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CLINICAL PERSPECTIVES

A Biochemical Hypothesis for the Effectiveness of Acupuncture in the Treatment of Substance Abuse: Acupuncture and the Reward Cascade

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Abstract: This paper explores the physiological basis of the acupuncture effect in the treatment of addiction and focuses on the relationship of acupuncture to the reward "cascade." It proposes that the reward cascade combined with endorphin mechanisms may provide the biochemical framework to explain the mechanisms by which acupuncture provides relief from the symptoms of drug withdrawal, aids in the recovery from addiction, and may help prevent recidivism.

THE EFFICACY of acupuncture in the treatment of substance abusers and drug withdrawal has been amply demonstrated to the scientific community. While many still regard acupuncture with skepticism, clinical trials and scientific investigations have proven its effectiveness.[1-4] In fact, acupuncture has become standard procedure in many detoxification programs worldwide.[1,3,5,6] However, the mechanisms underlying the effectiveness of acupuncture in the treatment of addiction remain relatively obscure. In the following, we offer a possible explanation for this effect, which involves two theories.

Excerpts from a paper presented to the 32nd World Congress of Alternative Medicine, Colombo, Sri Lanka, November 27,1994.

I. The Endorphin Mechanism

Many cite acupuncture's most heralded biochemical action - the stimulation of endorphin production - as the primary physiological basis for its success in the treatment of substance abuse.

Although the natural painkilling neurotransmitter endorphin is best known for its role in analgesia, according to recent research it may also be partially responsible for drug craving and physical withdrawal symptoms.[6-8] It is thought that

when a person's endorphin receptor sites are filled by *endogenous* opioid peptides (e.g., endorphin, enkephalin), they experience feelings of wellbeing and, therefore, biological craving for addictive substances does not develop. *Exogenous* opioids, such as morphine and heroin, are endorphin *agonists* that is, they have an affinity for and stimulate physiologic activity at cell receptors normally stimulated by naturally occurring endogenous opioids. Thus, substitution of endogenous opioids at receptor sites by agonists (again, such as morphine, heroin, and possibly alcohol) produce the same feeling of wellbeing as when the receptor sites are filled by, e.g., enkephalin. This feeling of wellbeing provides positive reinforcement and contributes to the continued abuse.

Chronic use of exogenous opiates or alcohol interferes with opiates or alcohol interferes with opioid receptors and through a negative feedback system results in a decrease of opioid peptides. Hence, when exogenous substances attach to opioid receptor sites, the feedback system is, in effect, "short circuited" and the presynaptic neurons receive the message that endogenous opioid transmission is normal, thus resulting in a reduction in the synthesis of those neurotransmitters.[9] When the exogenous substance is withdrawn, the body must once again begin manufacturing the supplanted endogenous opioids. However, during this time there is a net depletion in the amount of opioids in the body. This is in part responsible for the painful withdrawal symptoms associated with drug detoxification.[10]

Investigators have hypothesized that acupuncture relieves withdrawal symptoms by triggering the body to produce more endorphins, thus bringing the body back to equilibrium.[6-8] Normalization of endorphin mechanisms may explain the effectiveness of acupuncture in treating withdrawal symptoms of opiate-related addictions (heroin, morphine, etc.),[11-13] but it does not explain why acupuncture is as effective in detoxification and treatment of non-opiate related addictions such as alcohol,[3] tobacco,[14-15] and cocaine.[2-4] Furthermore, in one study, patients detoxified with acupuncture exhibited a recidivism rate of only 5% compared to 20%-25% in non-acupunctured controls 12 months after detoxification.[5] This cannot be explained merely by changes in endorphin levels, which only remain elevated for a relatively short time after treatment.[7]

Acupuncture has proved to be clinically effective for substance abuse,[2,3,5] and the endorphin mechanism does provide a partial explanation for its success,

