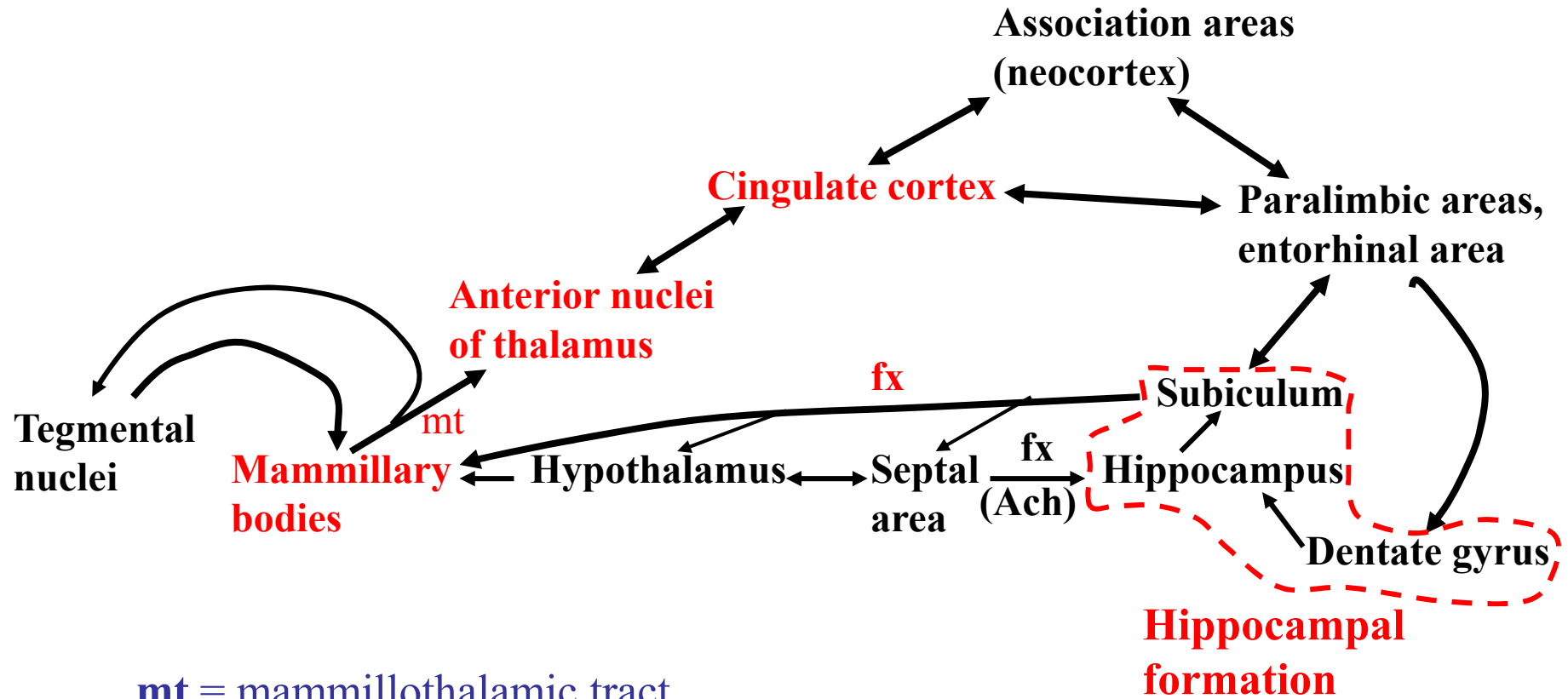


**Fig 26-5**

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From previous classes:

# Papez' circuit brought up to date:



mt = mammillothalamic tract

fx = fornix bundle (output of hippocampus)

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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 is the dominant input to this circuit, if it is not olfaction?*

Neocortex, mostly the multimodal association areas, via the entorhinal cortex.



## Questions, chapter 29

- 1) What are the most direct routes (monosynaptic and disynaptic) from neocortex to the hypothalamus?

*Alternative question:*

**How can neocortex influence the autonomic nervous system?** (*See Brodal pp. 420-423, and other sources*)

- *We can use the Papez' Circuit figure. Why?*
- *We can also refer to Mesulam's figure (following slide), to illustrate this influence.*

In red, the connections from neocortex that most directly influence the autonomic nervous system.

The **amygdala** is a major player in this kind of connection. We focus on the amygdala next.

