Conceptualizing Addiction From an Osteopathic Perspective: Dopamine Homeostasis

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Addiction is a public health crisis in the United States. Understanding the cause and providing effective treatment for patients—in particular, those with substance use disorders—is challenging. Research has demonstrated that addiction is not a flaw in one's moral fiber or a disease of choice; rather, it is driven by alterations in neuronal mechanisms, especially those that involve the neurotransmitter dopamine, which plays a critical role in the brain's reward pathway. Much of osteopathic philosophy is based on the concept of total body homeostasis and allostasis. This article discusses the role of achieving dopamine homeostasis as part of a comprehensive biopsychosocial treatment strategy in the effective management of addiction. The authors aim to motivate osteopathic primary care physicians to incorporate osteopathic philosophy into the treatment of patients with substance use disorders.

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Addiction is a public health crisis in the United States.[1] Former US Surgeon General of the United States Vivek H. Murthy, MD, released a report[2] in 2016 highlighting the challenges of addiction in the United States. The report cited the following 5 key areas that require immediate attention: (1) understanding of the neurobiological mechanisms of substance use, misuse, and addiction; (2) prevention programs and policies; (3) early intervention and management of substance use disorders (SUDs); (4) recovery options; and (5) health care systems with respect to treatment services and costs related to SUDs. These recommendations are based on the fact that 21 million people in the United States older than 12 years have a diagnosis of SUD, and an estimated 2 million people with an SUD have not received a diagnosis.[3] To put this number in perspective, more people have an SUD than diabetes, and addiction is 1.5 times more prevalent than any type of cancer in the United States.[4] However, unlike cancer or diabetes, only 10% of patients with an SUD receive any form of treatment.[5] In an accompanying letter to his report, Murthy asserted, "We can never forget that the faces of substance use disorders are real people."[6(p vi)] He called for expanding prevention and treatment programs in the community, increasing access to care, and enhancing the training of primary care physicians to better recognize and begin early treatment for patients with SUDs.

Despite significant efforts to better understand the core mechanism of addiction through research efforts, its cause remains poorly understood, often viewed as a flaw in

a person's moral character, not a real disease.[7] This lack of understanding has resulted in significant prejudice experienced by persons with SUDs.

Osteopathic Philosophy

Osteopathic medical education emphasizes the importance of treating patients using a comprehensive biopsychosocial approach, not merely focusing on an organ of dysfunction. Osteopathic medical schools also provide a solid primary care foundation for all students. Most importantly, osteopathic philosophy emphasizes the critical role of homeostasis and allostasis in maintaining health and wellness, as well as the management of disease and discomfort.[8] This concept may play an important role in understanding and managing SUDs.

Reward Deficiency Syndrome

In 1995, Kenneth Blum, PhD, first proposed the concept of reward deficiency syndrome (RDS) as a core cause of all addictive disorders.[9,10] Febo et al[11] demonstrated deficits in mesocorticolimbic dopamine functioning—key brain circuitry involved in the brain reward pathway. Blum et al[12] explored genetic, molecular, and neuronal circuitry involved with dopamine homeostasis and discovered its role as a potential driver of drug-seeking behavior.

When the dopamine reward pathway of the brain is subjected to repeated stimulation, associations are formed between cues related to the stimulus and the subsequent dopamine surge.[13] Because of this learned behavior, thoughts of a drug often trigger dopamine release, leading to craving and subsequent bingeing. Over time, repeated stimulation of the dopamine reward pathway results in an acquired desensitization—notably, persons with an SUD report less of a high after prolonged use. Medical desensitization of the pathway likely requires a 'reset' beyond short-term medication treatment.[14] However, longer-term use of methadone or buprenorphine only targets the withdrawal and craving symptoms and in the long run may even reinforce the disturbed dopamine homeostasis. For long-term solutions, alternative treatment options need to be considered.