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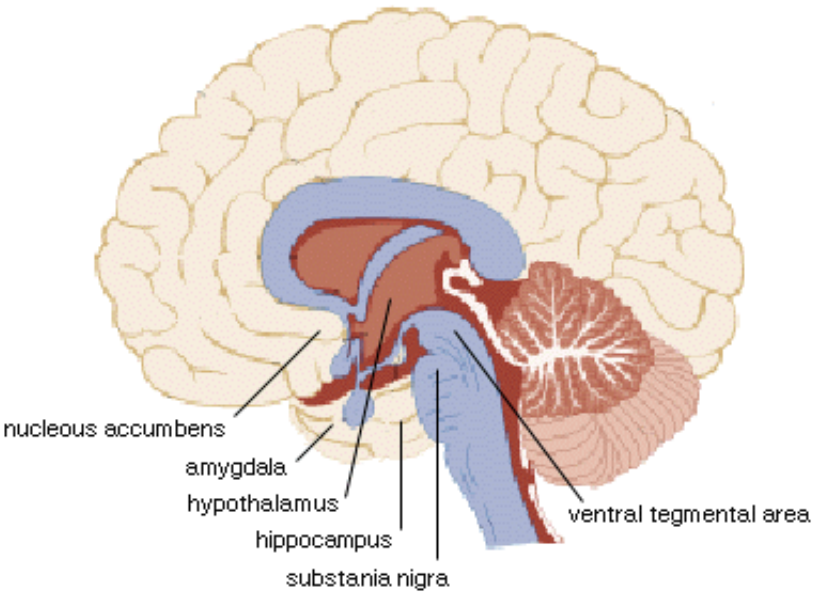

Figure 1.

The limbic system contains structures that play a vital role in the expression of emotions and the activity of the reward system of the brain. A cascase or chain of neurons within the limbic system that interact through various signaling molecules or neurotransmitters is responsible for the experience of pleasure and the modulation of reward. Researchers have proposed that the craving associated with addiction may stem from a biochemical deficiency in one or more of these neurons or signaling molecules. This deficiency can replace an individual's sense of well being with a feeling of anxiety or anger, and produce a craving for a substance that can alleviate the negative emotions.

particularly in relieving withdrawal symptoms. However, it does not adequately explain how acupuncture works in *non-opiate* addictions and how it prevents relapse. A large body of emerging work in neuroscience may shed some light on the complex mechanisms of drug addiction and its subsequent relief by acupuncture.

II. The Reward Cascade

According to our review of current theories, the most attractive is the "reward cascade" theory proposed by addictive behavior and genetics research scientist Kenneth Blum et all (University of Texas Health Center, San Antonio).[16] It involves a deficiency of the neurotransmitter *dopamine* in the limbic system of the brain (see Figure 1). The limbic system

consists of a group of brain structures, including the hippocampus, amygdala, and their interconnections and connections with the hypothalamus, septal area, and portions of the tegmentum. It contains many of the centers which control basic life processes such as appetite and sexual desire. It also contains centers related to pleasure, satiety, emotional behavior and drive.

Animal studies have confirmed these neuroanatomical connections. Dr. James Olds placed electrodes in the limbic system of rats and found that they would press a bar that activated the electrode and stimulated these centers to the exclusion of all other activity.17 Thus, the craving associated with addiction may stem from pathology within the limbic system. Because it occurs in the area of the brain responsible for maintaining fundamental life processes, it has been hypothesized by Ericson that, unconsciously, the addict perceives his drug as being as necessary to life as eating or drinking water.[18]

Addiction involves subtle changes in neurochemistry. Current research is focusing on various parts of the brain such as the *nucleus accumbens* and *ventral tegmental* area. Extrapolating from the work of Blum, et al, we suggest that pathology in these centers may result in hypersensitivity to the pleasurable effects of drugs.

