Commentary:
New View on Treatment of Drug Dependence

Mina Ranjbaran [1], Hedayat Sahraei [1*]

1. Neuroscience Research Center, Baqiyatallah (a.s.) University of Medical Sciences, Tehran, Iran.

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ABSTRACT

In the 1960s, discovery of pleasure system (defined as reward system) in the brain that may underlie drug reward and addiction encouraged many scientists to investigate the mechanisms by which drug abuse affects central nervous system function. In this regard, investigators developed several drugs targeting the brain reward system for drug dependence therapy. However, no positive results obtained in drug addiction treatment. It seems that more brain systems other than brain reward system must be considered in this regard.

1. Introduction

In the 1960s, Olds et al. discovered a pleasure system in the brain that may underlie drug reward and addiction (Olds and Milner, 1954); since then, many scientists investigated the mechanisms by which drug abuse affect central nervous system function and lead to addiction. It was found that all drugs of abuse stimulate, directly or indirectly, the dopaminergic neurons located in the ventral tegmental area (VTA) and thereby increase the dopamine tone (Baxter and Murray, 2002). This discovery led to the hypothesize that the VTA form is the main part of the brain reward system (BRS), which plays a key role in the initiation and maintenance of drug abuse and addiction (Koob, 2009). The BRS comprises mainly dopaminergic neurons, whose cell bodies are located in the VTA and whose projection targets are in forebrain structures, including the nucleus accumbens (NAc), hippocampus, amygdala, and prefrontal cortex (Baxter and Murray, 2002). Several studies show that drugs of abuse increase the basal tone of the dopaminergic neurons within the VTA, and consequently increase the dopamine concentration in their projection targets, including the NAc (Di Chiara and Imperato, 1988). This finding and various electrophysiological, pharmacological, and brain imaging data formed the basis of several therapeutic strategies for addiction treatment (Pulvirenti and Koob, 1994). Dopaminergic agents, including bromocriptine (Pulvirenti and Koob, 1994) and bupropion (Etter and Schneider, 2012) used as medications for drug addiction treatment. In recent years, opioid receptors partial agonists such as buprenorphine (Bhupal, 2012) or antagonists such as naltroxone (Kelty and Hulse, 2012) used for drug addiction treatment. Several studies reported that these drugs are useful in the short term, but due to a drastic reduction in the study sample size over a few weeks, they were unable to confirm the usefulness of the drugs in the long term (Kreek et al., 2008). Thus, due to its resolution requires great improvements of our knowledge of addiction biology, drug addiction treatment remains a challenging problem. In recent years, investigators focused on the neurobiological basis of drug addiction prevention, specifically, why and how drug abuse is initiated and continued (For rev see: Koob, 2009). Several studies on this topic suggested that stress plays a key role in the initiation and maintenance of drug abuse (Moller

* Corresponding Author:
Hedayat Sahraei1, PhD.
Neuroscience Research Center, Baqiyatallah (a.s.) University of Medical Sciences, Tehran, Iran.
Tel: +98-21- 26127286
E-mail: h.sahraei@bmsu.ac.ir

2012). Stress, described as any disturbance in the internal milieu, can activate brain areas that are considered to represent the brain stress system (BSS). The BSS comprises the main parts of the limbic system, including the amygdala, hippocampus, hypothalamus, and pituitary gland as well as the adrenal gland (both medulla and cortex) (McEwen 2007). The BSS can normalize adverse stresses and help the body to adapt to new situations (McEwen 2007). Many Studies showed that the BSS is in close functional relation with the BRS, so that any change in the BSS can activate several parts of the BRS (Koob and Kreek, 2007). Furthermore, neurons within BRS structures such as the VTA and NAc are very sensitive to glucocorticoids, and their function is altered by stress (Koob and Kreek, 2007). In animal models, these neurons showed long-term potentiation (LTP) when the animals experienced stressful events; in addition, glucocorticoid antagonists inhibited the rewarding properties of drugs of abuse in animal models (For rev see: Lu et al., 2003). Moreover, stress-relieving treatments can improve the stability of drug addiction treatments (Sinha et al., 2011). These findings led us to hypothesize that medical treatments of drug addiction must target the BSS. Our observations from Congress 60, a nongovernmental organization (NGO) that deals with drug addiction therapy (www.congress60.org), confirm this hypothesis. The NGO currently treats drug addiction by ensuring that patients receive and use drugs in a regular manner, which reduces the stress associated with taking drugs. In addition, the patients' families are also engaged in a series of programs that teach methods of stress amelioration. In returning the patient's BSS to its normal state, this dual approach can be effective. Thus, it appears that the best approach to drug addiction treatment is stabilization of the BSS; this approach differs greatly from the methods currently used to treat drug addiction.

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