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Depression and addiction: A review

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Abstract
We devised a set of survey questions to measure happiness. Although an abstract quality, ones happiness index can be boiled down to several circumstantial evidences. The survey also included questions regarding the volunteer's drug use habits and reasons. After collecting the results, we found a direct positive correlation between the happiness index and drug use. The following research was done to find a cause behind this relationship. We targeted specific brain neurotransmitters because they are responsible for mood regulation and also heavily effected by drug use. The study concerns three neurotransmitters, gamma-amino butyric acid, serotonin and dopamine. These are some of the most important mood regulatory neurotransmitters. The study analyses the effects of the three most commonly recorded drugs in our survey: nicotine, cannabis and alcohol respectively. Each drug negatively affects the particular neurotransmitter in a different way thus affecting its functions, which have a direct influence on depression.

Keywords: depression, circumstantial, neurotransmitters, analyses

Introduction
This was an independent psychological research done by students to find a correlation between Depression and Addiction. The research was prompted by a casual observation about how most people who abuse illegal drugs also seem much more likely to be depressed or anxious.

Hypothesis
People who are addicted are more likely to be depressed than people who dont have an addiction, showing a direct relationship between addiction and depression.

1. Gamma-Aminobutyric Acid
What is it?
GABA is a chemical that is made in the brain. It sends chemical messages through the brain and the nervous system and is involved in regulating communication between brain cells. The role of GABA is to inhibitor reduce the activity of the neurons or nerve cells.

Description/ relevance with happiness
GABA Is an inhibitory neurotransmitter, which means that it weakens or slows down signals. Because of its inhibitory function, GABA plays an important role in anxiety. When nerve signals fire too quickly and carry anxiety-inducing signals, GABA acts to slow the signals down, reducing overwhelming feelings of anxiety. GABA is taken by mouth for relieving anxiety, improving mood, reducing symptoms of premenstrual syndrome (PMS), and treating attention deficit hyperactivity disorder (ADHD). It is also used for promoting lean muscle growth, burning fat, stabilizing blood pressure, and relieving pain.

Synthesis/ site of concentration
It is synthesized by glutamic acid decarboxylase (GAD) from glutamate. Once synthesized, it is collected into synaptic vesicles by vesicular inhibitory amino acid transporters. Synaptic vesicles (SVS) are small, electron-lucent vesicles that are clustered at High concentrations of GABA and receptors are found in the limbic presynaptic terminals. High concentrations of GABA and GABA receptors are found in the limbic system, an area of the brain where personal feelings and emotional memories are generated and stored.

Effects of drugs
Nicotine
There is a hypothesis that frontal lobe and limbic/cingulate cortical structures might be the sites affected most Young and healthy 9 cigarette smokers (all males, 24-33 years, average, 26.4) were included. After prohibiting them from smoking for 15 hours, CBF was measured using a Xenon CT-CBF system. CBF (cerebral blood flow) is defined as the blood volume that flows per unit mass per unit time in brain tissue. In 8 subjects with a relatively high feeling, CBF increased mainly in the frontal lobe, hippocampus, uncus, thalamus, and caudate nucleus. Too much blood (a condition known as hyperaemia) can raise intracranial pressure (ICP), which can compress and damage delicate brain tissue

Deduction
The use of nicotine increases CBF in the hippocampus, thalamus i.e. the limbic system - Long-term increase of CBF can lead to damage of brain tissue i.e., Parts of the limbic system. - The limbic system is a major concentration site for GABA. > GABA is responsible for managing anxiety and overall mood stability, damage to Limbic system results in abnormal GABA Abnormal GABA concentrations may cause general mental unrest and thus unhappiness in the

long term.

2. Serotonin

What is it?

Serotonin is a chemical that has a wide variety of functions in the human body. The scientific name for serotonin is 5-hydroxytryptamine, or 5-HT. It is mainly found in the brain, bowels, and blood platelets. It is also produced in the central nervous system (CNS), specifically in the Raphe nuclei located in the brainstem.

Functions/ relevance with happiness

Serotonin impacts every part of your body, from your emotions to your motor skills. Serotonin is considered a natural mood stabilizer. It's the chemical that helps with sleeping, eating, and digesting. Serotonin also helps reduce depression, regulate anxiety, heal wounds, stimulate nausea, and maintain bone health. But this study will primarily focus on its

Functions regulating mood.