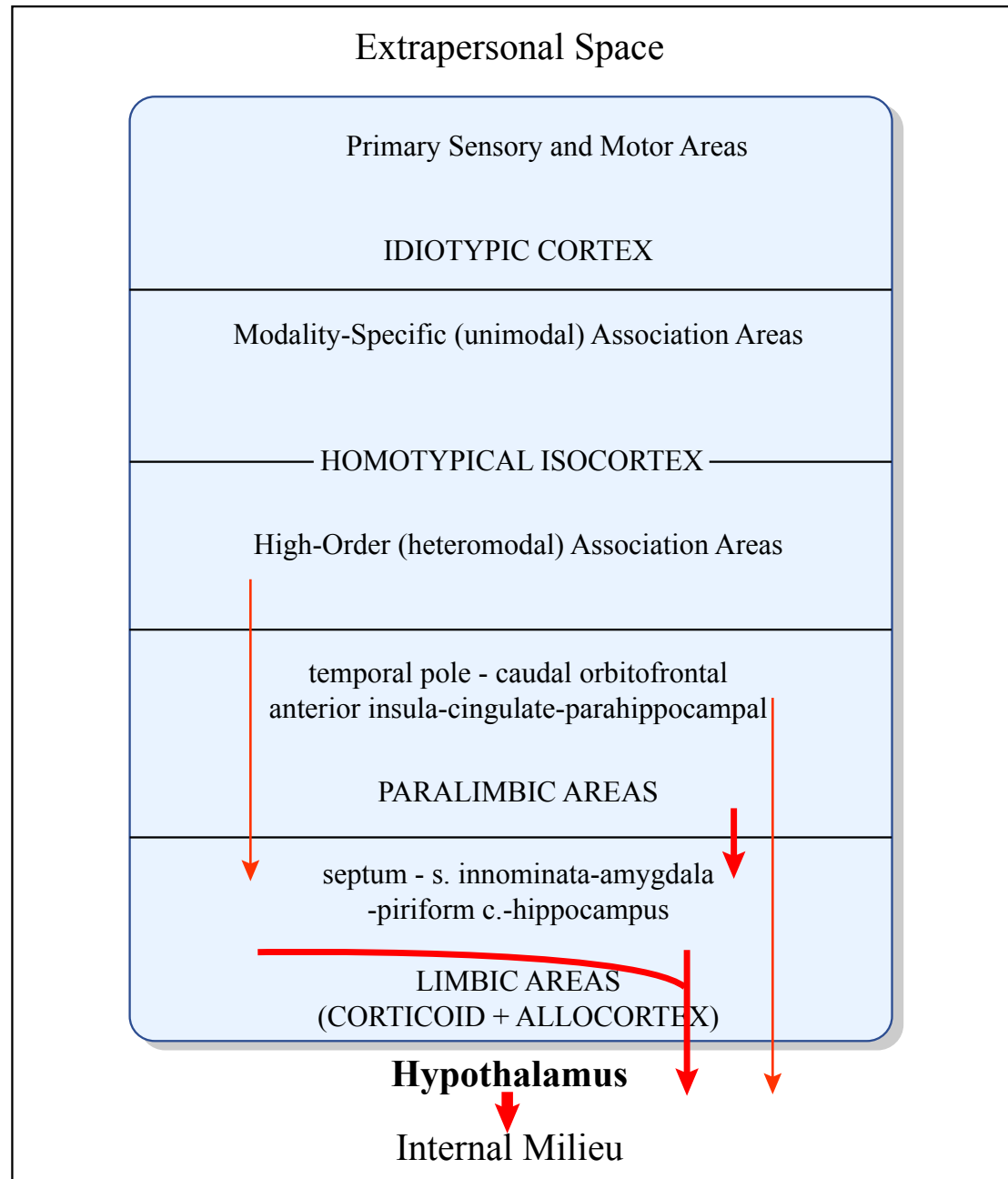
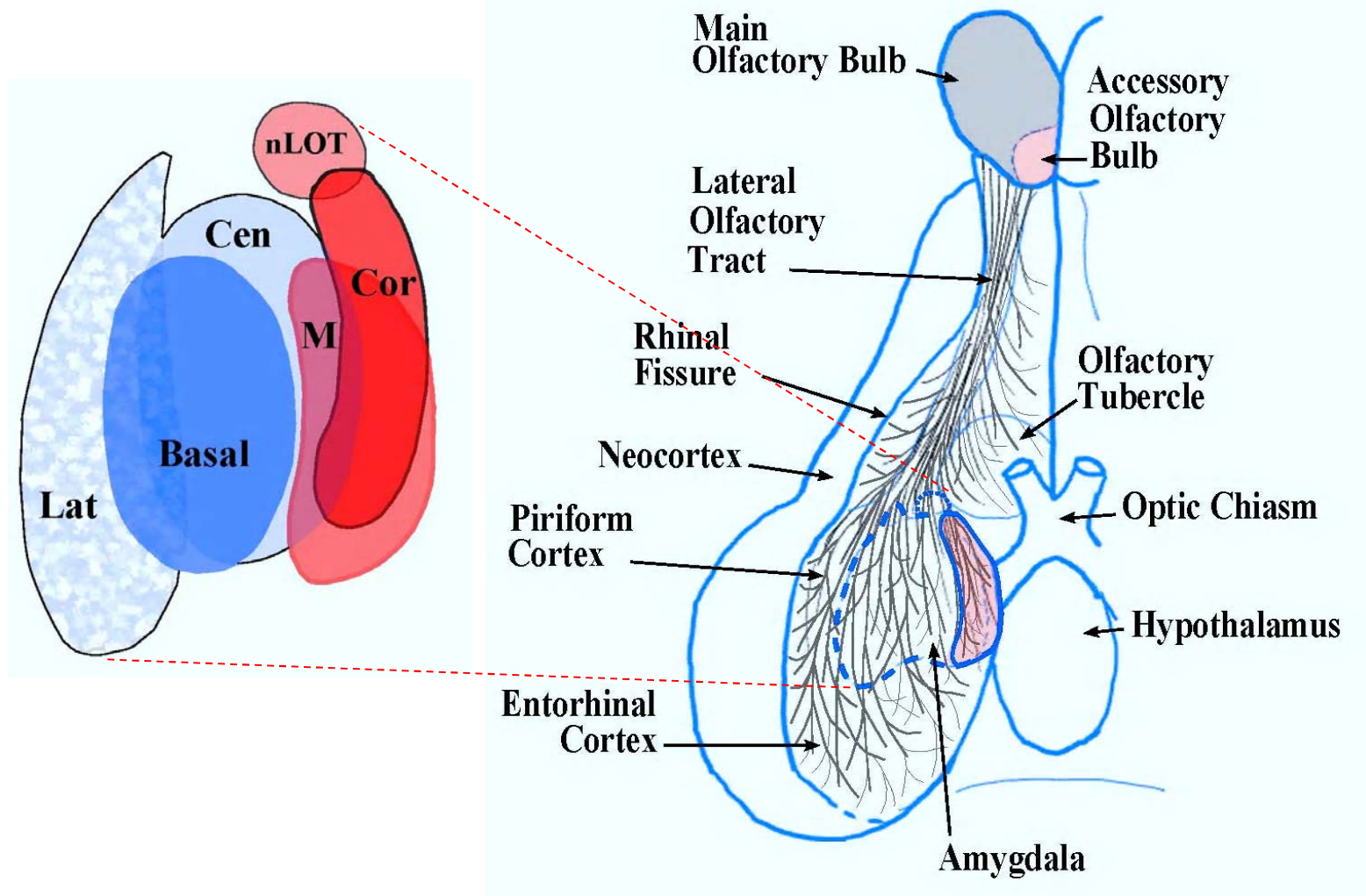


Image by MIT OpenCourseWare.

- ♥ But first, **what is the amygdala?** We can think of it as a modified part of the corpus striatum (*more broadly, a part of the basal ganglia*): It is a caudo-ventral part which abuts the tail of the striatum in the temporal lobe.
  - It also includes pallial components
- ♥ As in the striatum, connections in the amygdala are **plastic: Associations** are formed between perceived objects & sounds on the one hand, and affects & autonomic changes on the other. It gives objects in the world valences, or “affective tags”.
- ♥ *See also the detailed descriptions and ideas of L. W. Swanson (textbook, 2000; 2003)*



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## **Amygdala: some major connections**

**Corticomedial:** Inputs from olfactory bulbs, hypothalamus & lateral amygdala; outputs to hypothalamus, amygdala, ANS

**Basolateral:** Inputs from thalamus, neocortex, hippocampus; outputs to prefrontal cortex, ventral striatum, other amygdala nuclei

**Central:** Intra-amygdalar inputs; outputs through stria terminalis (see later slides)

# **Amygdala: some major connections**

*(See Brodal edition 2, fig 10.3)*

**Corticomедial:** *Inputs from olfactory bulbs, hypothalamus & lateral amygdala; outputs to hypothalamus, other nuclei of amygdala, ANS*

**Basolateral:** *Inputs from thalamus, neocortex, hippocampus; outputs to prefrontal cortex, ventral striatum, other amygdalar nuclei*

**Central:** *Intra-amygdalar inputs; outputs through stria terminalis (see later slides)*

Pallial derivatives

Striatal derivatives

## Questions, chapter 29

- 2) Describe the stria terminalis: its origins, course, and major connections.

## The “stria terminalis” (*st*): a major output pathway from the amygdala

Long axons of the pathway go to the hypothalamus, by a route similar to that of the fornix fibers coming from hippocampal formation to the hypothalamus.