A potential solution for resensitizing the brain's reward circuitry comes from examining people with naturally altered dopamine homeostasis. Advanced neuroimaging has revealed dysregulated resting state networks of dopamine functioning.[15] This dysregulation of dopamine results in unbalanced functional networks that drive the brain's reward pathway. Specifically, Badgaiyan et al[16] demonstrated that in persons with attention-deficit/hyperactivity disorder, a known subset of RDS whereby untreated patients have a high risk for SUD, tonic release of dopamine is attenuated, and the phasic release is enhanced in the right caudate. This finding strongly suggests a hypodopaminergia in RDS. Badgaiyan et al[16] also demonstrated a statistically significant decrease in phasic dopamine in the ventromedial striatum as the rate of cocaine intake increased.

Dopamine Receptor D2

Genetic variation plays a part in the predisposition to disruption of dopamine homeostasis. The *DRD2* A1 variant has been shown to result in fewer dopamine D2 receptors expressed, which leads to dopamine resistance and a higher threshold of dopamine stimulation before a person perceives satisfaction.[17-19] This excessive stimulus requirement manifests as a dopamine craving, which is often self-medicated through substances that raise dopamine levels, such as alcohol, nicotine, and stimulants. However, self-medication does not solve the dopamine-resistance problem—it makes it worse. A possible treatment is KB220Z, a prodopaminergic nutraceutical that increases dopamine sensitivity in the brain.[20] By addressing the root problem arising from the *DRD2* A1 variant, KB220Z may help normalize a person's physiologic dopamine homeostasis.

Management of SUDs

As more genetic variants involved in addiction are discovered, personalized medicine may be able to treat

patients with SUDs or prevent SUDs from developing. Such an approach is already having an effect on patient care, as genetic testing offers enhanced accuracy in developing treatments for patients with diseases such as cancer. However, there is a disparity between fields, such as oncology, and addiction medicine.[21] In oncology, tumors may be readily located, and biopsies allow for in vitro testing to identify biomarkers as candidates for therapy. Conversely, addiction medicine is largely limited to clinical history and end-stage organ dysfunction resulting from drug toxicity. Adding to the problem of limited scientific advances is the disparity in federal research funding. Since 1993, of all funding provided by the National Institutes of Health, 17% has gone to the National Cancer Institute, 10% to the National Heart, Lung and Blood Institute, and only 5% to the National Institute on Drug Abuse and National Institute on Alcohol Abuse and Alcoholism.[22] Within the National Cancer Institute, only 2.6% of the budget was allocated for tobacco research.[22] Although addiction medicine would be a great candidate for personalized medicine, it would require additional funding, which could result in significant positive outcomes for the economy and overall well-being for a large portion of the population.

Addressing the disruption in dopamine homeostasis in patients with SUDs could play an important role in better understanding and, ultimately, treating these patients with this complex clinical phenotype.[23] Successful management of SUDs requires a comprehensive biopsychosocial strategy. Gold et al[24] highlighted the need for ongoing, long-term interventions, including appropriate pharmacologic and behavioral support and close monitoring of sobriety status. Osteopathic primary care physicians could identify patients in their practices that may have an SUD and initiate treatment grounded in core osteopathic principles of treating the whole patient, not just specific symptoms or behaviors.

Like other chronic diseases, such as diabetes and hypertension, the key to long-term clinical success requires ongoing monitoring and continuation of treatment after acute stabilization is achieved. All of the extant clinical literature supports the need for a balanced approach to treatment from a biopsychosocial perspective.[25] Once cravings are controlled, maintaining long-term sobriety is a realistic goal. Dopamine homeostasis may be an important component of achieving this outcome when combined with effective psychosocial interventions and adherence to a healthy lifestyle, including balanced nutrition, regular sleep, and an enjoyable exercise program. The role of OMT needs to be better evaluated as a potential treatment for patients with somatic and emotional dysfunction.[26] This strategy is one that Andrew Taylor Still, MD, DO, would likely have endorsed.

Conclusion

Substance use disorder is a clinical disease that requires an integrated collaborative effort by physicians and researchers to develop effective, long-term treatment interventions. The concept of maintaining homeostasis is not only a key tenet of osteopathic philosophy, but it is likely the keystone of addiction management.

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