The neurotransmitter's effect on mood is also why it's often a target of medications that are used to treat depression, anxiety, and other mood disorders. For example, serotonin plays a starring role in treatments with the class of antidepressants known selective serotonin reuptake inhibitors (SSRI)

Effects of low serotonin

Generally, the normal range for serotonin levels in your blood are 101 283 nanograms per millilitre (ng/ml.).

Some mental/ physical effects of low serotonin include

- Mood instability
- Depression Anxiety
- Schizophrenia
- Memory issues Sleep changes
- Sexual function Attention-deficit
- Hyperactivity
- Somatic symptoms: Some people may experience physical symptoms that are actually rooted in psychological distress or report chronic pain that has no clear physical origin.
- Movement issues: People with low serotonin may have trouble with movement, balance, or coordination. Parkinson's disease, which damages neurons and can cause shaking and other movement problems also correlate with low serotonin.
- Premature orgasm or ejaculation: Serotonin increases the length of time it takes to orgasm. Low serotonin may therefore play a role in early ejaculation etc.

Effect of cannabinoids over-consumption on serotonin levels

As Jason Socrates Bardi (a writer and editor specializing in the sciences) explains, researchers have studied the ways that drugs affect the brain's serotonin levels. Bardi reports that fluctuations in serotonin may explain why so many people experience depression, anxiety, and other symptoms of lowered mood when going through withdrawal.

Molecules such as terpenes and cannabinoids fit into specific receptors within the ECS (The Endocannabinoid System), Researchers would say that molecules such as THC activate certain cannabinoid receptors, i.e., the CB1 receptors.

Although only recently discovered, cannabinoid receptors are believed to play a very important role in the human body. When the receptors are activated by cannabinoids (like THC or CBD), they are thought to alter how the body regulates itself. Up until today, only two cannabinoid receptors have been discovered the CB1 and CB2 receptors, and both have very different responsibilities within the human body. CB1 receptors are important to general health. Researchers have discovered that mice that don't have CB1 receptors demonstrate "psychological abnormalities" like enlarged amygdalae (the part of the brain responsible for motivation and emotions) and increased anxiety. Genetic studies report that CB1 receptors are crucial for reducing and controlling anxiety at times of high-stress. Ultimately, having less or no CB1 receptors could cause complications. THC (Tetrahydrocannabinol, the principal psychoactive constituent of cannabis) interacts with the CB1 receptors within the endocannabinoid system, the majority of which are located within the brain; this allows it to interact with so many different functions within the brain. The CB1 receptor is, among many other things, at least in part responsible for the release of serotonin in the brain.

We know that when THC is imbibed, it attaches itself to the CB1 receptors and begins to stimulate them. Over time THC can change how the EC system works in these brain areas, which can lead to problems with memory, addiction, and mental health. Theories suggest this is caused by depletion of CB1 receptors due to overconsumption of THC.

Deduction

- Long-term overuse of cannabinoids results in the deterioration of the CB1 receptors.
- CB1 receptors control serotonin release in the CNS
- Consequently, serotonin levels are reduced.
- Serotonin functions as a major mood booster
- Lack of serotonin has shown to be directly related to depression (hence selective serotonin reuptake inhibitors

3. Dopamine

What is it?

Dopamine is the neurotransmitter that controls brain's reward circuit. It is an organic chemical of the catecholamine and phenethylamine families. Dopamine is responsible for reward-driven behaviour and pleasure seeking. Every type of reward seeking behaviour that has been studied increases the level of dopamine transmission in the brain. Nearly all-addictive drugs increase dopamine production. It is critical for central nervous system functions such pleasure motivation mode and attention.

Effect of drugs on dopaminergic reward system

Evidence suggests that the intense reward sensation of drug intoxication create a strong and rapid learning in the brain, associating drug use with feelings of pleasure. This association led to higher and more frequent drug administration in order to feel pleasure of reward response more often. As a result, cravings for the rewards associated

with the drug continue to occur, even during drug use, which leads to compulsive, repetitive use. Continued, long-term use also results in the brain reducing the number of dopamine receptors in the brain to adjust for the increased dopamine in the system. This production and dopamine receptors please do compulsive self-administration of drugs and also results in a state known as anhedonia or a loss of pleasure in activities that were once enjoyed. Anhedonia is a core feature of depression.

