Molecular Neurobiology for Practicing Psychiatrists, Part 1: Overview of Gene Activation by Neurotransmitters

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Issue: *Molecular biology is increasingly relevant to practicing psychiatrists because it helps to explain the biological basis of mental disorders and especially the molecular and pharmacologic mechanism of action of psychotropic drugs. The ultimate action of neurotransmitters and drugs that act at receptors is to alter the activity of neuronal genes.*

This feature begins the first of a series of articles on molecular neurobiology for the practicing psychiatrist. Shown here is the "visual vocabulary" for each of the critical elements in the activation of neuronal genes by neurotransmitters.[1] Subsequent lessons will demonstrate how each element of this visual vocabulary relates to the others, resulting ultimately in the expression of genes that regulate neuronal functioning in the target neuron.

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Figure 1. Neurotransmitter Receptors

Neurotransmission begins with "first messenger" neurotransmitters (such as the monoamines serotonin, norepinephrine, and dopamine) occupying their receptors (usually a member of the receptor superfamily known as 7 transmembrane region G protein–linked second messenger system), which results in activation of second messenger systems.

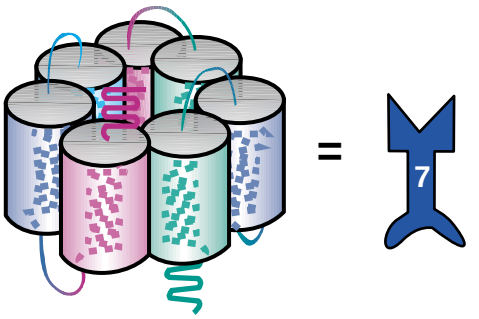


Figure 2. Enzymes

The second messengers then hand the message off to an enzyme that participates in the regulation of gene activation by changing the messenger into another form, such as transcription factors. The most important enzyme, protein kinase, phosphorylates various intracellular proteins, especially various transcription factors. Other important enzymes include dephosphatase enzymes, which reverse the phosphorylation process, and RNA polymerase, which transcribes DNA into RNA.

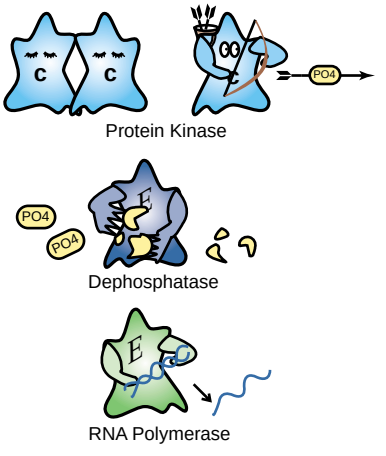
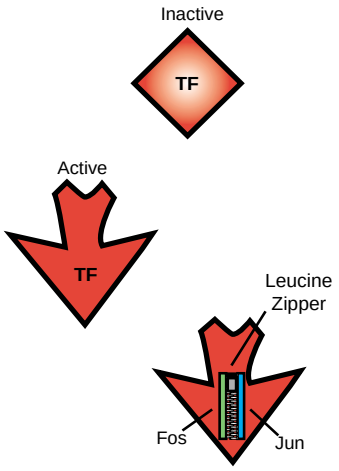


Figure 3. Transcription Factors

Transcription factors are molecules that activate genes by allowing RNA polymerase to spring into action.



Take-Home Points

- Chemical neurotransmission can be described as a cascade of biochemical events resulting in changes in the expression of genes in the target neurons.
- Molecular elements in this cascade include not only the neurotransmitter and its receptor, but also second messengers, enzymes, transcription factors, genes, and gene products.

Figure 4. Genes

It is estimated that there are over 100,000 genes in the human genome, including a category known as immediate-early genes (early response genes), with exotic names such as c-*fos* and c-*jun*, which are some of the very first to be transcribed directly following neurotransmitter action at postsynaptic receptors. Late-onset genes are turned on by the products of these early-onset genes and perpetuate the cascade begun way back with the neurotransmitter.

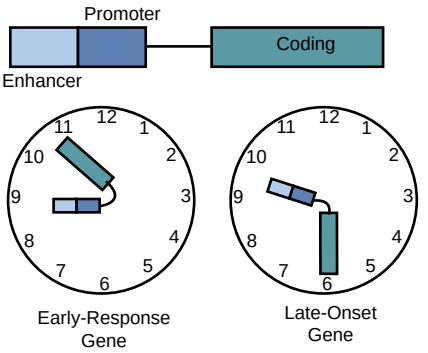
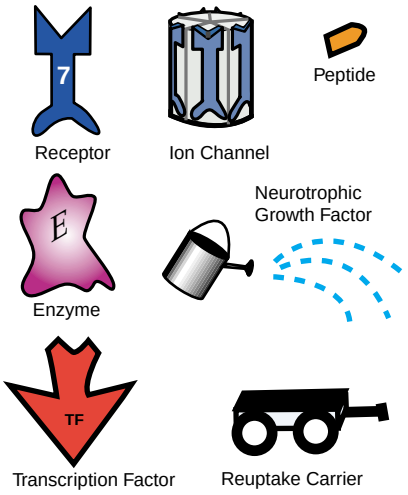


Figure 5. Gene Products

Late-onset genes are the ultimate regulators of the postsynaptic neuron, as their gene products include all of the important proteins made by the target neuron, including enzymes, receptors, transcription factors, growth factors, structural proteins, and many more. In addition to the role of these players in chemical neurotransmission, each molecule is a known or potential site of drug interactions. Each is also a theoretical site of malfunction that could contribute to a nervous or mental disorder.



REFERENCE

1. Stahl SM. Essential Psychopharmacology. 2nd ed. New York, NY: Cambridge University Press. In press

Coming Next Issue

PART 2: HOW NEUROTRANSMITTERS ACTIVATE SECOND MESSENGER SYSTEMS