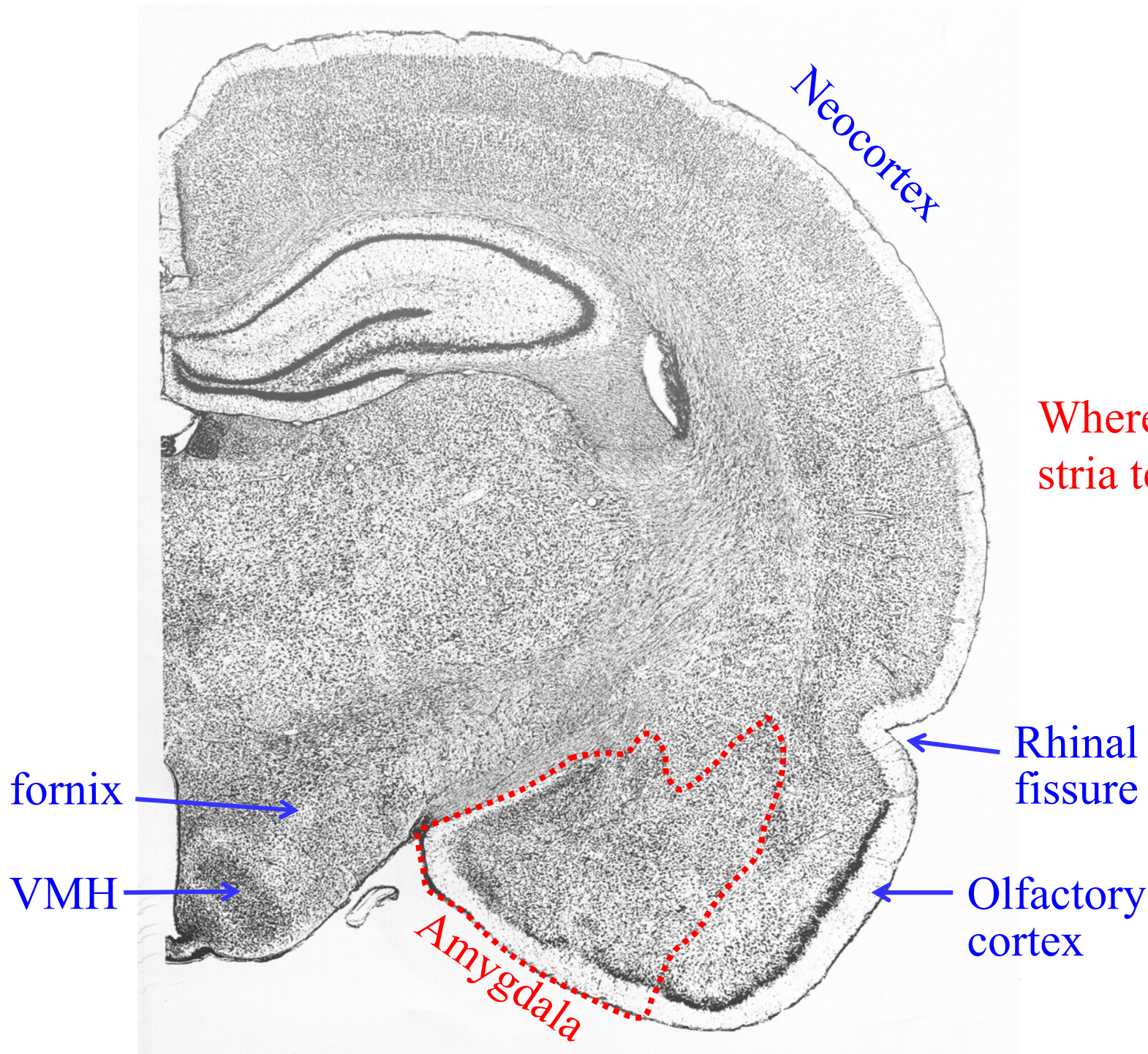
By this connection, the amygdala strongly influences motivational states.



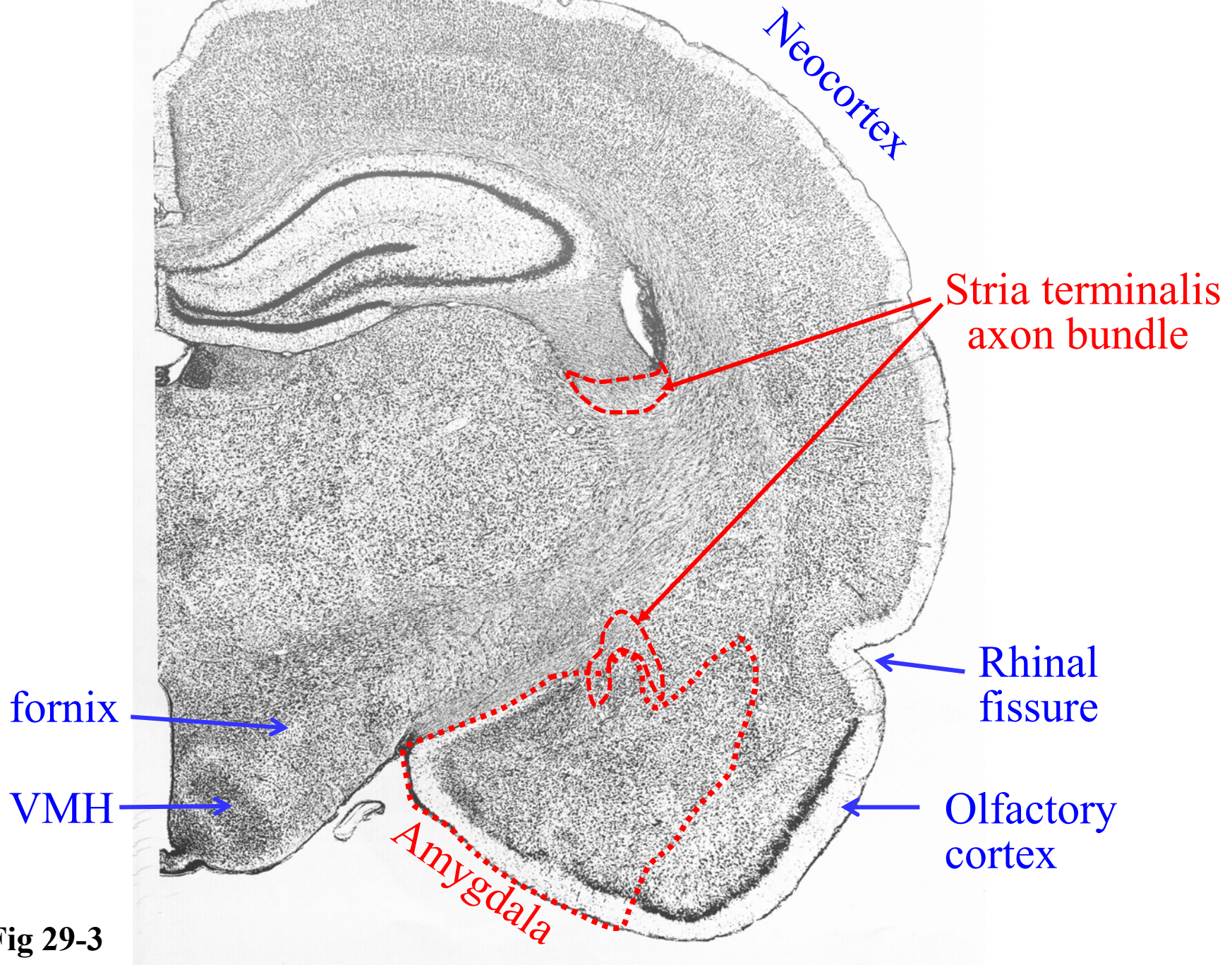
**A good way to begin answering the question is by showing the stria terminalis on a brain section:**

The sections illustrate the cytoarchitecture of rat 'tweenbrain & endbrain showing the amygdala and one of its major targets.