Sites of highest concentration or production

Eventually, Carlson's group developed an assay that could measure dopamine concentration in the brain and mapped out where the highest concentration of dopamine was present. They determined that dopamine was found in high concentrations in the striatum, the largest component of the basal ganglia.

Alcohol

While a large part of the population consumes alcohol, many people actually develop in alcohol use disorder (AUD).

Alcohol is a central nervous system depressant (a drug that reduces function or nervous activity) whose short-term effects are blurred vision, slurred speech, difficulty walking and impaired memory. This happens because the substance directly affects the brain's chemistry by altering the levels of neurotransmitters in the brain. However, in the long run, persistent use of alcohol can have adverse effects on the physiology of the brain. According to The National Institute on Alcohol Abuse and Alcoholism (NIAAA), long term abuse of alcohol leads to brain shrinkage and causes the brain's inner cavity to grow larger. NIAAA conducted a research on using MRI and DTI to assess brain damage in alcoholics. According to this study, "Brain imaging using conventional magnetic resonance imaging (MRI) has revealed that several brain structures in people with a history of chronic alcohol dependence are smaller in volume than the same brain structures in non-alcoholic control subjects." Alcoholics assessed before and after a period of abstinence showed some revival of tissue volume. DTI- a new MR technique called Diffusion tensor imaging- helped in identifying degeneration of fibres (white matter) that carry information between brain cells (grey matter), caused by excessive chronic alcohol consumption. Subjects also indicated thinning of corpus callosum, a band of white matter fibres connecting the brain's hemispheres. Recent data are discussed showing that reduced neuronal activity as well as dysfunctional connectivity between the ventral striatum and the dorsolateral prefrontal cortex is associated with alcohol craving and impairment of new learning processes abstinent alcoholics. In detoxified alcohol-dependent patients, brain imaging studies with positron emission tomography (PET) revealed a reduction of availability and sensitivity of central dopamine D2-receptors, which may reflect a compensatory down-regulation and which was correlated with lifetime alcohol intake. Further PET studies showed that a low dopamine synthesis capacity measured with 3,4-Dihydroxy-6-fluoro-DL phenylalanine (F-DOPA) PET was specifically correlated with alcohol craving in detoxified alcohol-dependent patients who also displayed reduced dopamine D2 receptor availability in the ventral striatum including the nucleus accumbens.

Deduction

- Dopamine plays a role in how we feel pleasure and is typically associated with happiness.
- It is expressed in the central nervous system, specifically in the hippocampal dentate gyrus and sub ventricular zone, highest concentrations are found in the striatum.
- Long term over consumption of alcohol results in reduced connectivity and sensitivity in the striatum among many other parts of the CNS.
- This causes lower dopamine levels in the brain and hence sadness or depression.

