Medical Neuroscience | Tutorial Notes

Neurotransmitters

MAP TO NEUROSCIENCE CORE CONCEPTS[1]

NCC2. Neurons communicate using both electrical and chemical signals.

LEARNING OBJECTIVES

After study of the assigned learning materials, the learner will:

1. Name the major small molecule neurotransmitters and neuropeptides in the CNS and briefly state the function of each.
2. Account for the factors that determine the effect of neurotransmitters on postsynaptic neurons.

TUTORIAL OUTLINE

I. Overview of neurotransmitters

- A. review mechanisms of chemical synaptic neurotransmission (see **Figure 5.3**[2])
- B. two broad classes based on molecular size and chemical class (see **Figure 6.1**)
  - 1. small-molecule neurotransmitters
    - a. typically mediate **rapid synaptic effects** (i.e., post synaptic potentials are relatively brief, a few msec) when bound to ionotropic receptors
    - b. however, they may elicit long-lasting effects when bound to metabotropic receptors – see below
    - c. most important representatives
      - **(i)** **glutamate**: major excitatory neurotransmitter in the CNS
        - review the organization of glutamatergic synapses by viewing a short online animation that accompanies *Neuroscience, 5th. Ed.*, Chapter 6: Animation 6.2 Neurotransmitter Pathways: Glutamate [click here]
      - **(ii)** **GABA**: major inhibitory neurotransmitter in the brain
      - **(iii)** **glycine**: major inhibitory neurotransmitter in the spinal cord

[1] Visit **BrainFacts.org** for *Neuroscience Core Concepts* (©2012 Society for Neuroscience) that offer fundamental principles about the brain and nervous system, the most complex living structure known in the universe.
[2] Figure references to Purves et al., *Neuroscience, 5th Ed.*, Sinauer Assoc., Inc., 2012. [click here]

(iv) **acetylcholine**: excitatory neurotransmitter of somatic motor neurons, major excitatory neurotransmitter in autonomic ganglia and post ganglionic parasympathetic fibers, and special modulatory systems in the CNS

- for an overview of a central cholinergic synapse, see **Figure 6.2**
- review the organization of cholinergic synapses by viewing Animation 6.1 Neurotransmitter Pathways: Acetylcholine [click here]

(v) **biogenic amines (dopamine, serotonin)**: involved in motivation and reward systems; also linked to several neuropsychiatric disorders and movement disorders (see **Boxes 6B** & **6E** and **Figures 6.11** & **6.13**)

review the organization of dopaminergic synapses by viewing Animation 6.3 Neurotransmitter Pathways: Dopamine [click here]

- review the organization of serotonergic synapses by viewing Animation 6.5 Neurotransmitter Pathways: Serotonin [click here]

2. neuropeptides

   a. mediate **slower and more long-lasting synaptic effects** (i.e., post synaptic potentials may last 100s of msec to seconds, or even minutes and longer) when bound to metabotropic receptors

   b. most important

      (i) **substance P**: a neurotransmitter of pain and temperature fibers that synapse in the spinal cord

      (ii) **opioids**: have analgesic effects in brain; also inhibit release of substance P in spinal cord

      (iii) hypothalamic releasing hormones (affect secretory cells in anterior pituitary) & posterior pituitary hormones

3. "unconventional" (i.e., poorly understood) neurotransmitters

   a. ATP and other purines

      (i) ATP may be co-released with other small molecule neurotransmitters

      (ii) Once in extracellular spaces, ATP is metabolized into adenosine, which has its own biogeneic activity

      (iii) Adenosine is now thought to be an important signal (in the hypothalamus, at least) that modulates wakefulness by promoting sleepiness

(iv) Xanthines (including caffeine) block adenosine receptors (which is why caffeine fights sleepiness!)

b. Endocannabinoids

(i) produced from membrane lipids and bind to receptors that also bind the psychoactive component of marijuana

(ii) hydrophobic; hence, they readily diffuse through neuronal membranes and leave neurons where they can interact with membrane bound receptors on other cells

(iii) play a role in the plasticity of inhibitory circuits in the brain (see **Figure 6.19**)

c. Nitric oxide (NO)

(i) Gas produced from the metabolism of the amino acid, arginine – a process regulated by calcium

(ii) Since it is a gas, if can diffuse freely across neuronal and glial cell membranes to influence a local volume of brain tissue

(iii) Some actions of NO are mediated by the activation of an enzyme guanylyl cyclase, which when activated produces the second messenger, cGMP (see **Figure 6.20**)

(iv) a passing note of interest … Viagra and related drugs work by affecting NO-mediated signaling

II. Neurotransmitter cycle for small-molecule neurotransmitters and neuropeptides (see Table below and **Figure 5.5**; see also **Figure 6.5** for glutamate cycle)

	Small-molecule neurotransmitters	**Neuropeptides**
Synthesis	in presynaptic terminal by specific enzymes	in cell bodies in the form of pre-(pro)-peptide and later cleaved into active transmitter
Packaging & release	small vesicles near active zone in presynaptic terminal low frequency of neural activity sufficient for release docked vesicles released with influx of even low levels of Ca^{++} rapid onset	large vesicles away from active zone high frequency of neural activity are required for release vesicles only released with influx of high levels of Ca^{++} slower onset
Removal of neurotransmitter	passive diffusion reuptake into presynaptic terminal uptake into astrocytes enzymatic degradation	passive diffusion -- -- enzymatic degradation

III. Activities of neurotransmitters

A. the actions of a neurotransmitter is NOT dictated by the chemical structure of the neurotransmitter

B. *the response elicited by any given neurotransmitter will depend upon the post synaptic receptor and the associated types of channels and second messenger systems* (more on this topic in the next tutorial)

STUDY QUESTIONS

Q1. Which of the following substances is associated with fast, excitatory neurotransmission in the central nervous system?

A. dopamine
B. acetylcholine
C. gamma aminobutyric acid
D. endorphin
E. glutamate

Q2. Which of the following substances plays a role in the plasticity of inhibitory circuits in the brain?

A. gamma aminobutyric acid
B. endocannabinoids
C. adenosine
D. nitric oxide
E. dopamine