A SEARCH FOR BIOCHEMICAL SIMILARITIES IN THE EFFECTS BETWEEN ALCOHOL/CAFFEINE AND SPEED/HERION MIXTURES

Abstract. A neurochemical review is done at the receptor level. In all cases, agonist or antagonist of neurotransmitter receptors was the principle biochemical effect of the drugs. The results indicate the mixtures do have a similar pharmacology although there are numerous differences as well.

1. Comparison of amphetamine and caffeine

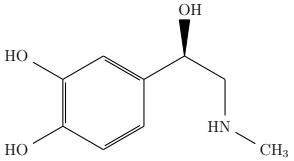
The effects of alcohol, caffeine, amphetamine and heroin on the human body can be understood in terms of the underlying biochemistry, specifically, that of receptors and their agonist and antagonist.

Biochemical receptors are large protein molecules that can be activated by the binding of a ligand (such as a hormone or drug). Ligand binding changes the conformation (three-dimensional shape) of the receptor molecule. This alters the shape of the protein, changing the interaction of the receptor molecule with associated biochemicals. If the ligand binding leads to the normal cellular response mediated by the associated biochemical pathway, the ligand is said to be an agonist of the receptor. However, some ligands called antagonists block receptors from binding to other ligands without inducing any response themselves. Receptors can be activated or inactivated by either endogenous (such as hormones and neurotransmitters) or exogenous (such as drugs) agonists and antagonists, resulting in the stimulation or inhibition of a biological response.

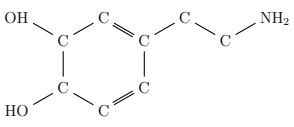
In the central nervous system, receptors can be membrane-bound on the cell membrane of neurons such as at synapses, or intracellular, such as on the surface of vesicles containing neurotransmitters. Binding occurs as a result of noncovalent interaction between the receptor and its ligand, at locations called the binding site on the receptor. A receptor may contain one or more binding sites for different ligands. Binding to the active site on the receptor by it's agonist regulates receptor activation directly. For example, the neurotransmitter dopamine is an agonist for the dopamine receptor, and the cellular response is a synaptic nerve signal to the post-synaptic neuron. The activity of receptors can also be regulated by the binding of a ligand to other sites called allosteric sites, on the receptor. Antagonists prevent agonist from effecting a receptor response. This may be accomplished by binding to the active site thus effectively "blocking" the agonist, or binding to the allosteric site. In the latter case, the receptor is altered conformationally rendering the agonist unable to bind to it.

In short, agonists turn "on" a single cellular response by binding to its receptor, and antagonists turn "off" that response by interfering or 'blocking' the ability of the agonist to effect the receptor.

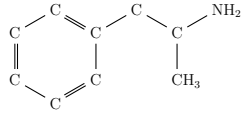
This study focuses on agonists and antagonist of receptors affected by alcohol, heroin, caffeine, and amphetamine. To study the amphetamine and caffeine system, two groups of molecules can be identified. Group one is a set of three phenylpropylamines:



Adrenalin

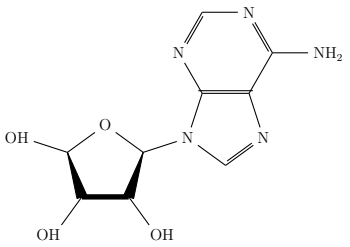


Dopamine

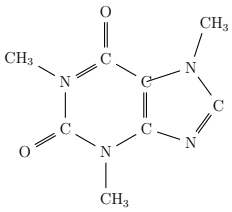


Amphetamine,

and group two, a set of two purines:



Adenosine



Caffeine.

One can't help notice a similarity in structure between the members of each group and that is no conincidence. Many drugs exert their effects by resembling a receptor ligand and this is the case for the two groups above.

Group one includes the neurotransmitter dopamine. From Wikipedia:

> "The brain includes several distinct dopamine systems, one of which plays a major role in reward-motivated behavior. Every type of reward that has been studied increases the level of dopamine in the brain, and a variety of addictive drugs, including stimulants such as cocaine, amphetamine, and methamphetamine, act by amplifying the effects of dopamine. Other brain dopamine systems are involved in motor control and in controlling the release of several important hormones."[2]

Amphetamine amplifies the effects of dopamine, serotonin, and norepinephrine by acting as an antagonist to the corresponding reuptake receptors. Amphetamine enters neurons via transport by the monoamine transporters. Once inside, amphetamine inhibits the vesicular monomine transporter on the transmitter vesicles which causes dopamine, serotonin, and norephinephrine to accumulate in the cytoplasm. This concentration increase induces the corresponding reuptake transporters to operate in reverse, pumping neurotransmitter into the synaptic junction. Amphetamine also inhibits an enzyme responsible for breaking down dopamine in the cell and promotes an enzyme involved with the synthesis of a precursor to dopamine, L-Dopa. These combined effects cause amphetamine to release more dopamine into the synapse than most other stimulants including cocaine.

