Abstract
Studies performed during the past decade have shown that the rates at which certain neurons produce and release their neurotransmitters can be affected by precursor availability, and thus by the changes in plasma composition that occur after ingestion of the precursors in purified form or as constituents of foods. Thus, tryptophan administration or a plasma ratio of tryptophan to other large neutral amino acids, thereby raising brain tryptophan levels, increasing the substrate saturation of tryptophan hydroxylase, and accelerating the synthesis and release of serotonin. Tyrosine administration or a high-protein meal similarly elevates brain tyrosine and can accelerate catecholamine synthesis in the CNS and sympathoadrenal cells, while the consumption of lecithin or choline increases brain choline levels and neuronal acetylcholine synthesis. The physiologic and biochemical mechanisms that must exist in order for nutrient consumption to affect neurotransmitter synthesis have been characterized and include: 1) the lack of significant feedback control of plasma levels of the precursor; 2) the lack of a real "bloodbrain barrier" for the precursor, i.e. the ability of the plasma level of the precursor to control its influx into, or efflux from, the CNS; 3) the existence of a low-affinity (and thus unsaturated) transport system mediating the flux of the precursor between blood and brain; 4) low-affinity kinetics for the enzyme that initiates the conversion of the precursor to the transmitter; and, 5) the lack of end-product inhibition of the enzyme, in vivo, by its ultimate product, the neurotransmitter. The extent to which neurotransmitter synthesis in any particular aminergic neuron happens to be affected by changes in the availability of its precursor probably varies directly with the neuron's firing frequency. This relationship allows precursor administration to produce selective physiologic effects by enhancing neurotransmitter release from some but not all of the neurons potentially capable of utilizing the precursor for this purpose. It also allows the investigator to predict when administering the precursor might be useful for amplifying a physiologic process, or for treating a pathologic state. (for example, tyrosine administration raises blood pressure in hypotensive rats, lowers it in hypertensive animals, and has little effect on blood pressure in normotensive animals; the elevation in blood pressure probably reflects enhanced catecholamine release from sympathoadrenal cells, while the reduction in hypertensive animals probably results from increased catecholamine release within the brain-stem.) Such predictions are now being tested clinically in many institutions. Available evidence suggests that lecithin or choline administration can diminish the frequency of abnormal movements in patients with tardive dyskinesia...