- The photo shows the rat brain in coronal section, Nissl stain (cell bodies)
- The major target is the Ventromedial Nucleus of the Hypothalamus (VMH)

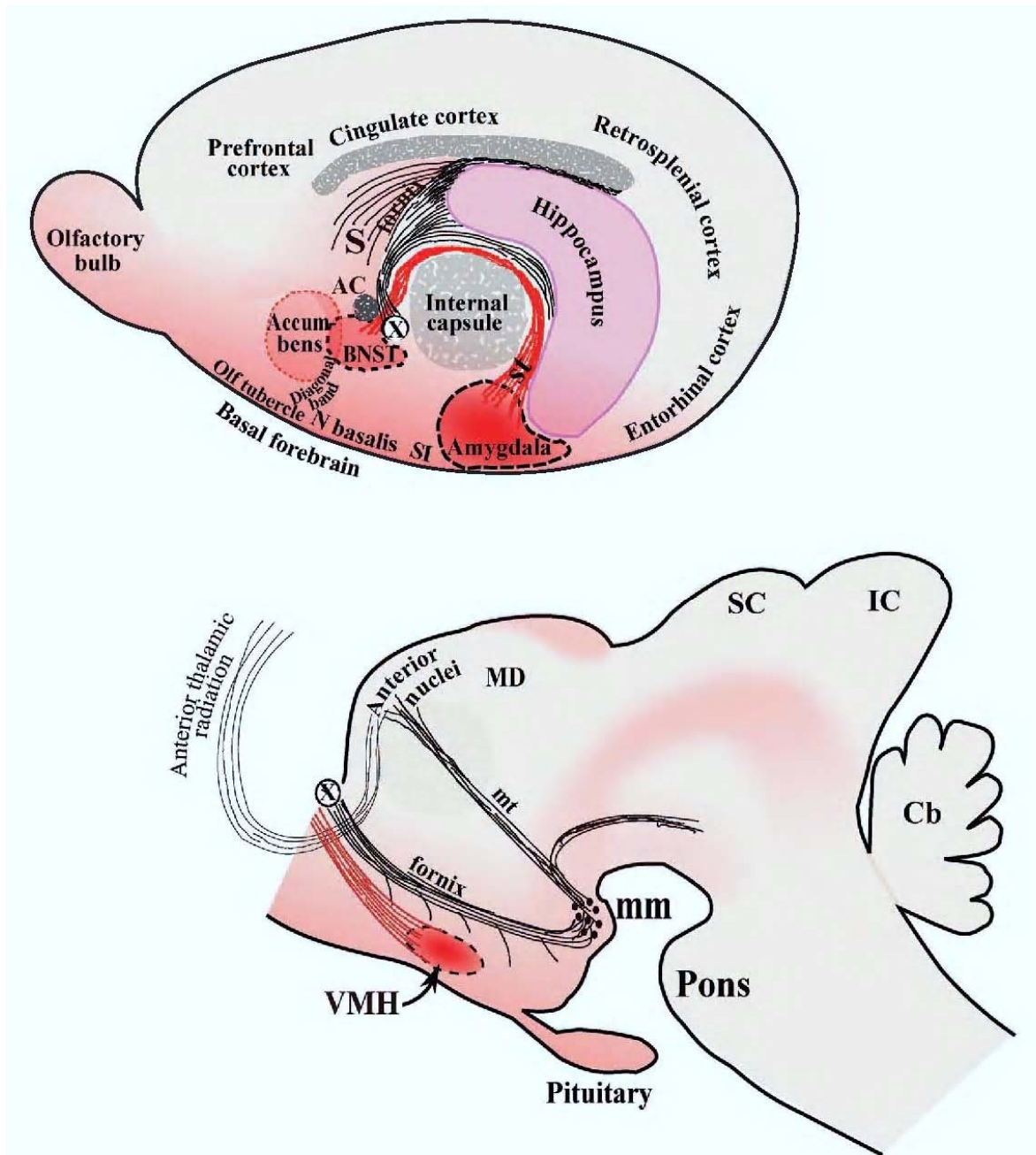


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**Fig 29-3**

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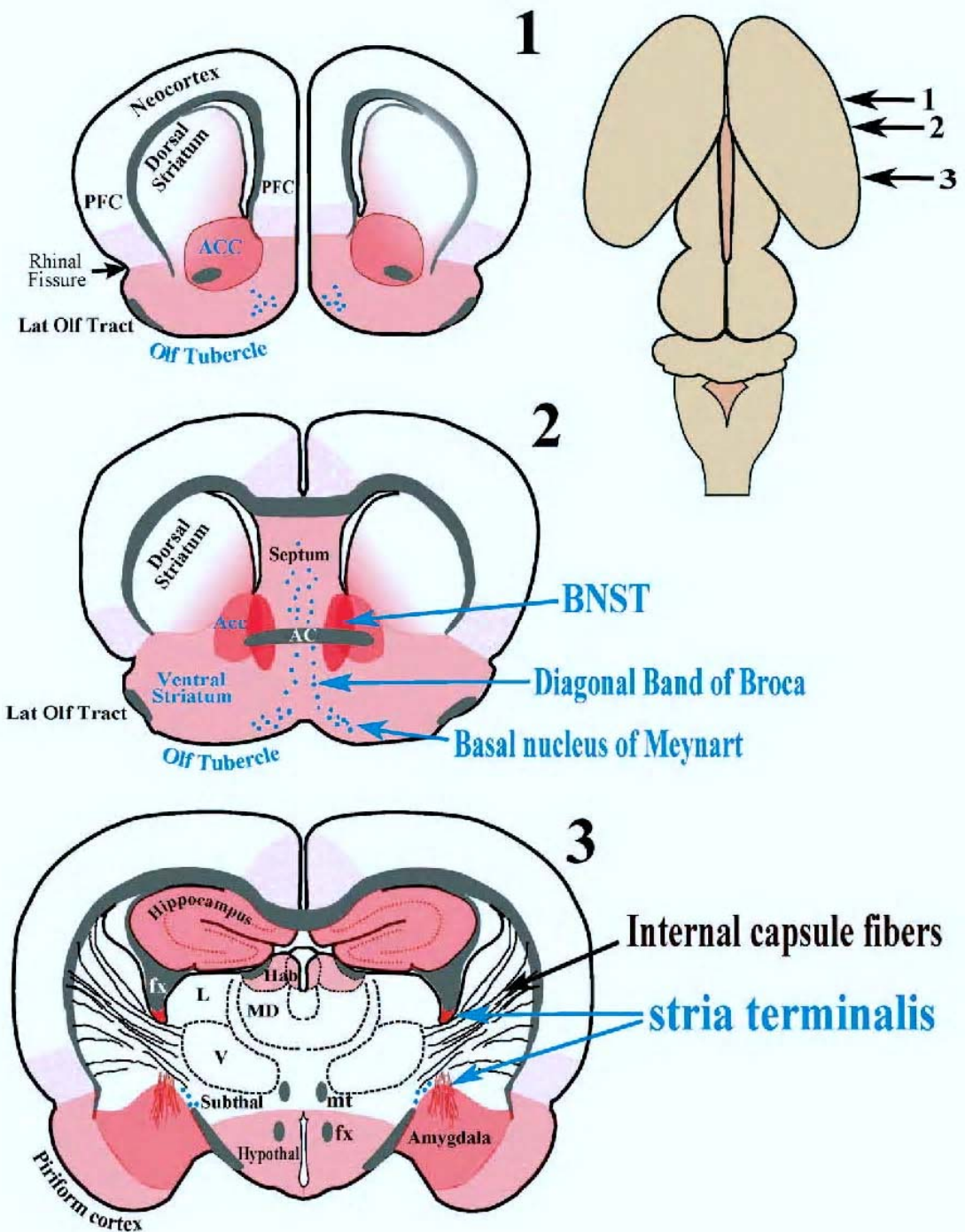
**Fig 29.5**

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

# Frontal sections: the limbic system of rodent

Find the Amygdala,  
the Stria Terminalis,  
and the Bed Nucleus  
of the Stria Terminalis

Can you also identify the  
positions of the fornix  
fibers from the  
hippocampal formation?



