

Contributions to theory

Study of how organized sequences of movement are produced, and how they can change, has led to the development of basic ideas about how the brain works.

Basic concepts in theories of CNS functions: The circuit level (“connectionist” models)

- 1 • Straight-through processing concepts
 - Reflexes, S-R models
 - Input analysis, or filtering
- 2 • Feedback control
 - “Reverberating circuits” (positive feedback)
 - Reciprocal inhibition
 - Homeostatic mechanisms
- 3 • Endogenous CNS activity (“spontaneous” activity)
 - Rhythmic activity; periodic bursts of activity
 - Maintained excitatory states
- + • Plasticity in the above mechanisms, usually meaning a change in connections
 - Molecular (synaptic change, etc.)
 - Anatomical (sprouting of various kinds)
- + • Modulation of the same mechanisms by neuromodulators that can alter the “brain state”—our next topic
 - Experimental and modeling studies of invertebrates, especially those in the laboratory of Eve Marder (Brandeis University)

Part 8:

The overall state of the brain

- What controls brain state changes?
- How many states are possible?

See chapter 17 of *Brain Structure and Its Origins*

Brain state changes

The structures and pathways underlying behavioral state control, including activity rhythms

- What is the **anatomy of brain-state changes** that underlie changes in behavioral state, such as
 - Going to sleep
 - Becoming aroused from sleep or drowsiness
 - Becoming hyperattentive when danger is near
 - Becoming dominated by feelings of hunger
 - (There are many other brain state changes that are scarcely studied, or not studied at all.)
- Changes in some of these states have been correlated with changes in membrane potential rhythms in the cortex.
Seen with electroencephalograph recordings (EEG).

Questions, chapter 17

- 1) What are two different types of mechanisms whereby the overall state of all or much of the brain can be changed?

Behavioral state control:

Brain states influenced by

- (A) widely projecting axon systems, and by
 - (B) chemical secretions
-
- State changes involve pathways fundamentally different from the type we have been discussing.
 - Examples:
 - The “reticular activating system”
 - Monoamine systems
 - Widely projecting neurons of the lateral hypothalamus
 - Secretions into the cerebrospinal fluid, e.g., during sleep onset.

Questions, chapter 17

- 2) Describe four axonal systems that are very widely projecting—systems where activity changes may change the overall state of the brain.

