Lecture 2:
Neurotransmitters and Drugs
Osher Series

Karen Dobkins
Psychology Department
University of California, San Diego

Today's Lecture Outline

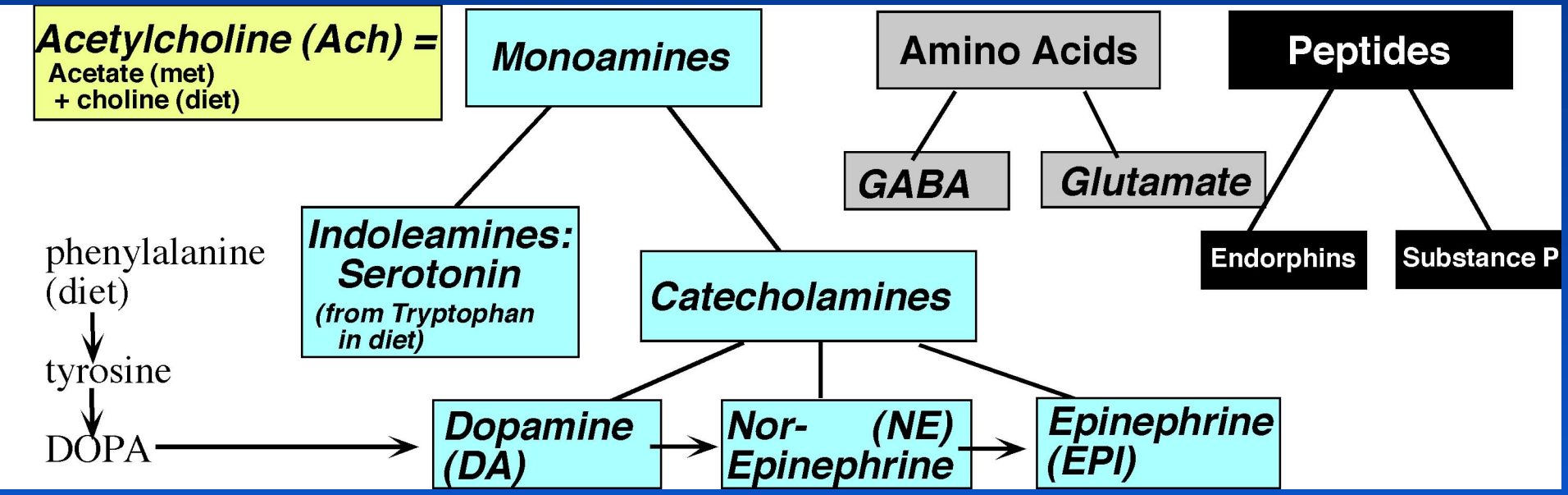
1) Neurotransmitter (NT) Types

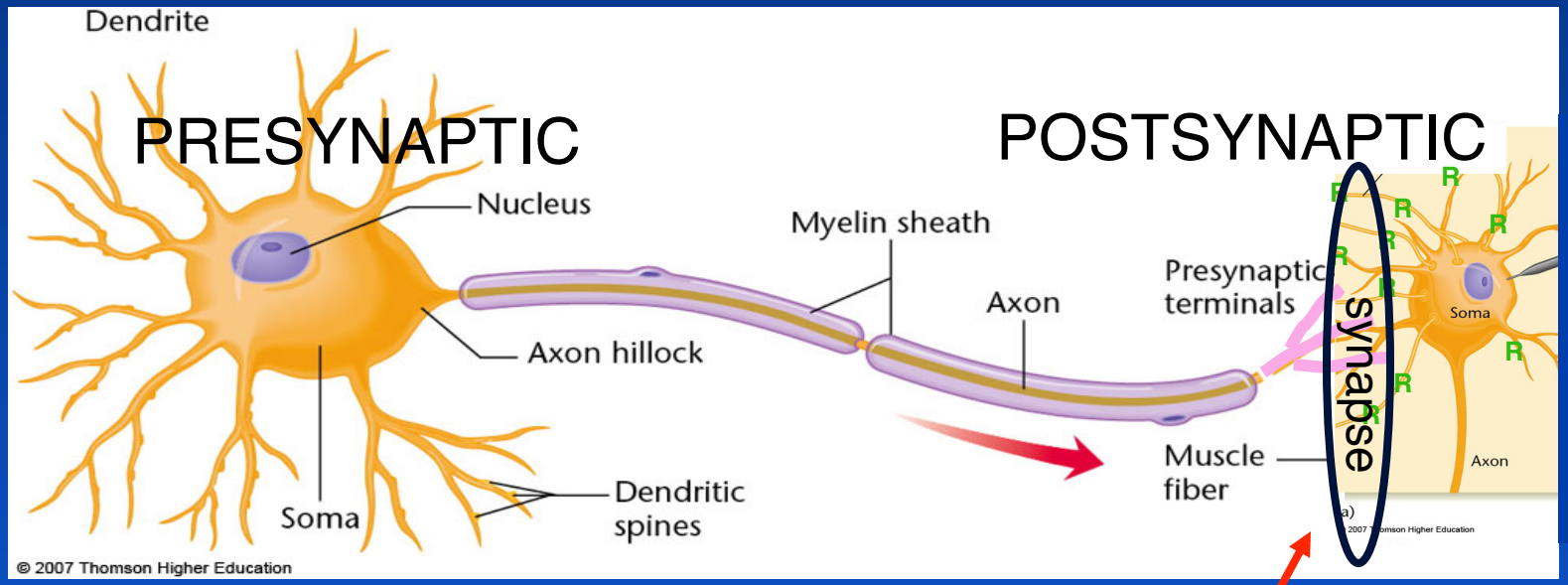
