NEUROBIOLOGICAL BASIS OF DRUG ADDICTION (2): IMPAIRED RESPONSE INHIBITION AND SALIENCE ATTRIBUTION

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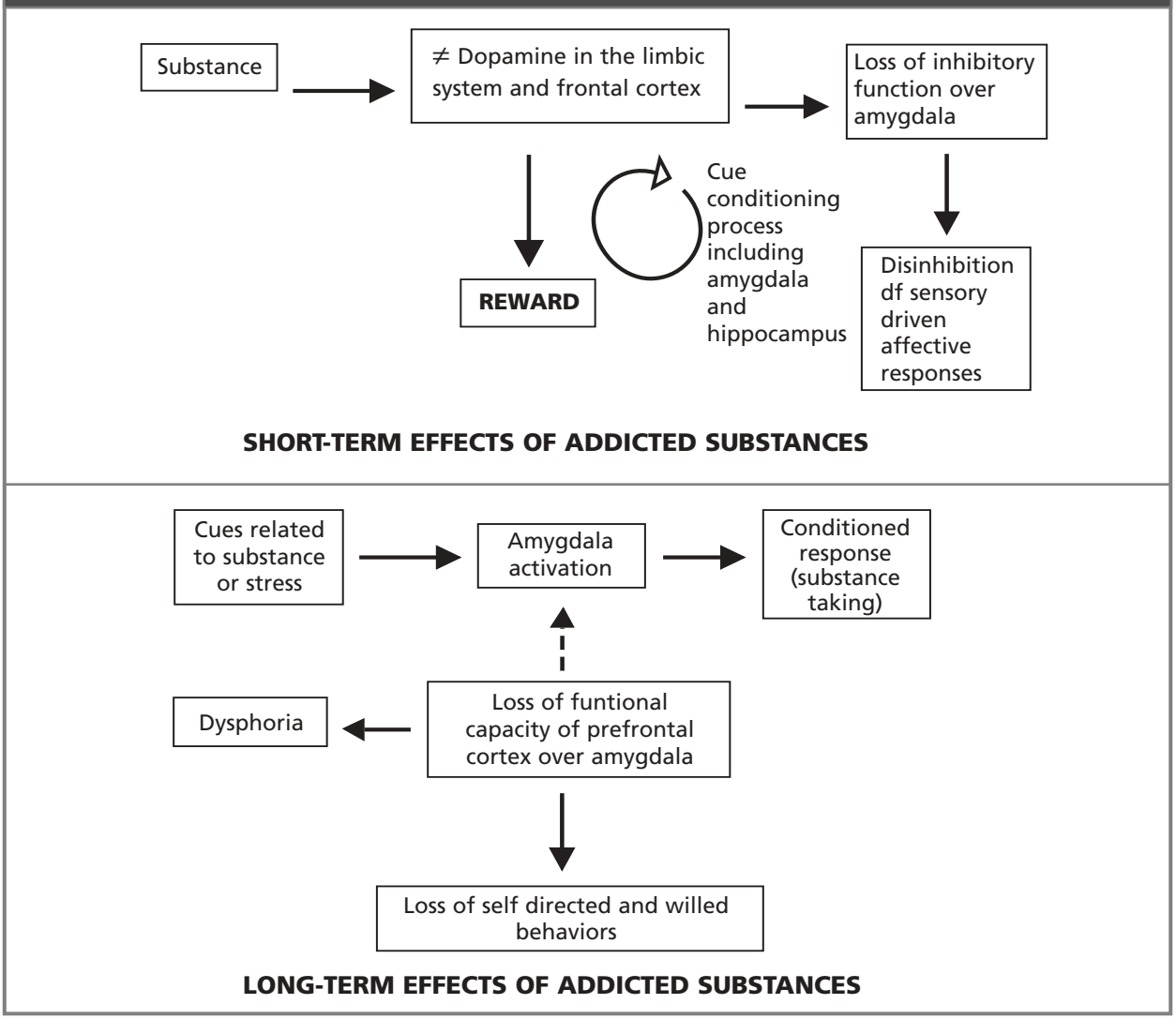
Until recently, many researchers have focused on the role of dopamine in the process of drug addiction. What makes dopamine so popular is the ability of addicted substance to increase the brain dopamine concentrations in the limbic regions of the brain. The reinforcing effect of dopamine makes it number one suspected neurotransmitter in the area of addiction research. However, the increase in the dopamine per se is insufficient to account the process of addiction, since drugs of abuse increase dopamine in naïve as well as addicted subjects. The magnitude of drug-induced dopamine incre-

Figure 1: Schematic description of impaired response inhibition and salience attribution



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ases, and intensity of self-reports of the drug's reinforcing properties appear to be smaller in the addicted than in naïve patients. This difference can not be attributed solely on receptor changes. It has been recently shown that self administration of cocaine, but not food, results in morphological changes in dentrites and dentritic spines in the prefrontal cortex and nucleus accumbens. In structural volumetric studies volume losses in the prefrontal cortex has been reported in heroin, alcohol and cocaine-dependent substance. Thus dopamine and related mechanisms in the addiction process, causes changes in the prefrontal cortex.

It is very interesting that dopamine controls the medial frontal cortex which has a very important function of suppressing amygdala. Indeed, during intoxication losing of inhibition over amygdala releases behaviors that are normally kept under close monitoring. In the long-term substance via dopaminergic and other related mechanisms disturb the cellular structure and functional capacity of prefrontal cortex and resulted in attenuation of the relevance of motivational, higher cognitive, and self-monitoring functions. It is later understood that not only with substance intake but also during craving and anticipation of a future drug reward in the addicted patients, this process is going on.

It is proposed that behaviors and associated motivational states that are the core of the addiction are distinctly processes of loss of self-directed and willed behaviors to automatic sensory-driven formulas and attribution of primary salience to the drug of abuse at the expense of other available rewarding stimuli. With the rewarding effect addicted substance become cue conditioned and turn out to be a chronic tendency. With the loss of prefrontal cortex control over amygdala, this conditioned response takes palace with every cue. Thus, Goldstein and Volkow conceptualized drug addiction syndrome as syndrome of "impaired response inhibition and salience attribution".

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