Dopaminergic (DA) neurons extend from the vental tegmentum to the region of the limbic system concerned with emotionality and reward. Another bundle of DA neurons proceeds to the frontal cortex where emotions and thoughts are integrated. Parkinson's disease,[10,19] depression,[16, 20] and addiction[16] are all linked to deficient dopamine in key brain areas. Interestingly, these are all disorders in which acupuncture has proved to have substantial clinical effectiveness.[19,20]

Pathology in the reward centers of the brain is the focus of Blum et al's biochemical theory of the addictive process. They suggest that the tendency toward addiction stems from a neurochemical imbalance in the reward cascade that leads to feelings of craving and dysphoria, which many addictive substances relieve for a time. The reward cascade begins in the hypothalamus, which is a principle site for emotion and reward.[16,21] According to Blum et al, under normal conditions the reward cascade operates as follows (see Figure 2):

- Neurons in the hypothalamus release serotonin (5HT)
- Serotonin activates the opioid peptide methionine enkephalin
- Met-enkephalin is released at the ventral tegmental region and interacts to inhibit receptors controlling the release of gamma-aminobutyric acid

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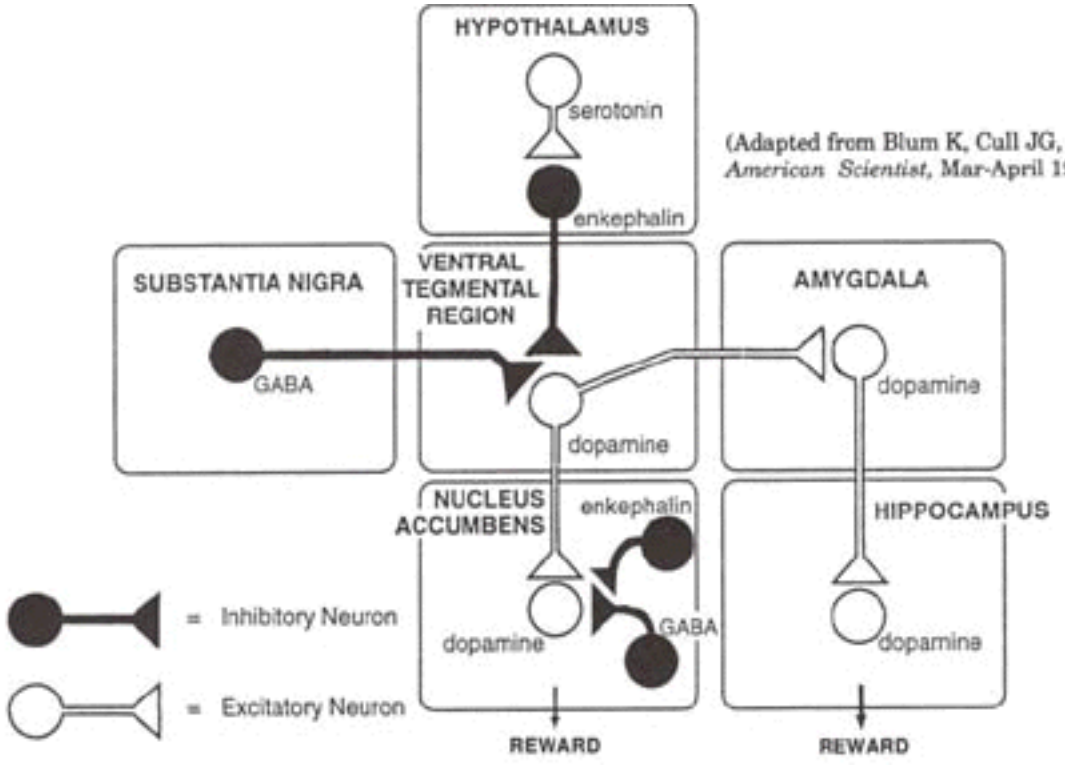

Figure 2.