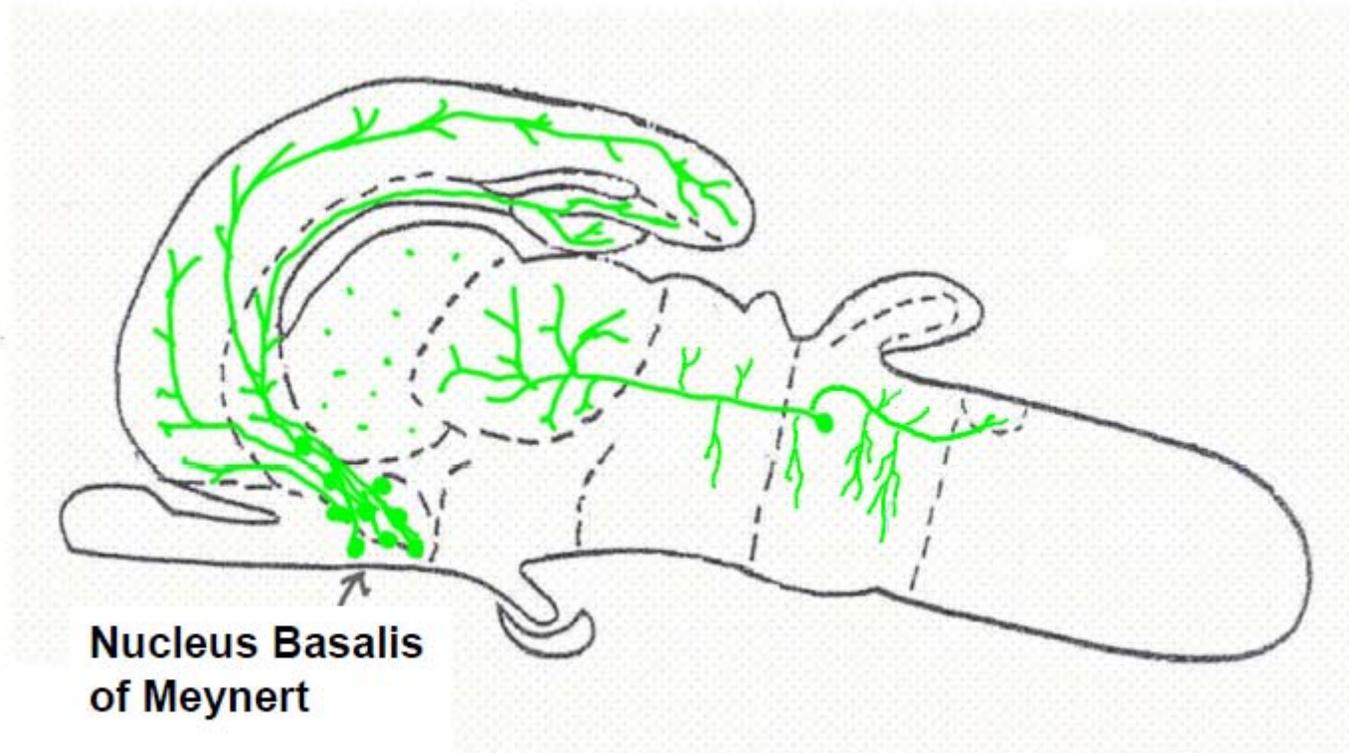
Reticular activating system: Example of a widely distributed axon from hindbrain

Figure removed due to copyright restrictions.

Many such cells use acetylcholine as their transmitter.

Cholinergic cells with widely distributed axons are also found in the basal forebrain; the axons project to neocortex (next slides).

Cholinergic neurons of the basal forebrain and hindbrain



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.

Cholinergic cells and axons

Figure removed due to copyright restrictions.

Please see: Nolte, John. "The Human Brain: An Introduction to Its Functional Anatomy." (2002).

Monoamine systems

- **Serotonin** (5 hydroxytryptamine, 5-HT)
 - Neurons of the raphe nuclei with widely distributed axons
 - Already in place in *Amphioxus*
 - Role in sleep and waking/arousal
 - Additional roles in mood stabilizationalization. *See Allman pp 19-27*
- **Catecholamines**
 - **Norepinephrine**-containing axon systems, *e.g.*, from the locus coeruleus of the rostral hindbrain
 - Role in sleep and waking/arousal
 - **Dopamine**-containing axon systems, *e.g.*, from the ventral tegmental area of the limbic portions of the midbrain
 - Role in reward/ reinforcement in learning processes

Serotonin-containing axons

Figure removed due to copyright restrictions.

Please see:

Heimer, Lennart. *The Human Brain and Spinal Cord: Functional Neuroanatomy and Dissection Guide*. Springer-Verlag Publishing, 1983.

**The widespread
projections of the
raphe nuclei of
midbrain &
hindbrain**

From: *Lennart Heimer,
The Human Brain and
Spinal Cord, 1983*

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Please see course textbook or:
Heimer, Lennart. *The Human Brain and Spinal Cord: Functional Neuroanatomy and Dissection Guide* . Springer-Verlag Publishing, 1995.

The rostral raphe nuclei give rise to two distinct kinds of axons with differences in projections.

Figure removed due to copyright restrictions.

Please see figure 17-5 of the course textbook or:

Törk, Istvan. "Anatomy of the Serotonergic Systema." *Annals of the New York Academy of Sciences* 600, no. 1 (1990): 9-34.

Norepinephrine-containing axons (noradrenergic systems)

**The Locus Coeruleus,
“The blue place”**

**(less than 25,000 cells in
humans; less than 1000
in smallest mammals)**

Figure removed due to copyright restrictions.

