Biogenic Amine Transporters: Targets for Drugs of Therapy and Abuse

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An important aspect in the life cycle of a neurotransmitter molecule is its transport across the plasma membrane of a neuron or glial cell. This process serves two important functions. The transport, or re-uptake, process terminates the action of extracellular transmitter on cell surface receptors and it also provides a mechanism for recycling the transmitter molecule so that it can be reused. For the biogenic amines serotonin, dopamine, and norepinephrine, three closely related membrane proteins mediate the reuptake process. An indication of the relative importance of these proteins in brain physiology is the dramatic effect of drugs that inhibit the transport process. Substances that inhibit the serotonin transporter or the norepinephrine transporter have proven to be clinically useful as antidepressants. Psychostimulants such as cocaine and amphetamines block biogenic amine transporters or cause them to release intracellular transmitter. Molecular studies aimed at understanding the nature of the transporters have revealed many aspects of the transporter structure. They indicate that the transporters exist as oligomers and that specific amino acid residues are involved in binding substrates and functioning as gates that allow substrates to pass through the membrane.