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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

- 3) What sensory inputs come to the cortical and medial nuclei of the amygdala without passing through the neocortex?  
Comparative studies indicate that these inputs are very ancient.
  
- 4) The lateral nucleus of the amygdala receives various sensory inputs via neocortical association areas. What sensory pathways come to the lateral amygdala directly from the thalamus?

# Sensory pathways to the amygdala.

## 1. More ancient inputs

Corticomedial nuclei receive direct **olfactory** projections, also direct inputs from the **taste** nucleus in the hindbrain (parabrachial nucleus), and probably from the cortex of the anterior insula.

Also, **pain** inputs reach the central nucleus by a route from the hindbrain.

# Sensory pathways to the amygdala

## 2. More recently evolved inputs

Lateral nucleus receives **auditory** inputs directly from the thalamus. Inputs about **visual** objects reach this area via temporal lobe association cortex.

The amygdala, particularly the Basal nucleus, is reciprocally connected to prefrontal cortex.



# Projections from MGB to Lateral Amygdala and Auditory Neocortex in Opossum, Hedgehog, and Tree Shrew [REVIEW]

Figure removed due to copyright restrictions. Please see course textbook or:  
Frost, Douglas O. "Anomalous Visual Connections to Somatosensory and Auditory Systems  
Following Brain Lesions in Early Life." *Developmental Brain Research* 3, no. 4 (1982): 627-35.

# Amygdala connections in a medical textbook

This seems complicated at first. Remember that it depicts the human brain, which is difficult to visualize.

**Just note the inputs from, and outputs to, limbic system structures.**

**Also note the olfactory and visual inputs.**

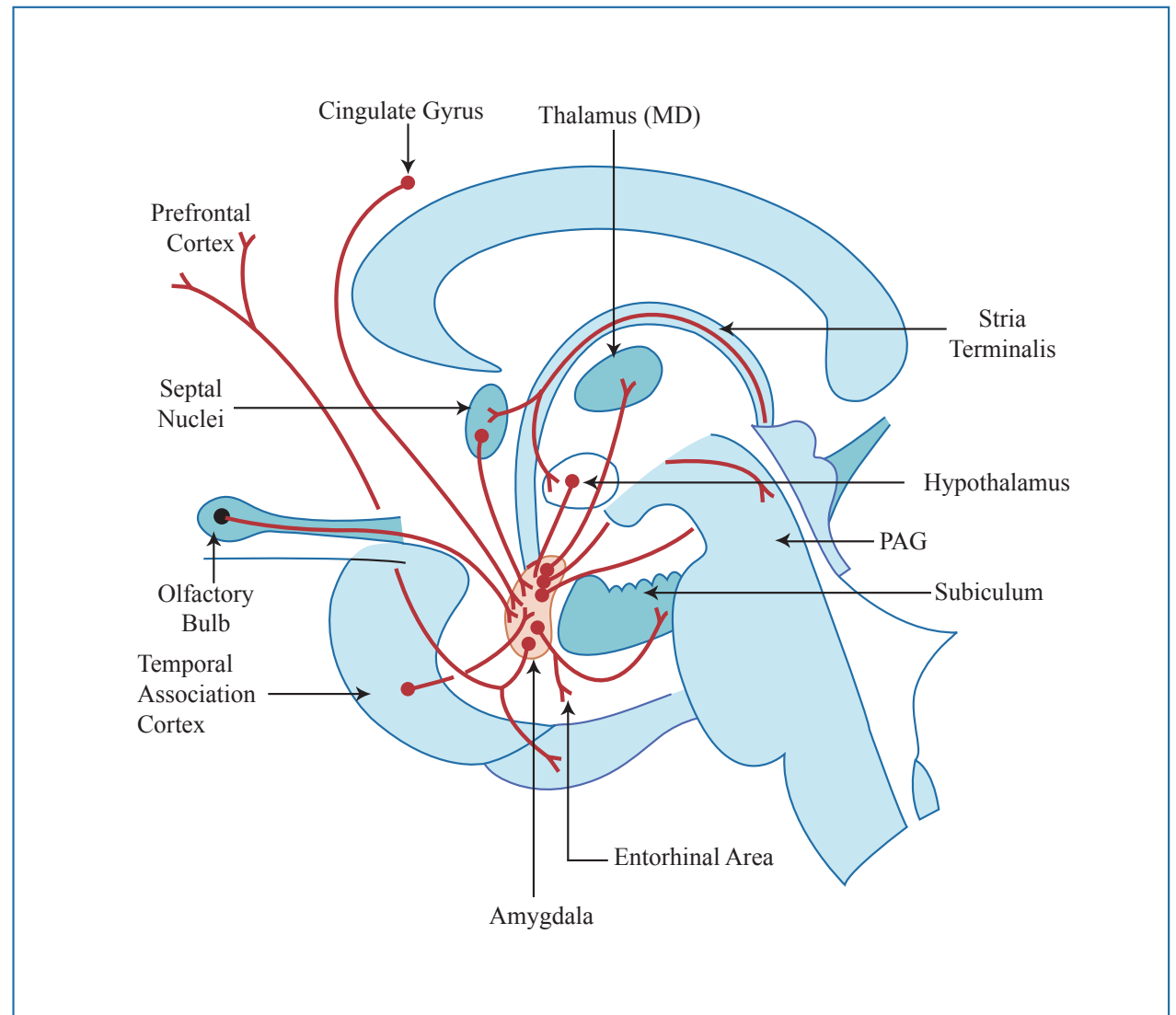


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Gluhbegovic, Nedzad, and Terence H. Williams. *The Human Brain: A Photographic Guide*. Harper & Row, 1980.

**Fig 29-6**

## *Amygdala in human cerebral hemisphere*

## Some effects of electrical stimulation of the amygdala

- Corticomedial amygdala: Lip smacking, salivation, licking, chewing; inhibition of voluntary movements; elimination behavior
- Basolateral amygdala: Arousal and attentiveness; fear or rage; humans have shown anxiety and other strong emotions, also *déjà vu* experiences
- Negative emotions have been stressed for amygdala functions, although both negative and positive feelings involve amygdala activity

# Behavioral effects of lesions of the amygdala

- “Tameness” in monkeys: Loss of normal defensiveness and aggressiveness in social interactions
- These monkeys become socially isolated, with loss of sensitivity to social dominance relationships
- Loss of normal fear in response to visual inputs
- Humans with amygdala lesions have shown loss of autonomic reactions accompanying fear and anxiety.
- Altered dietary preferences and hypersexuality have also been seen.

## Questions, chapter 29

5) The amygdala is involved in habit learning.  
What kind of habits?

Habits of feelings/ emotional reactions to objects and individuals.

# Auditory Fear Conditioning: dependent on amygdala in rats

Figure removed due to copyright restrictions. Please see course textbook or:  
LeDoux, Joseph E. "Emotion, Memory and the Brain." *Scientific American* 7, no. 1 (1997): 68-75.