2) Reminder about Neural Communication

3) A Day in the Life of a NT

4) Synapses & Drugs

MAJOR NEUROTRANSMITTER (NT) TYPES





Overview of Events:

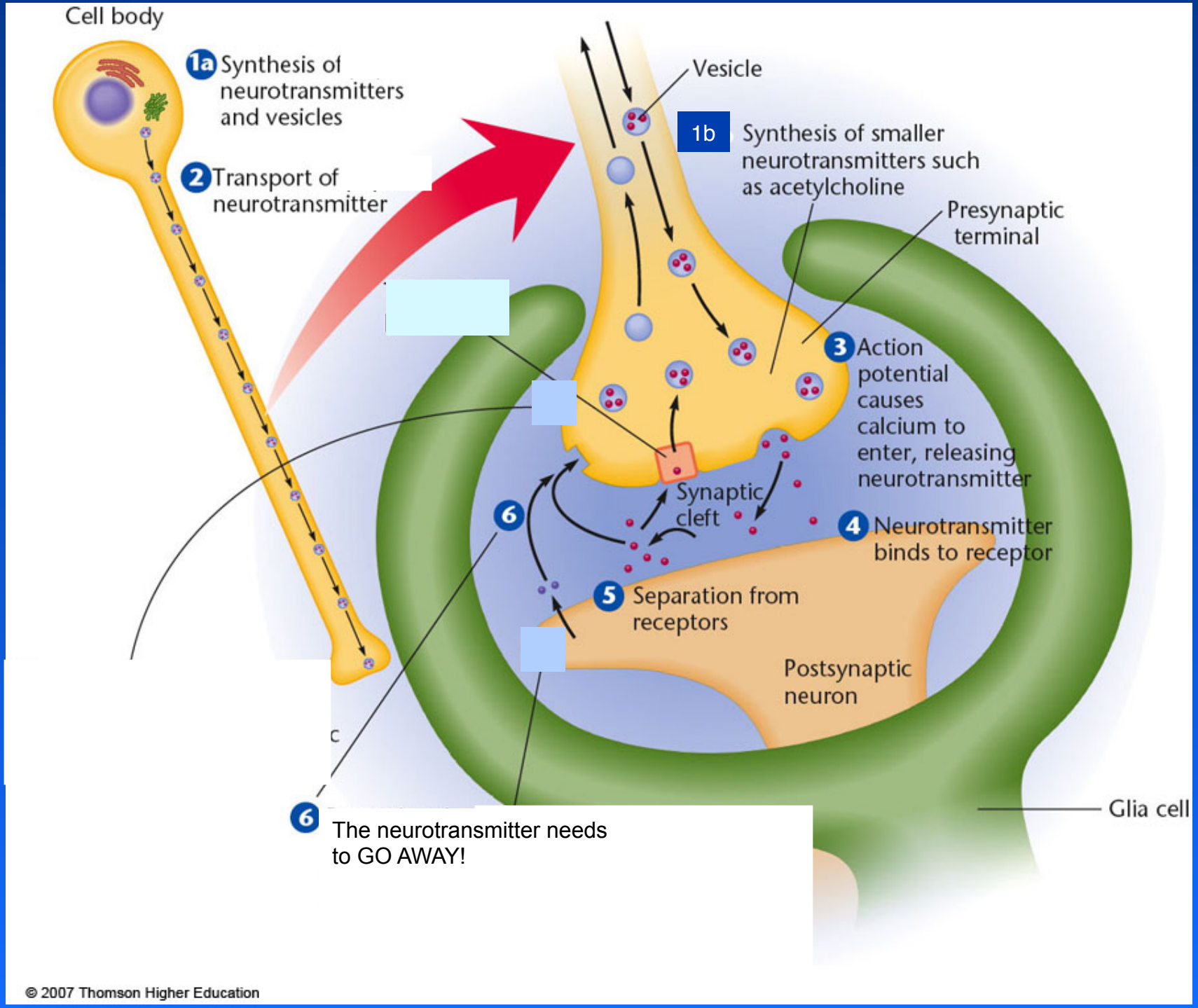
1) Electrical signal starts in the *presynaptic* neuron and travels down the axon to the presynaptic terminals.