Please see:

Heimer, Lennart. *The Human Brain and Spinal Cord: Functional Neuroanatomy and Dissection Guide*. Springer-Verlag Publishing, 1983.

From: *Lennart Heimer,
The Human Brain and
Spinal Cord, 1983*

(Figure was altered for the book because of various mistakes in the original, and for the sake of simplification.)

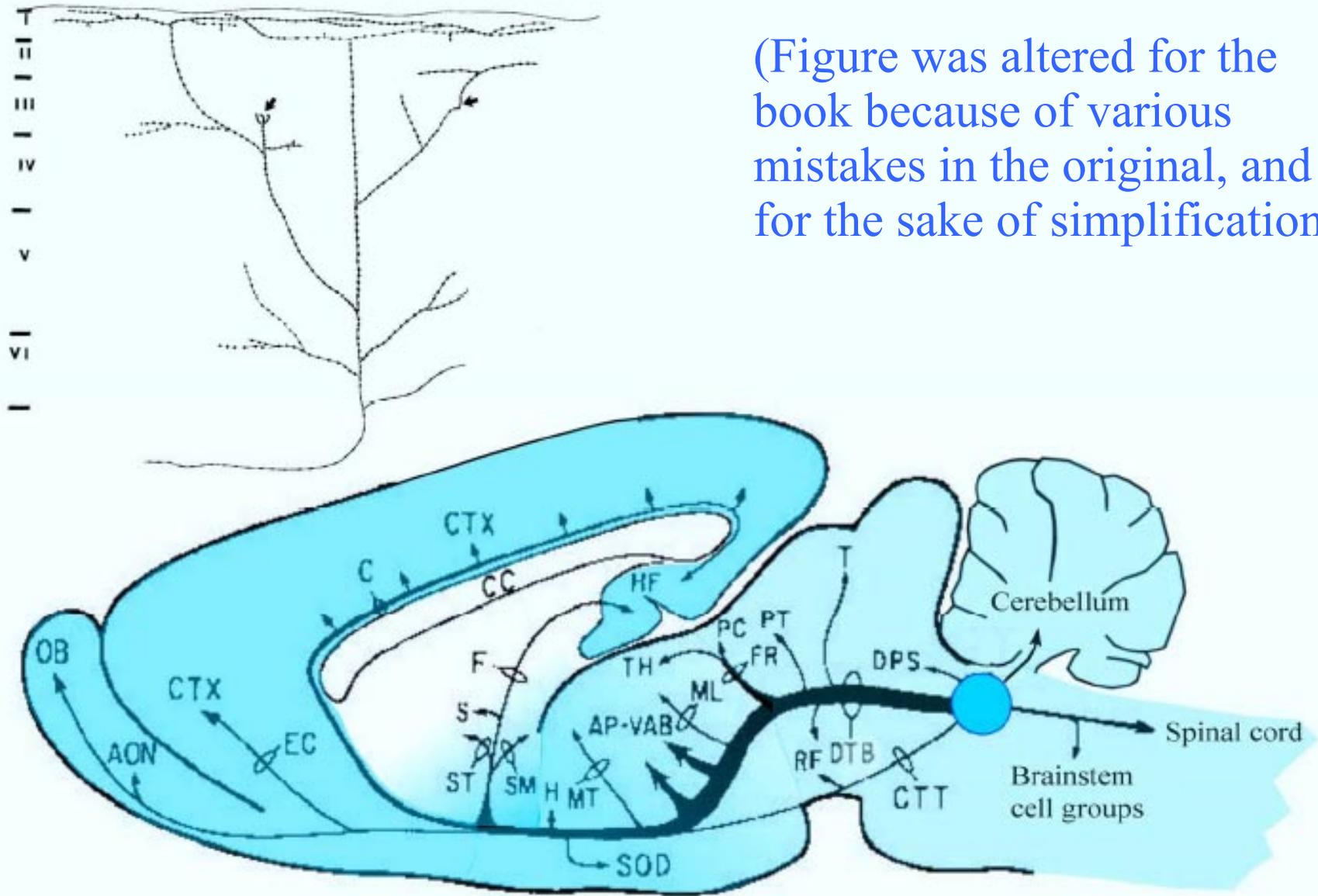


Fig 17-2

The noradrenergic system

Dopamine-containing axons (dopaminergic systems)

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Please see:
Heimer, Lennart. *The Human Brain and Spinal Cord: Functional Neuroanatomy and Dissection Guide*. Springer-Verlag Publishing, 1983.

