Molecular Neurobiology for Practicing Psychiatrists, Part 2: How Neurotransmitters Activate Second Messenger Systems

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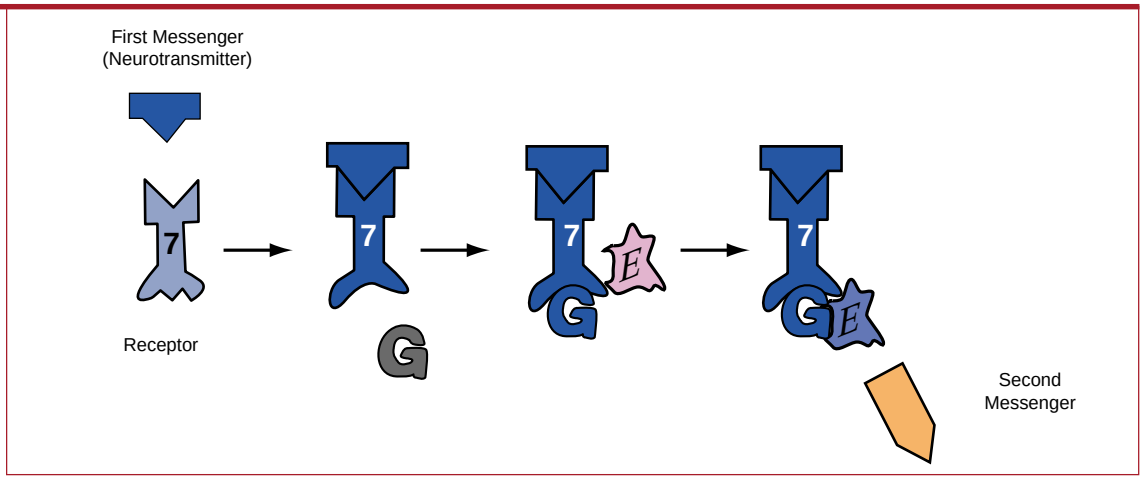
Issue: *Chemical neurotransmission begins when receptor occupancy by a neurotransmitter is converted into an intracellular second messenger that carries the information from the neurotransmitter deep into the target neuron. For clinicians, it is this transfer of neurotransmitter information all the way to the genome that hypothetically explains the therapeutic actions of many psychotropic drugs. This also accounts for why drugs that modify neurotransmission may take time to fully develop their clinical actions.*

This feature is the second in a series on molecular neurobiology for the practicing psychiatrist. Last month's BRAINSTORMS[1] provided a visual vocabulary of the elements involved in translating neurotransmitter-occupied receptors into genes expressed in the target neuron. Here we begin with the first step in this process, namely, formation of an intracellular second messenger triggered by occupancy of a neuronal membrane–bound receptor by its neurotransmitter.[2] Next month, we will show how this second messenger activates intracellular enzymes and transcription factors.

A second messenger system includes several elements: (1) the first messenger (neurotransmitter), (2) the neurotransmitter's receptor, (3) a second receptor called a G protein that interacts with the neurotransmitter receptor, (4) an enzyme triggered into action by the interacting pair of receptors, and (5) a second messenger molecule manufactured by this enzyme. The 2 best known examples of second messengers are cyclic AMP and phosphatidyl inositol (PI). The systems that produce these second messengers are also sometimes known as the cyclic AMP second messenger system, and the PI second messenger system, respectively. Although the actions of a stimulatory G protein are shown here, other types of G proteins are inhibitory and slow down or prevent coupling of the receptor with the enzyme that makes the second messenger.

Overview



Thus, the handoff of first messenger to second messenger is accomplished by means of a molecular cascade: neurotransmitter to neurotransmitter receptor (Figure 1); neurotransmitter receptor to G protein (Figure 2); binary complex of 2 receptors to enzyme (Figure 3); and enzyme to second messenger molecule (Figure 4). ◆

REFERENCES

1. Stahl SM. Molecular neurobiology for practicing psychiatrists, part 1: overview of gene activation by neurotransmitters [BRAINSTORMS]. J Clin Psychiatry 1999;60:572–573
2. Stahl SM. Essential Psychopharmacology. 2nd ed. New York, NY: Cambridge University Press; In press

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Figure 1.