In the limbic system, the reward cascade is composed of both inhibitory and excitatory neuropathways that are modulated by neurotransmitters. Under normal conditions, the reward cascade begins with the release of serotonin by excitatory neurons in the hypothalamus. Serotonin activates the opioid peptide methionine-enkephalin. Met-enkephalin is released at the ventral tegmental region and interacts to inhibit the release of gamma-aminobutyric acid (GABA) from the substantia nigra. The primary role of GABA is to control the output of dopamine in the ventral tegmental region. Disinhibition by GABA results in an increase in dopamine supplies. Dopamine released by this GABA inhibition has effects on two distinct sites; a direct effect on the nucleus accumbens and an indirect effect on the hippocampus via the amygdala, causing the release of dopamine in both sites, permitting the completion of the reward cascade.

(GABA). Met-enkephalin and/or other opioid peptides thus finely tune the system.

- The primary role of GABA is to control the output of dopamine (DA) in the ventral tegmental region. The result of inhibiting GABA activity is an increase in dopamine supplies.
- Dopamine released by GABA inhibition has effects on two distinct sites: a

direct effect in the nucleus accumbens and an indirect effect on the cluster type CAI cells of the hippocampus after relay to the amygdala. In both areas it acts as the target messenger of reward.[16,21]

When in balance this system provides homeostatic regulation of activity and inactivity. However, if a neurochemical becomes dysfunctional or its receptor site is unresponsive, this homeostatic balance is upset, causing changes in feelings and behavior. Mackler and Eberwine (1991) postulated that such imbalances can arise due to genetic factors or through chronic use of addictive drugs through a negative feedback system.[9]

III. Acupuncture and the Reward Cascade

Blum et all proposed that serotonin is the neurotransmitter which initiates the reward cascade. Evidence suggests the importance of serotonin in acupuncture, particularly high frequency (50-2000Hz) electroacupuncture. Most of this evidence comes from research into the analgesic effects of acupuncture.6,22,23 We suggest that acupuncture directly affects the reward cascade by increasing the amount of serotonin in the hypothalamus.

Investigations have shown that acupuncture activates the descending serotonergic pathways via the anerolateral tract.[24] When acupuncture stimulation is applied at the correct points, neural impulses are received in the dorsal horn of the spinal cord. These impulses are conveyed to a variety of fibers of the spinoreticular and spinomesencephalic tracts, project to the midbrain where they directly influence the descending serotonergic pathways.[24] The hypothalamus and midbrain have interconnecting feedback or modulatory neuronal pathways. Therefore, by stimulating the descending serotonergic pathways with acupuncture, serotonin within the reward cascade is directly affected leading eventually to an increase in dopamine in the nucleous accumbens and amygdala, and a subjective sense of wellbeing.

Most detoxification clinics use auricular acupuncture in the treatment of substance abusers. In particular, the ear point "lung" has proved to be very effective in the treatment of withdrawal symptoms and should be included in any program of relapse prevention. This point has a unique location at the most superficial branch of the vagus nerve. Stimulation of the vagus nerve by use of this point is believed to produce neural impulses that restore activity of the nervous cells of the reticular formation that, in turn, stimulate the hypothalamus,[6] which initiates the reward cascade.

Conclusion

By increasing serotonin in the hypothalamus, acupuncture may help to normalize the complex functioning of the reward cascade. Hence, addicts treated with acupuncture not only experience a reduction of withdrawal symptoms, but also a reduction of the craving for the drug. When the reward cascade is functioning normally, the patient feels a sense of peace and wellbeing that lasts beyond the detoxification treatment. Thus, it is possible that the scope of acupuncture is not limited to the withdrawal phase of chemical dependence, but may also play a role in relapse prevention.

A disruption in the reward cascade may also play a role in a number of mental disorders other than addiction. Acupuncture seems to relieve many of the symptoms of mental disorders through serotonergic mechanisms within the brain. It seems that acupuncture is also particularly effective in alleviating depression and other mood disorders through its serotonin activating mechanism. However, the role of the reward cascade in the normal functioning of the brain remains obscure.

The reward cascade hypothesis raises many intriguing possibilities for deepening our understanding of substance abuse and the possibility of regulation with acupuncture. Further consideration and investigation of these mechanisms is urgently needed.

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