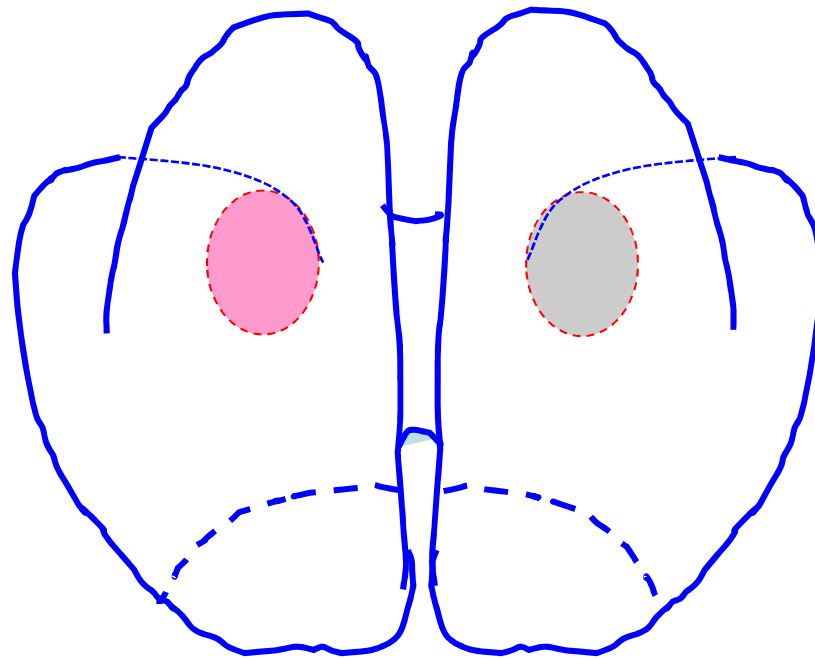
## Questions, chapter 29

- 6) Describe the lesions, made in monkeys by Downer, that produced a loss of learned fears (e.g., in social interactions) when one eye was closed and not when the other eye was closed.

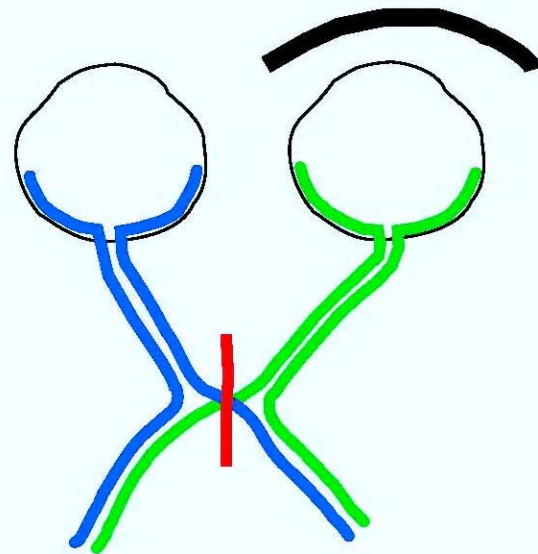


Amygdala symptoms in a monkey when it was looking with one eye but not the other eye (Downer, 1962)

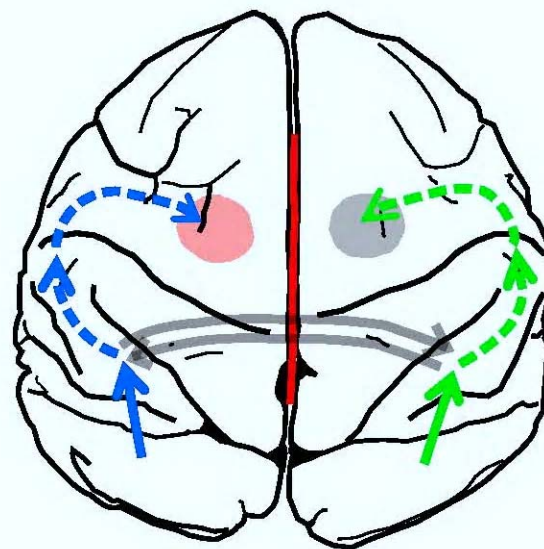
Downer's experiments were carried out in split-brain monkeys with unilateral amygdalectomy.



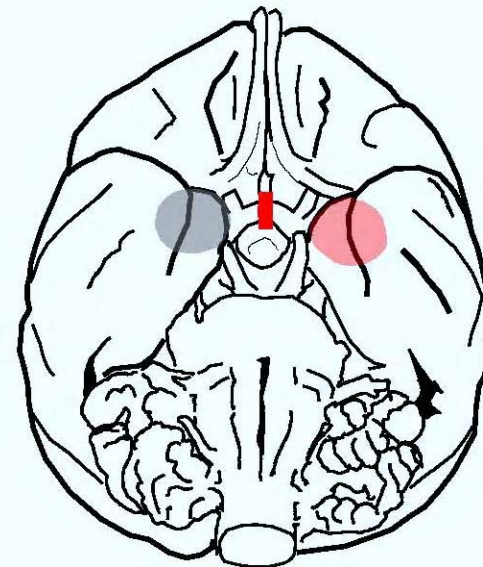
What additional lesions were necessary?



**Eyes, optic nerves,  
optic tracts; split  
optic chiasm**



**Dorsal View**



**Ventral View**

**Fig 29-7**

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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 behaviors that can become clinical problems are tied to amygdala functions

- Aggression in males, related to androgen levels
- Learned fear (*as already discussed*)
- Stress and anxiety
- Social insensitivity, as in autism

# Androgen and aggression, *via* effects on limbic-system structures

Figure removed due to copyright restrictions.

# Corticotrophin Releasing Hormone in the amygdala

What does CRH have to do with the amygdala?

*(See Brodal p. 422, right-hand column)*

*CRH-containing neurons are found in the central nucleus, which also receives CRH-containing axons.*

*CRH neurons project to paraventricular nuc. of hypothalamus, which projects to median eminence. In the ME, CRH enters bloodstream and goes to anterior pituitary → release of ACTH. Cortisol levels in bloodstream rise.*

Such knowledge makes possible the targeting of drugs for treatment of emotional problems.