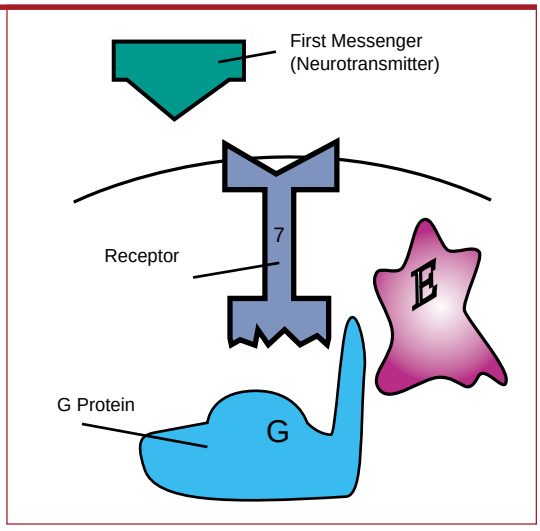


Figure 2.

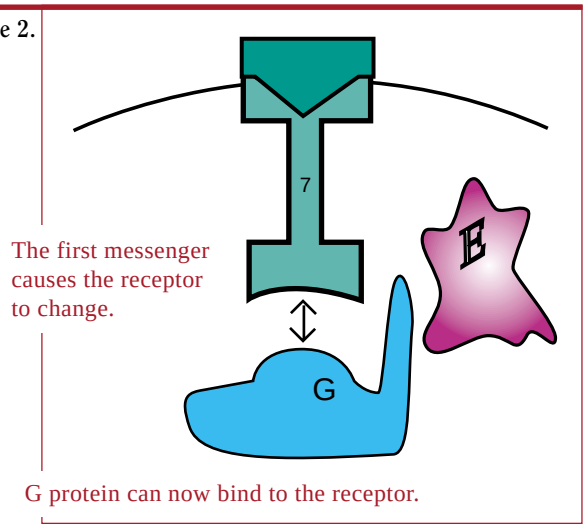


Figure 3.

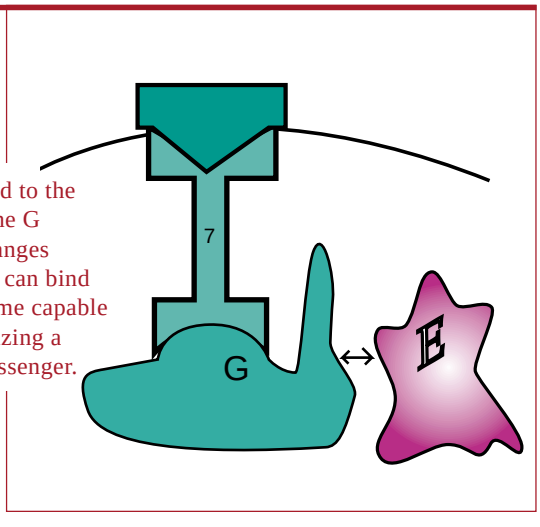
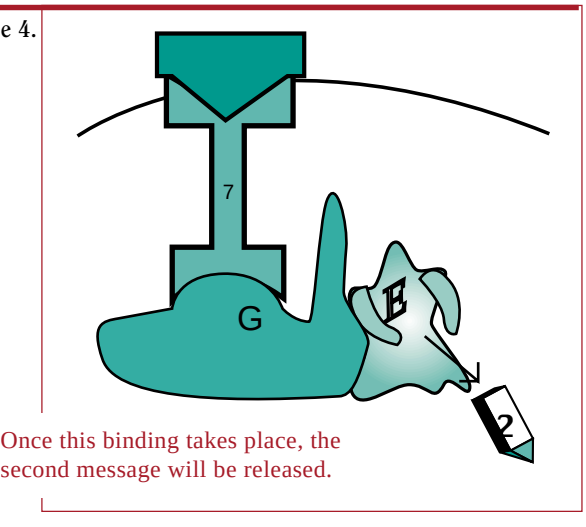


Figure 4.



Coming Next Issue

PART 3: HOW SECOND MESSENGERS "TURN ON" GENES BY ACTIVATING PROTEIN KINASES AND TRANSCRIPTION FACTORS