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Perspective

Signal Transduction Mechanism in the Brain

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DESCRIPTION

The brain is composed of 150 billion nerve cells (or neurons), each of which can create synapses with thousands of other neurons. The amazing complexity of the brain is illustrated by the specificity of this staggering number of synaptic connections, which underpins all aspects of brain function. An electrical impulse at the synapses causes a chemical messenger termed a neurotransmitter to be released from the terminal of one neuron (a nerve terminal). This neurotransmitter diffuses through space and attaches to specialized receptor proteins in the next neuron. The majority of these receptor sites are found on dendrites, which are the parts of neurons that receive signals.

Neurotransmitter attachment to the receptor causes changes in the neuron, including changes in other specialized proteins called ion channels, which cause electrical changes in the next cell. Other types of specialized proteins called transporters, which physically pump the neurotransmitter back into its nerve terminals for subsequent release, turn off the neurotransmitter signal in most circumstances. Langley coined the term "receptive substance" in 1905 to define the component of the cell that hormones, neurotransmitters, and neuromodulators interact with. Clark proposed in 1926 that acetylcholine and its receptive material undergo a reversible monomolar reaction, with the latter being a small constituent of the cell. Cell surface receptors (like those for acetylcholine) are divided into two categories: ligand-gated ion channels (like the nicotinic receptor) and G protein coupled receptor systems (such as for the muscarinic receptor). GTP binding (G) proteins connect receptors to a variety of effector systems in the latter.

To begin, most drugs of addiction affect the brain by interfering with synaptic transmission: that is, each drug of abuse binds to an antique protein target found at the synapse. Many drugs of abuse (opiates, nicotine, and marijuana) mimic many neurotransmitter chemicals found in the brain, as shown in the diagram. Other medicines, particularly stimulants (cocaine, amphetamine, and methamphetamine), target the dopamine transporter in various ways, but all result in increased dopamine signals at the synapse. Other medicines, such as alcohol and phencyclidine, work by affecting the excitability of neurons through the brain's ion channels.

Unfortunately, these immediate impacts of drugs do not account for the long-term consequences of repeated exposures, which are required to induce addiction. To comprehend such long-term impacts, scientists must look beyond the traditional synapse to a more comprehensive perspective that includes post-receptor, and intracellular messenger pathways. This means that, despite a drug's initial actions on the activity of a neurotransmitter or receptor system, the complex network of intracellular messenger pathways that mediate physiological responses to neurotransmitter-receptor interactions is ultimately responsible for the many effects of drugs on brain function. G proteins, second messenger systems, protein kinases, and protein phosphatases are only a few of the intracellular pathways. As a result of recurrent disturbance of these intracellular pathways, which eventually alter gene expression, repeated exposure to medicines induces molecular and cellular changes. Many aspects of addiction, we believe, are ultimately caused by these long-term adaptations.

CONCLUSION

Neuroprotective factors and their signaling pathways regulate many aspects of neuronal function and survival during development and in the adult central nervous system.

The discovery of these pathways has opened up many new target sites for the development of new drugs to treat a variety of neurologic and psychiatric disorders. Furthermore, understanding the functions of these pathways in the normal nervous system may lead to the discovery of aberrant circumstances that underpin pathologic illnesses. The introduction of growth factor action into neurosciences brings up possibilities that are just as rich and strong, if not more so, as those offered by more traditional neurotransmitter systems.

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