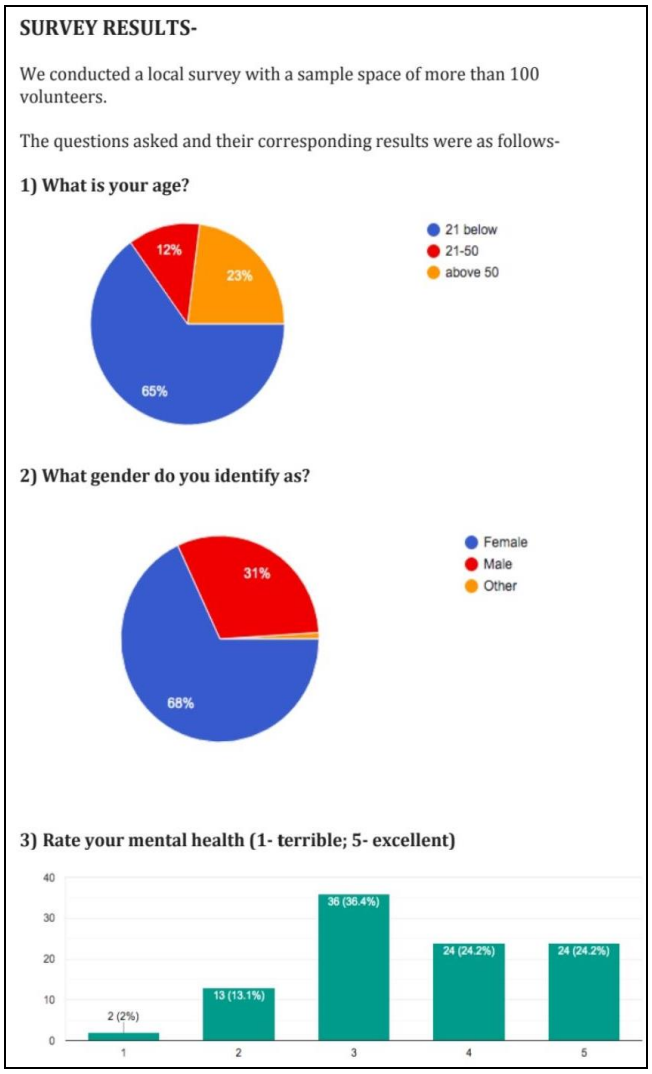
SURVEY RESULTS-
We conducted a local survey with a sample space of more than 100 volunteers.
The questions asked and their corresponding results were as follows-
1) What is your age?
12%
23%
65%
21 below
21-50
above 50
2) What gender do you identify as?
31%
68%
Female
Male
Other
3) Rate your mental health (1- terrible; 5- excellent)
40
30
20
10
0
2 (2%)
13 (13.1%)
36 (36.4%)
24 (24.2%)
24 (24.2%)
1
2
3
4
5

Fig 1

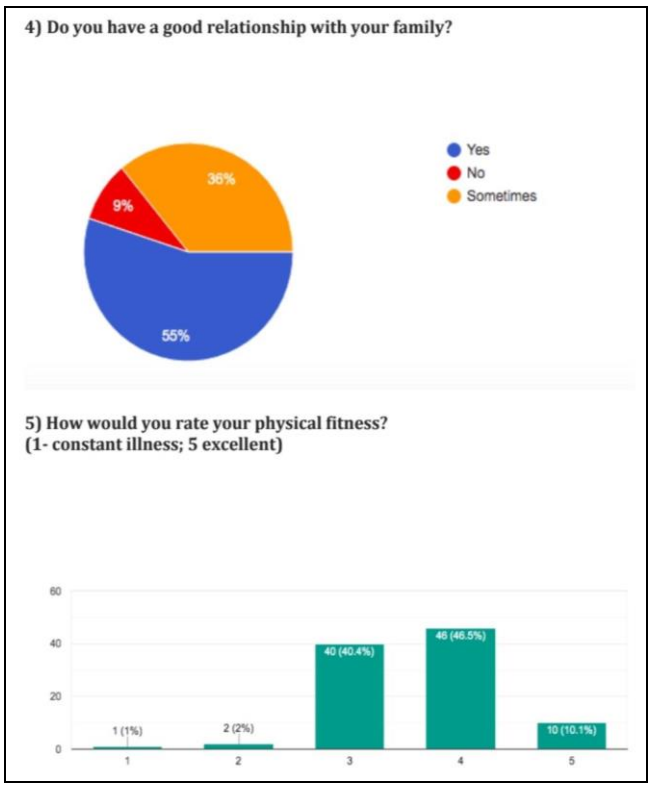
4) Do you have a good relationship with your family?
36%
9%
55%
Yes
No
Sometimes
5) How would you rate your physical fitness?
(1- constant illness; 5 excellent)
60
40
20
0
1 (1%)
2 (2%)
40 (40.4%)
46 (46.5%)
10 (10.1%)
1
2
3
4
5