# **The basal forebrain:**

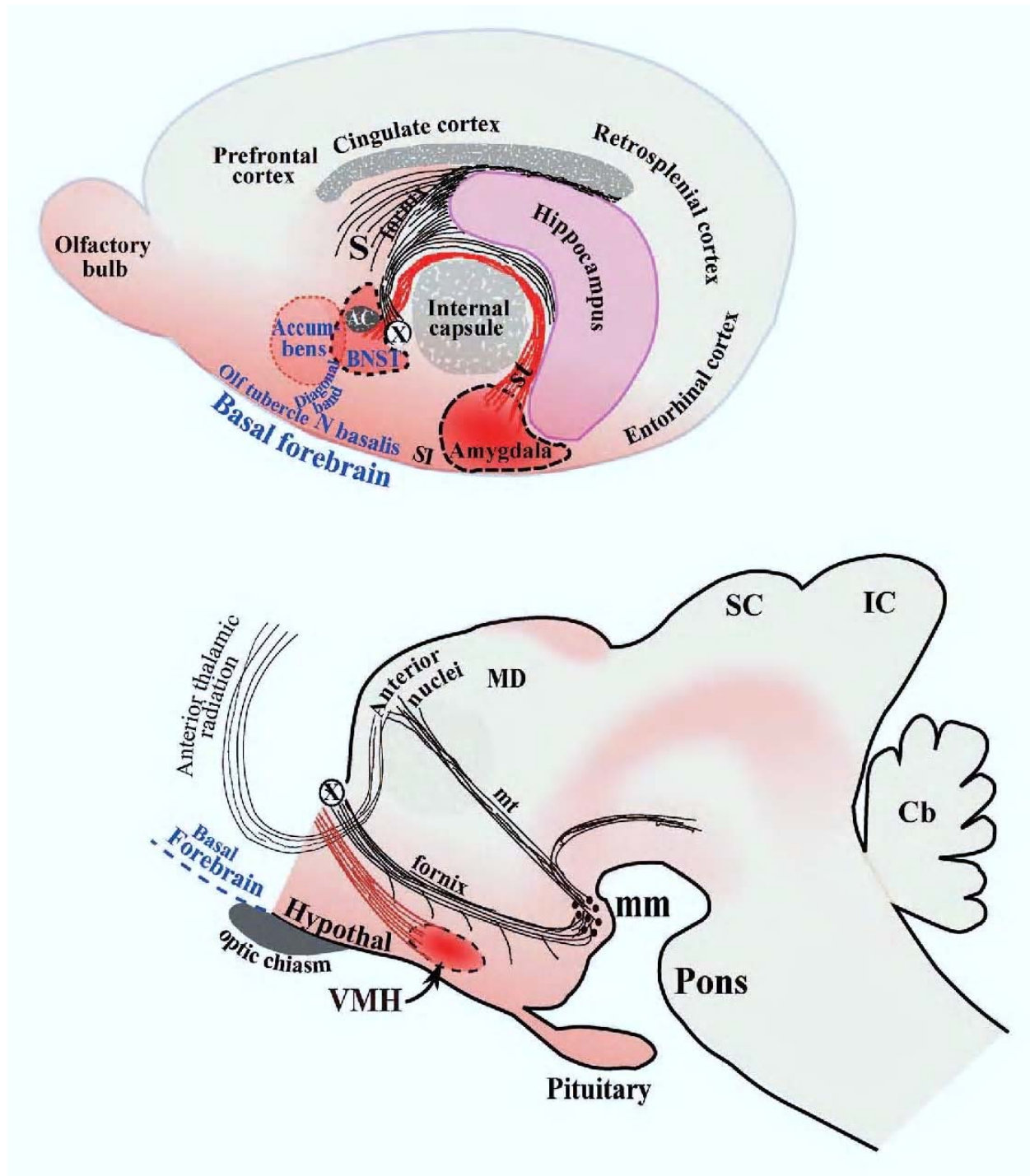
## **Questions, chapter 29:**

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

Next slide:

Cerebral hemisphere,  
medial view

**Basal Forebrain  
structures**



**Fig 29.9**

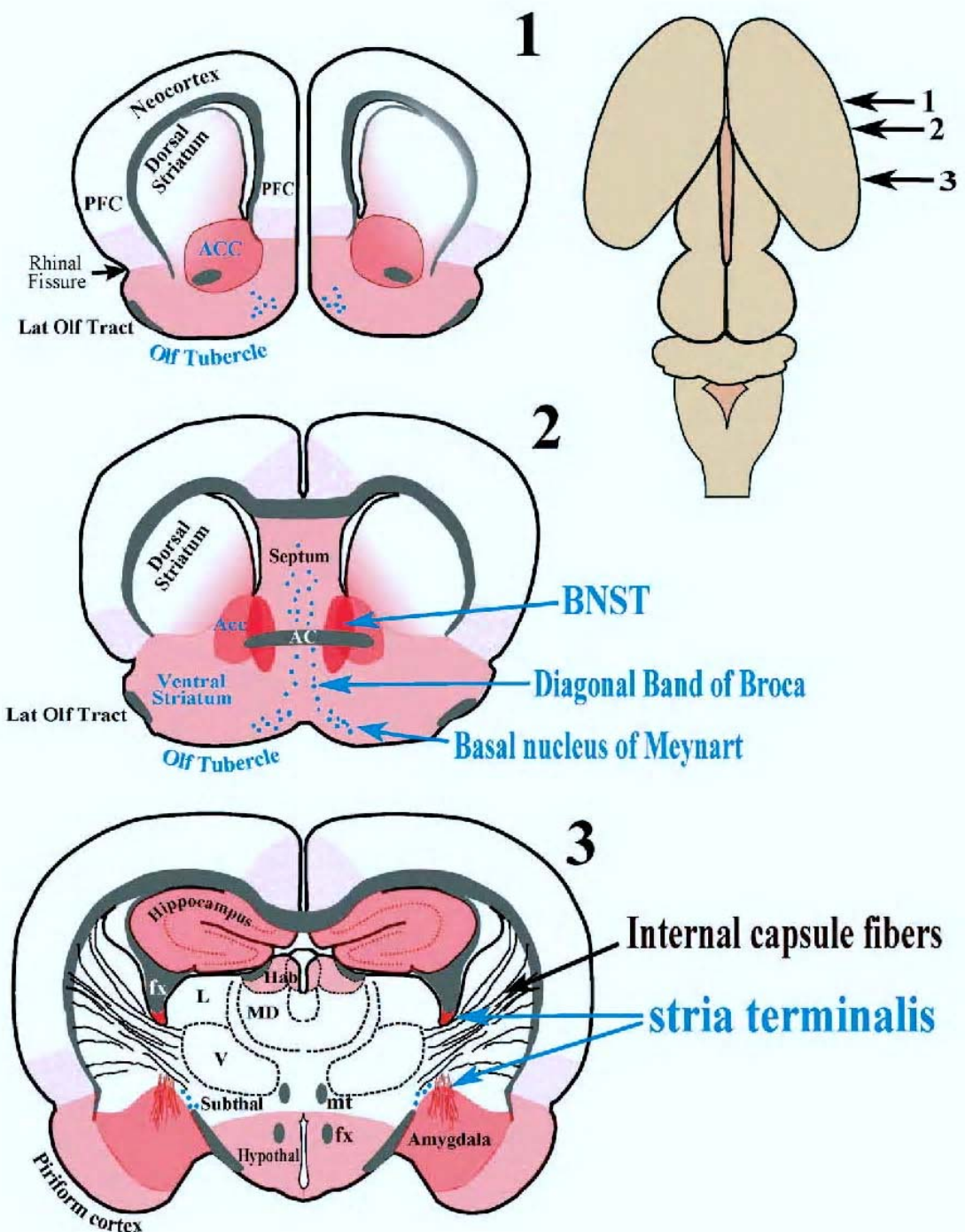
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# Frontal sections: the limbic system of rodent

Basal forebrain  
structures: Ventral  
striatum, including

- \* **Nuc. Accumbens**
- \* **Bed Nuc. of the Stria Terminalis**
- \* **Olfactory tubercle**
- \* **Basal nuc. of Meynart**
- \* **Diagonal band of Broca**