Some of the psychological effects caused by amphetamine can be explained by understanding which parts of the brain have nerves affected by dopamine, serotonin,and adrenalin. One part of the brain with a large amount of dopamine neurons is the reward system. This system is a collection of neurons which reinforce a behavior. For example, sex is a behavior reinforced by a sense of pleasure. And the major neural system in this reward system is a collection of dopamine neurons. Amphetamine exerts its psychological effect on the body by affecting dopamine and serotonin concentrations in this brain system and that is the source of the addictive properties of this drug. Its stimulating effects can be attributed to its affect on the production of norepinephrine. This chemical is normally released both in the blood and brain when physiological events are activated by a stressful event to transmit the flight-or-fight response. A host of physiological events are associated with this event including increasing heart rate, blood pressure, increasing glucogenesis, increasing oxygen to the brain, and increasing blood flow to the skeletal muscles. These affect alertness, arousal, and influences the reward system. Amphetamine can elevate cardiac output and blood pressure. The fact that amphetamine influences neurotransmitter activity specifically in regions implicated in reward offers insight into the behavioral consequences of the drug, such as the onset of euphoria. [5]

In the second group of compounds we have adenosine. This is a neurotransmitter affecting many areas of the brain and operate through several adenosine receptors. These receptors have inhibitory functions and presynaptically, reduces synaptic vesicle release.[3]

> "Adenosine acts as an inhibitor neurotransmitter that suppresses activity in the central nervous system. Consumption of caffeine antagonizes adenosine and increases activity in neurotransmission including acetylcholine, epinephrine, dopamine, serotonin, glutamate, norepinephrine, cortisol, and in higher doses, endorphins which explains the analgesic effect to some users. At very high doses (exceeding 500 milligrams) caffeine inhibits GABA neurotransmission. This evidence explains why caffeine causes anxiety, insomnia, rapid heart and

respiration rate. The caffeine molecule is structurally similar to adenosine, and is capable of binding to adenosine receptors on the surface of cells without activating them, thereby acting as a competitive inhibitor.[4]"

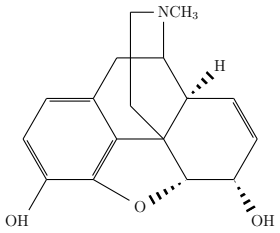
In general, adenosine has an inhibitory effect in the central nervous system (CNS). Caffeine's stimulatory effects, on the other hand, are primarily (although not entirely) credited to its inhibition of adenosine by binding to the same receptors, and therefore effectively blocking adenosine receptors in the CNS. This reduction in adenosine activity leads to increased activity of the neurotransmitters dopamine and glutamate. By nature of caffeine's purine structure it binds to some of the same receptors as adenosine.[3]

2. Comparison of alcohol and heroin

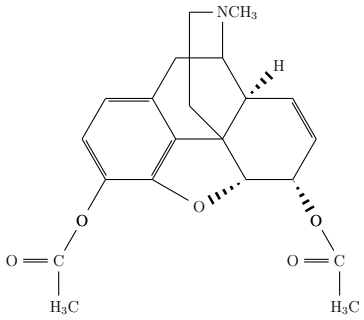
Ethanol acts in the central nervous system by binding to GABA receptors, increasing the effects of the inhibitory neurotransmitter GABA (i.e., it is a positive allosteric modulator). GABA is the chief inhibitory neurotransmitter in the nervous system.

Small doses of ethanol, in general, produce euphoria and relaxation; people experiencing these symptoms tend to become talkative and less inhibited, and may exhibit poor judgment. At higher dosages, ethanol acts as a central nervous system depressant, producing at progressively higher dosages, impaired sensory and motor function, slowed cognition, stupefaction, unconsciousness, and possible death.

Short-term effects of alcohol consumption include intoxication and dehydration. Long-term effects of alcohol include changes in the metabolism of the liver and brain and alcoholism (alcohol dependency). Alcohol intoxication affects the brain, causing slurred speech, clumsiness, and delayed reflexes. Alcohol stimulates insulin production, which speeds up glucose metabolism.



Morphine



Heroin

To understand the neurochemistry of heroin, one must understand the μ-opioid receptor,(MOR). This is a G-protein coupled receptor having a high affinity for enkephalins and endorphins with the principle agonist being morphine. Activation of MOR by an agonist causes analgesia, sedation, slightly reduced blood pressure, itching, nausea, euphoria, decreased respiration, miosis (constricted pupils) and decreased bowel motility often leading to constipation.[1]

MOR can mediate acute changes in neuronal excitability via "disinhibition" of presynaptic release of GABA,[1]. This implies MOR activation increases GABA concentrations.

3. Conclusions

Both amphetamine and caffeine increase the neurotransmission of several neurotransmitters including dopamine, serotonin, and ephinephrine and both alcohol and heroin increase levels of GABA.

References

Wikipedia, μ-opioid receptor.
Wikipedia, Dopamine.
Wikipedia, Adenosine Receptor
Wikipedia, Caffeine

Wikipedia, Amphetamine