NEUROBIOLOGY OF ADDICTION (PART 1)

THE SYNAPSE AS THE ACUTE TARGET OF DRUGS OF ABUSE

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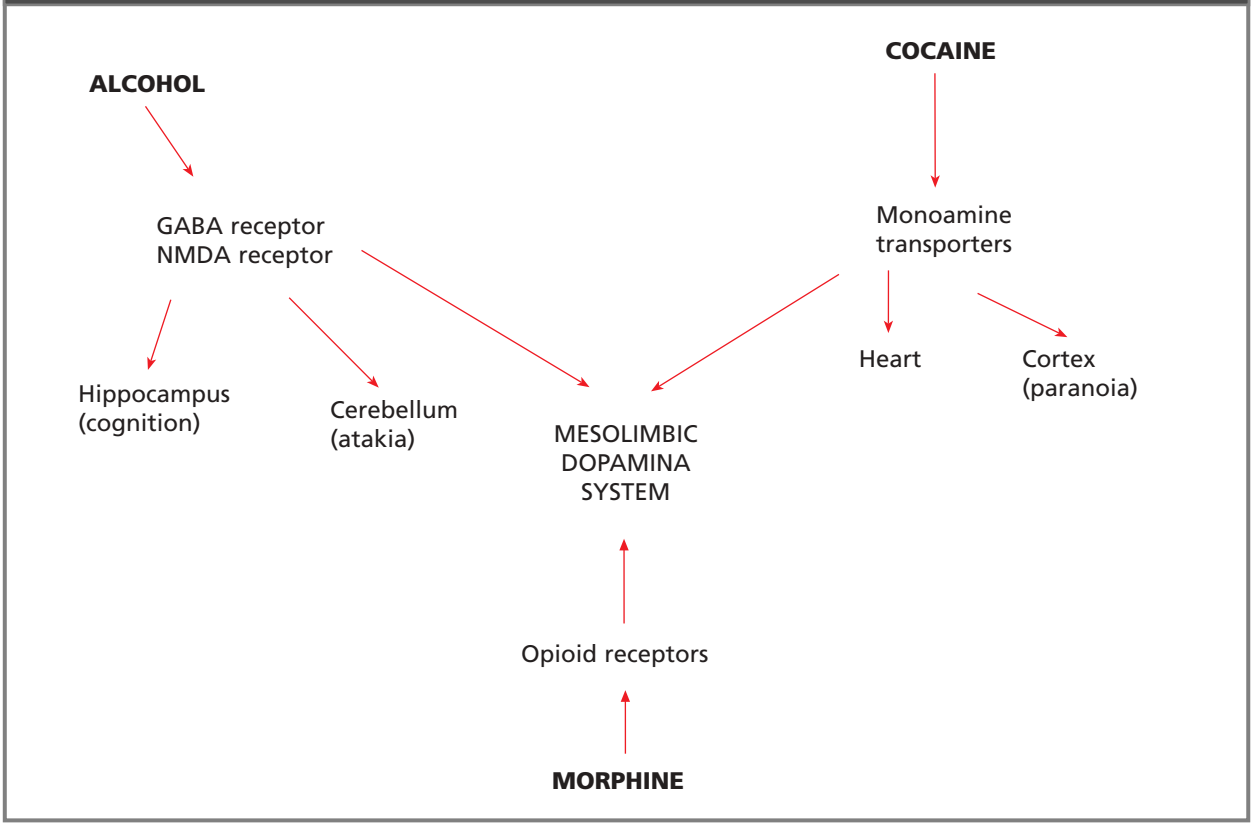
Drug addiction, also known as substance dependence, is a chronically relapsing disorder that is characterized by compulsion to seek and take drug; loss of control in limiting intake and emerge of a negative emotional state (e.g. dysphoria, anxiety, irritability) when access to drug is inhibited. An important goal of resent researches is to understand the neuropharmacological / neuroadaptive mechanism within specific neurocircuits that mediate the transition between occasional, controlled drug use and loss of behavioral control over seeking and drug taking that defines chronic addiction. However, the first step for researchers is understood what is going on in the synaptic cleft as acute target of drugs of abuse.

Opiates are agonists at μ, δ and κ opioid receptors. Cocaine increase synaptic levels of dopamine, serotonin and norepinephrine by inhibiting the presynaptic reuptake transporters for these amines. Amphetamine and its derivatives also increase the synaptic levels of monoamines, but via a distinct mechanism: by increasing release of them. One of the best established mechanisms belongs to alcohol (ethanol). It facilitates the activation of GABA A receptors by GABA. This action is similar to benzodiazepines and all other sedative-hypnotics. By the

Figure 1: The main final action is at mesolimbic dopamine system which consists of dopamine-containing neurons in the ventral tegmantal area and their axonal projections to the terminal fields in nucleus accumbens and prefrontal cortex.



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way, ethanol, unlike other sedative-hypnotics, also exerts potent effects on NMDA glutamate receptors. Ethanol inhibits the functioning of the receptor, again, not by blocking the glutamate binding site but via a more complex, which results in diminished glutamate-induced Na and Ca flux through the receptor ionosphere. This effect of ethanol may contribute to the intoxicating effect of alcohol and perhaps to the dissociative effects seen in people with high ethanol blood levels.

Other drugs of abuse have different receptors that they are partially or fully agonist. For example nicotine is agonist at nicotinic acetylcholine receptors, cannabioids are agonist at cannabinoid receptors. Hallucinogens are partially agonist at 5-HT2A serotonin receptors. Phencyclidine is antagonist at NMDA glutamate receptors. In contrast to the many disparate acute actions of drugs of abuse, the common effect they had on brain is reinforcement (Figure 1).

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