2) Causes release of *neuotransmitter* into the ***synapse***

3) *Neuotransmitter* binds to *receptors (R)* on *postsynaptic* neuron's dendrites

4) Triggers an *electrical signal* in postsynaptic neuron, and so on…..

A Day in the Life of a Neurotransmitter (NT)



6) The NT needs to go away!

a) NT is *re-absorbed* by the presynaptic terminals, i.e., *recycled*

e.g., Monoamines

b) NT is altered (in the synapse) to be *inactive*

i) broken down by <u>enzymes</u>

e.g., Acetylcholinesterase (AChe):
ACh -> acetate + choline
choline reabsorbed and added to acetate

ii) converted to an *inactive* state by <u>enzymes</u>

e.g., MAO (monoamine oxidase),
converts Monoamines to inactive state
- drugs that inhibit MAO are used for depression

c) Release of more NT is inhibited by activation of *presynaptic AUTO-receptors*

d) NOTE: NT will *float away* eventually (relevant to drugs that inhibit re-absorption)

MAJOR RECEPTOR TYPES (named for which NT binds to it)

But note: receptors are sometimes named for Drug they bind to (no standard rule…….)

Acetylcholine (Ach) Receptor:

~4 Nicotinic Receptor Types (Ionotropic, fast acting)

~5 Muscarinic Receptor Types (Metabotropic, slow acting)

(of course bind Ach too)

In PNS: at Neural-Muscular Junction

Nicotinic (skeletal muscle, e.g., bicep, diaphragm)

Muscarinic (smooth muscle, e.g., uterus)

In CNS: Both Nicotinic and Muscarinic Exist

Norephinephrine (NE): 2 receptor types

Alpha Receptors

Beta Receptors

Dopamine (DA): ~5 Receptors

Serotonin (5-HT): ~14 Receptors

How Drugs Affect Neurons

Agonist: mimics or increases the effect of a neurotransmitter system

Antagonist: blocks or decreases the effect of a neurotransmitter system

5 ways to be an **AGONIST:**

1) Drug Stimulates Receptor: Mimics NT

e.g., **Nicotine** attaches to *Nicotinic **Ach*** receptor
(and has roughly same effect)

e.g., **XANAX (Benzodiazepine)** attaches to *GABA* receptor
(GABA is INHIBITORY)

2) Drug stimulates release of more NT

e.g., **Amphetamines -> NE**
-> DA

3) Drug blocks re-absorption of NT at the synapse

e.g., Amphetamines & Cocaine (& Ritalin)
Cocaine blocks the re-absorption of DA
"Crashing" (depletion, because NT "floats away")

4) Drug acts as a precursor for the NT

e.g., **L-DOPA** synthesizes to DA (Parkinson's)

5) Drug inactivates enzyme that breaks down NT:

e.g., **Physostigmine** inhibits *Acetylcholinesterase*

Iproniazid inhibits *Monoamine Oxidase*

5 ways to be an **ANTAGONIST:**

1) Drug blocks receptor

e.g., **Curare** attaches to *Acetylcholine (Ach) receptor*, and keeps Ach from binding to receptor -> **muscle paralysis**

2) Drug inhibits NT release

e.g., Clostridium botulinum (bacteria) releases **botulin toxin** -> inhibits *release* of **Ach** -> muscle paralysis (called "botulism")

3) Drug inactivates synthetic enzyme

e.g., **AMPT** blocks enzyme that converts *tyrosine -> DOPA*

4) Drug makes the synaptic vesicles "leaky"

e.g., **reserpine**: *monoamine* vesicles

5) Drug stimulates autoreceptors

e.g., **Clonidine**: *NE autoreceptors*

Recreational Drugs

(not always clear if they are Agonists or Antagonists)

Hallucinogenic Drugs (LSD, PCP, mescaline, X)

Serotonin system. Agonist??

creates hallucinations, dream-like state

Raphe nuclei in brainstem (sleep and dreams)

Other Serotonin-Related (Agonist) Drugs

PROZAC (depression) -> prevents re-absorption

St. John's Wort for Depression (more natural?)

- social phobias, schizo, bulemia, autism

Opiates (Heroin, Morphine, Methadone)

endorphin receptor *AGONISTS*

used as "pain-killers" (more later in course)

produce "euphoria"

Marijuana (THC and other cannabinoids, from Cannabis plant)

acts on **cannabinoid** receptors (numerous in the brain especially in HIPPOCAMPUS). Agonist?

dissolve in body FATS

intensified sensory experience, time slows down

used clinically for pain, nausea, glaucoma, migraines

"Overdosing": shutting down the *medullary respiratory center*

Barbiturates and Opiates -> Yes

Marijuana -> NO

Ondine's Curse