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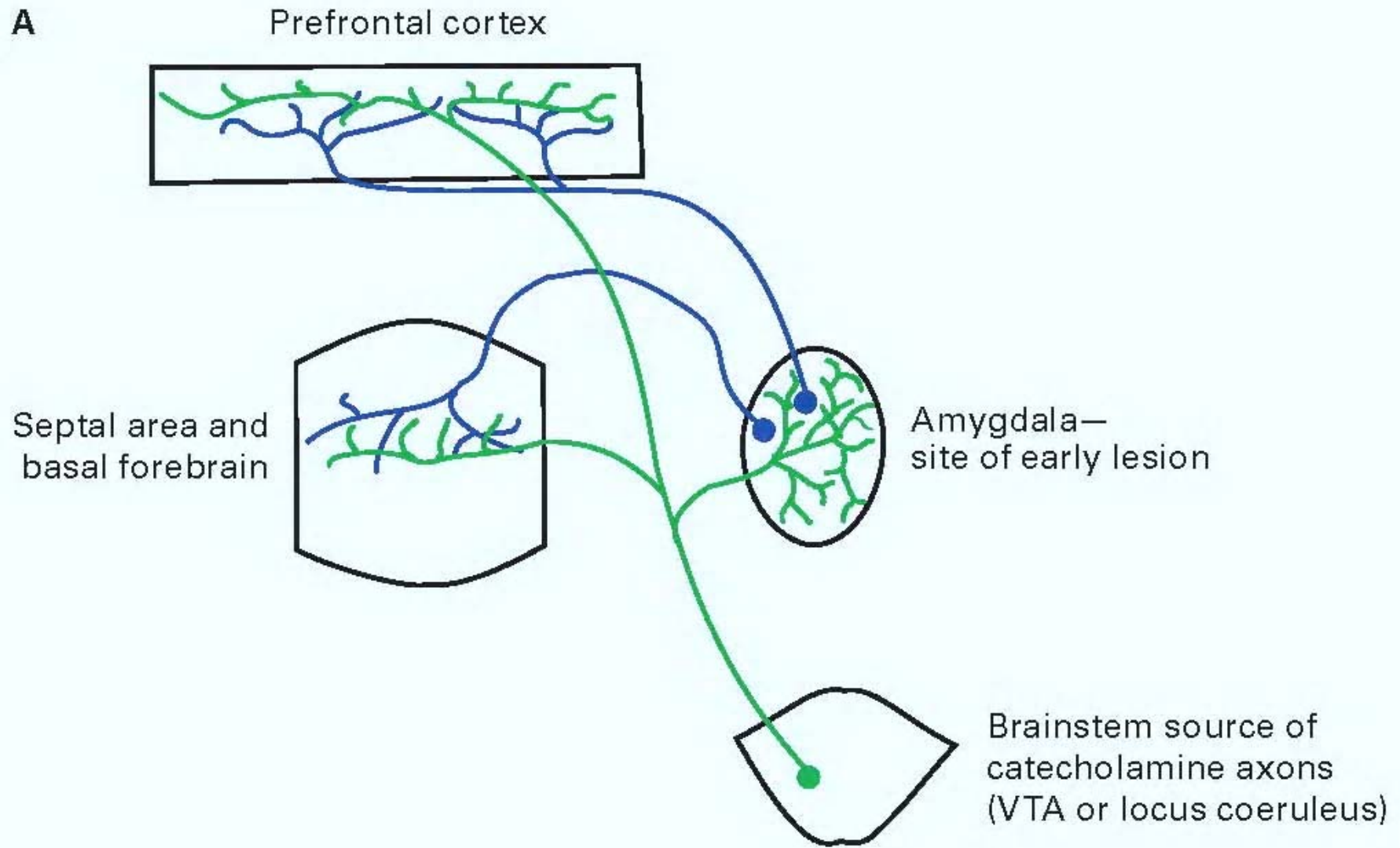
## Questions, chapter 29:

- 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:

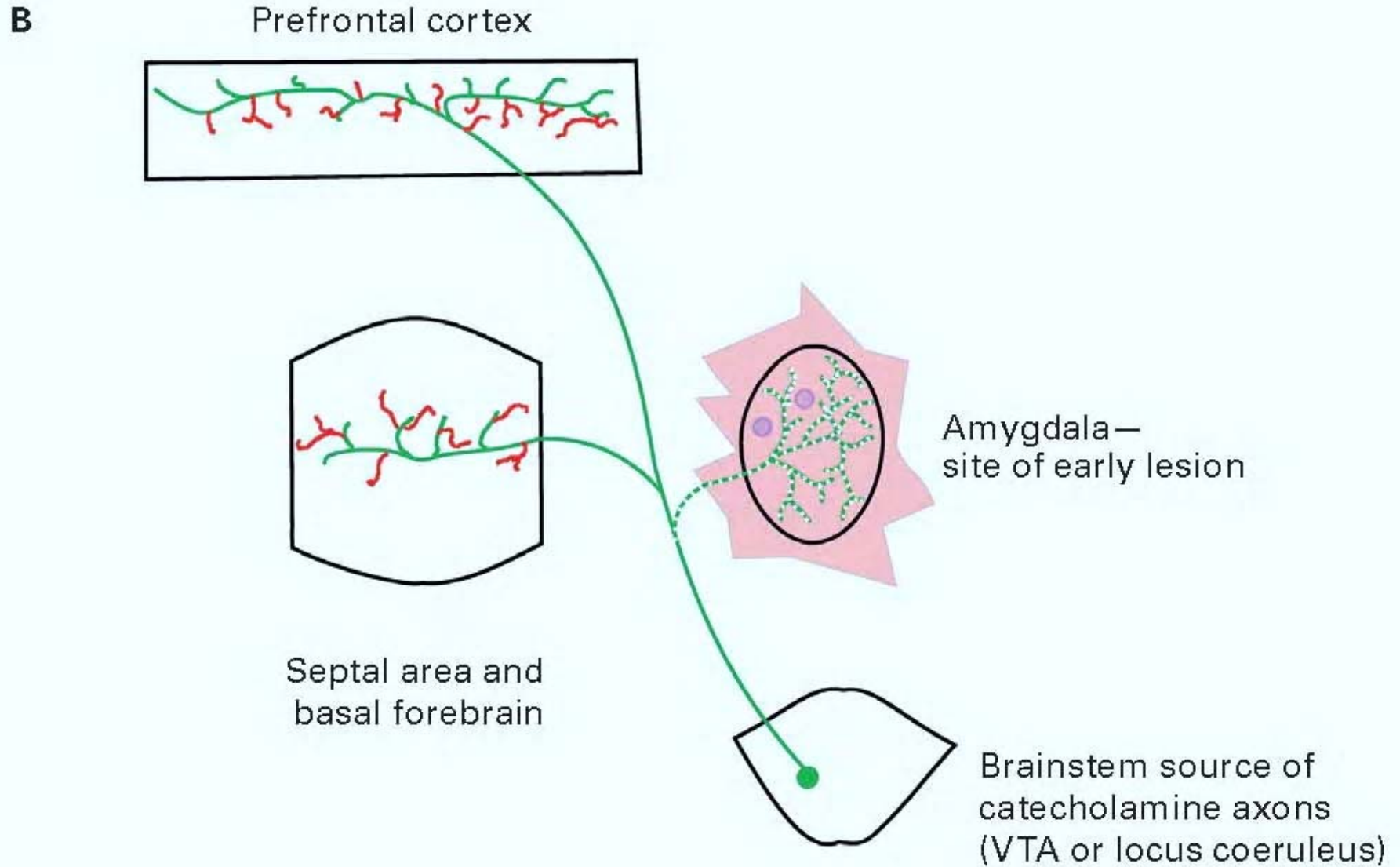
- *Prenatal lesion hypothesis of the etiology of some types of schizophrenia: Damage to amygdala*

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.



**Fig 29.12A**

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 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**

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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* 10, no. 3 (1990): 276-86.

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

Figure removed due to copyright restrictions.



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

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