Fig 2

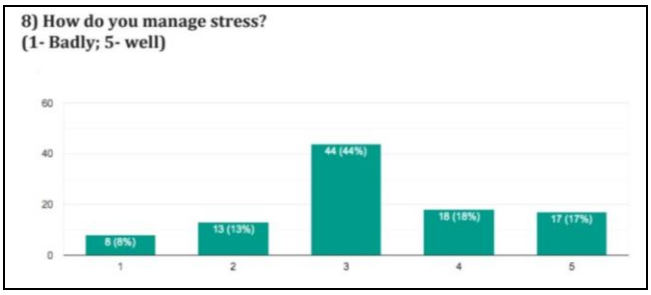

Fig 3

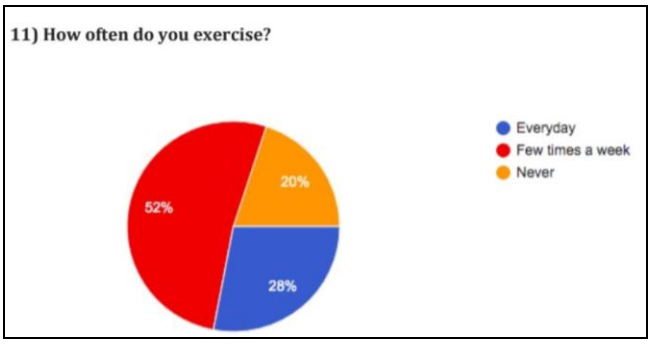

Fig 4

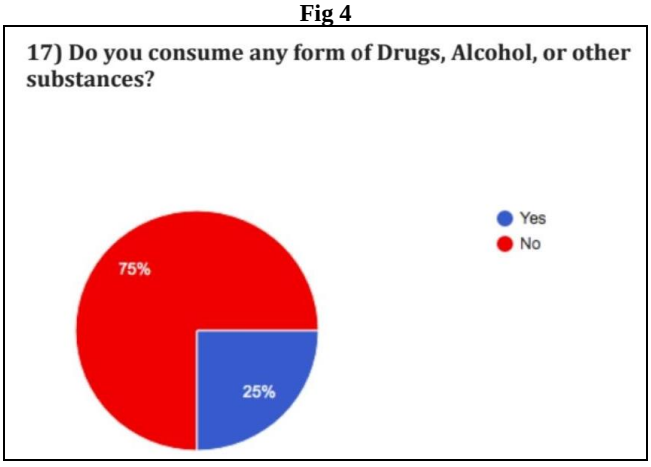

Fig 5

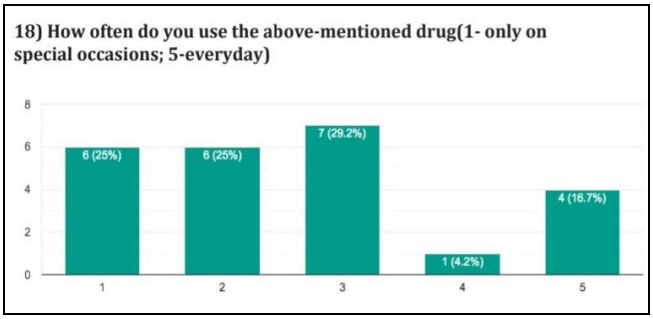

Fig 6

Survey Conclusion

- The purpose of the survey was to find a correlation between the amount of people who score low on the happiness index and those who abuse drugs.
- Of the 102 respondents, 15.1% rated their mental health below average.
- 21% manage stress badly. 19% lack close friendships.
- 20% never exercise.
- 14.2% were extremely dissatisfied with their upbringing or experienced childhood trauma. 15% think they live a life without purpose.
- 15.1% are either able to devote none or very less time to the things they enjoy.
- 18.2% are financially unstable.

This is a clear indication that 15 to 20 percent of the respondents scored severely below average on the happiness index. Consequently, exactly 16.7% have drug consumption as a part of their daily routine and 20% have been trying to quit using their mentioned drug. Thus, the survey served its purpose i.e., proving that addiction/ regular drug use and depression come together.

Link to the survey

https://docs.google.com/forms/d/e/1FAIpQLSd0CgWSa7_C672locvlcFbe_UW1IaSu3FdNIeMWoooGNyhAPQ/viewform

Link to the published survey results

https://docs.google.com/forms/d/1B-UjVDRY2T4CT084Y3x0ZQIGShmDxwMmmTR8spc4LE4/viewanalytics

Significance of Research/ Conclusion

The findings in this research can be used in improving the treatment of both depression and addiction. Before administering anti-depressants, one could focus on the patient's drug addiction, which might partially or even completely solve the depression. More research is necessary in this field.

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