Substantia Nigra

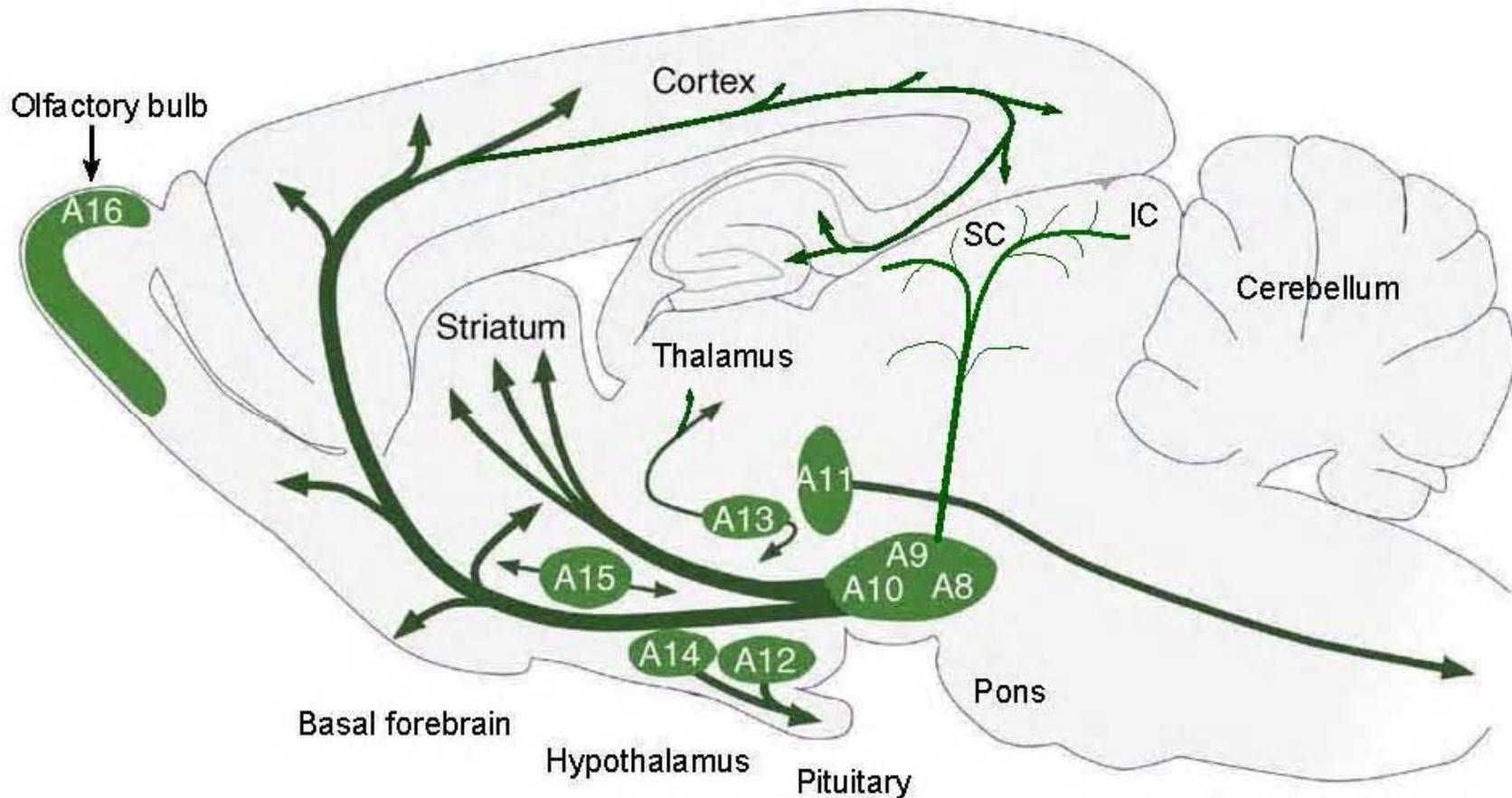
(source of DA to the striatum)

Ventral Tegmental Area

(source of DA axons to the limbic

From: *Lennart Heimer, The Human Brain and Spinal Cord, 1983.*

This picture has changed more recently (next slide)



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.

Dopamine-containing cell groups and axons (dopaminergic systems)

(The projection to the SC and IC is not very strong, and may originate in A13.)

Fig 17-3

Other widely projecting axon systems that influence behavioral state

- Cell groups in the midline and intralaminar nuclei of the thalamus (the “paleothalamus”)
 - Projections to large territories in the neocortex
 - ♥ One has projections to layer 1 of nearly the entire neocortex
- Cell groups in the lateral hypothalamus and adjoining subthalamus [Discoveries of Cliff Saper *et al.* at Harvard.](#)
 - One contains Melanin Concentrating Hormone
 - Another uses peptides Hypocretin/Orexin and Dynorphin as transmitters [\[NEXT SLIDE\]](#)
 - Mutations in the gene for H/O or its receptor cause narcolepsy
 - Another uses Corticotropin-releasing hormone (CRH), at least in anorexia states
- *See Swanson (2003), ch 7*

Figure removed due to copyright restrictions. Please see course textbook or:
Heydendael, Willem, Kanika Sharma, et al. "Orexins/Hypocretins Act in the Posterior Paraventricular Thalamic Nucleus during Repeated Stress to Regulate Facilitation to Novel Stress." *Endocrinology* 152, no. 12 (2011): 4738-52.

Blue: Norepinephrine axon distribution
Red: Orexin / hypocretin axons and cells

How many “brain states” are possible?

- Assume that there are four systems of the brainstem that can alter behavioral state, and that each of these systems has three possible states (e.g., no activity, low level of activity, high level of activity).
- Assume further that there are four diencephalic state-changing systems, discussed above, that each have three possible states.
- Assume that these eight systems can each operate independently.
- Calculate the number of possible states: $3^8 = 6,561$.
- If the 8 systems each have 4 possible states: $4^8 = 65,536$.

Remember that these “brain states” are largely independent of specific sensory, motor and cognitive activity. They interact with, but are at least partially independent of, emotional activities.

This is a bare-bones introduction to brain mechanisms that can change the state of much or all of the brain

- They were not all present in the earliest chordates
 - E.g., *Amphioxus* has only one catecholamine system/receptor—dopamine (but no norepinephrine).
 - Hagfish and lampreys have norepinephrine as well as dopamine
 - The monoamine Serotonin (5-hydroxytryptamine, or 5-HT) has been found in all of these animals.
- **However, the “primitive state” of many axons was that of widely branched and extensive distribution. In evolution, specific axon systems have become specialized for this kind of connection.**

Questions, chapter 17

- 3) How have changes in brain state been measured by the recording of electrical potentials? (This is not much discussed in the textbook.)

EEG recording patterns are correlated with various behavioral states, but the number of these EEG patterns are many fewer than the calculations of numbers of brain states in chapter 17.

- 4) How might brain-state control magnify the processing power of the neocortex? (This is a discussion question, touched on in some of the comments on suggested readings at the end of the chapter.) See slide 27. The same neuron may function in different ways in different states of the brain.

Review of chapters 1-17 and classes 1-18:

See the questions, names, terms posted for class 18. The midterm exam will be based on this review.

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9.14 Brain Structure and Its Origins

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